GETTING YOUR ASTHMA UNDER CONTROL USING THE SKILLS OF THE COMMUNITY PHARMACIST – FINAL REPORT

MEDICINES

ASSESSMENT REPORT

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DOCUMENT APPROVAL

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The technical information in this document is used by the Medical Services Advisory Committee (MSAC) to inform its deliberations. MSAC is an independent committee which has been established to provide advice to the Minister for Health on the strength of evidence available on new and existing medical technologies and procedures in terms of their safety, effectiveness, and cost effectiveness. This advice will help to inform government decisions about which medical services should attract funding under Medicare.

MSAC's advice does not necessarily reflect the views of all individuals who participated in the MSAC evaluation.

This report was prepared by Professor Carol Armour AM from Woolcock Institute of Medical Research.

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EXECUTIVE SUMMARY

MAIN ISSUES FOR MSAC CONSIDERATION

- Approximately 50% of people with asthma have poorly controlled symptoms, despite the availability of appropriate medications and public education campaigns. Improving asthma control can reduce the risk of exacerbations and resultant morbidity and mortality.
- Exacerbations result in increased use of health services, including emergency presentations and hospital admissions, as well as time lost from work while unwell.
- The majority of care for asthma occurs in primary care settings.
- We conducted a randomised controlled trial recruiting people with poorly controlled asthma to assess the effectiveness and costs of a Pharmacy Asthma Service delivered via three in-person private consultations between the pharmacist and the participant over a period of 12 months (at baseline, one month and 12 months), with one additional six-month telephone check-up. The comparator arm involved referral of the participants to their general practitioner (GP) following identification of poorly controlled asthma, and two telephone follow-ups by the pharmacist.
- There was a significant improvement in asthma control scores in both arms of the study. However, there was no significant difference between the intervention versus the comparator arm.
- By the end of the trial, 62% of intervention arm participants and 53% of comparator arm participants achieved control of their asthma from a starting point of having poorly controlled asthma.
- At the end of the trial, the intervention arm reported a significant improvement in asthma-related quality of life, when compared with the comparator arm.
- Improvements in asthma control reduced reliance on, and overuse of, reliever medicines (3-4 puffs or more each day). Inappropriate reliever use in the intervention arm reduced from 75% at baseline to 26% at approximately 12 months (p=0.034), whereas in the comparator arm, inappropriate use reduced from 63% to 43% (p=0.009).
- The intervention improved participant inhaler technique, and improvements were sustained at month 1 and month 12 for more than half of the participants.
- Participants in the intervention arm had a significant reduction in emergency department presentations during the trial compared to the 12 months prior to the trial. There was no significant reduction in emergency presentations in the comparator arm. The comparator arm required referral to a GP, and this arm was associated with a significant increase in GP visits during the trial.
- There was no significant difference in participant adherence to preventer medications in the intervention versus comparator arm according to review of dispensing records or Pharmaceutical Benefits Scheme (PBS) data. However, self-reported preventer adherence increased significantly in the intervention arm between baseline and the end of the trial.
- There was no significant difference in the annual Medicare Benefits Schedule (MBS) and PBS costs between the two arms of the study, for the 12 months in which each participant was involved in the trial.
- The cost to deliver the Pharmacy Asthma Service per participant was calculated to be AU$349.

MAIN ISSUES FOR MSAC CONSIDERATION

- A follow-up process evaluation was conducted to explore the involvement of the pharmacist in the comparator arm. At least 38% of comparator arm pharmacists who were interviewed reported performing extra interventions with their patients that were not prescribed in the trial and potentially influenced the improvement in clinical outcomes when combined with the GP referral. As such, these comparator arm pharmacists did not behave as a true control group, but were active in their efforts to improve outcomes for their patients.
- The degree of improvement in asthma symptoms in both arms during the trial suggests that the act of identifying people with poorly controlled asthma with a series of validated questionnaires serves as an important trigger for community pharmacists to implement strategies to improve asthma control.
- Thus, a structured intervention by pharmacists when compared to pharmacist-plus-GP interventions provided comparable improvements in asthma control, with the pharmacy intervention providing a greater improvement in patients' quality of life.
- Both pharmacists and participants in the intervention arm reported positive experiences.
- The Pharmacy Asthma Service was assessed across a range of locations in three states of Australia. The service could be particularly valuable to those in rural and remote communities, as these people with asthma often have limited access to care.
- Our research found that regular review and feedback provided by services within community pharmacies, as well as care provided by GPs following referral by pharmacists, can therefore benefit people with asthma, the health system and the community.
- Community pharmacies represent privately funded infrastructure that can be enabled throughout the country to deliver better asthma outcomes and cost savings for Australia.

GETTING YOUR ASTHMA UNDER CONTROL USING THE SKILLS OF THE COMMUNITY PHARMACIST

This submission-based assessment examines the evidence to support listing of a Pharmacy Asthma Service on the MBS. The service would be used in the pharmacy setting for the management of people with asthma. The target population are people with poorly controlled asthma. We propose that the successful listing of the Pharmacy Asthma Service will lead to improved clinical and quality of life outcomes in the target population as well as significant cost savings for the health system by reducing asthma associated morbidity and mortality.

ALIGNMENT WITH AGREED PICO CONFIRMATION

A PICO Confirmation outlining the proposed use of a pharmacy based clinical service for the management of asthma was not presented to the PICO Confirmation Advisory Subcommittee (PASC). The PICO elements presented are in accordance to the contracted agreement ratified by the Department of Health and delivered by the Woolcock Institute of Medical Research.

PROPOSED MEDICAL SERVICE

The new Pharmacy Asthma Service was delivered via three in-person private consultations between the pharmacist and the participant over a period of 12 months (at baseline, one month and 12 months), with one additional six-month telephone check-up mid-program. The service was designed to address three key factors associated with

poorly controlled asthma including: (1) suboptimal adherence characterised by underuse of preventer medication and/or overuse of reliever medication; (2) suboptimal inhaler technique; and/ or (3) uncontrolled allergic rhinitis.

Population

The target population for the Pharmacy Asthma Service was individuals: ≥18 years of age with poorly controlled asthma, as determined by a score ≥ 1.5 on the Asthma Control Questionnaire (ACQ); able to communicate with the pharmacist in English; who were a regular patient of the pharmacy (receiving medications from that pharmacy for the previous 12 months); and managing their own medications (as determined by the pharmacist). Patients were excluded from the trial if they had high dependence on medical care (more than five comorbidities and specialist care), a confirmed diagnosis of COPD (as reported by the patient), or a terminal illness.

Comparator Details

The comparator arm consisted of three interactions between the pharmacist and the participant over a 12-month period (at baseline, one month and 12 months), including one in-person initial consultation where baseline questionnaires were administered, and two subsequent telephone calls to collect comparative data (no interventions were made). Since participants in the comparator arm also had poorly controlled asthma, they were given a referral to their GP at the end of the baseline visit, as required by the Human Research Ethics Committee (HREC) to ensure duty of care was met.

Clinical Management Algorithm(s)

The clinical algorithms used in the Pharmacy Asthma Service to manage poorly controlled asthma include: (1) a medication adherence assessment to determine appropriate guideline-based therapy and dosing, with particular focus on preventer medications; (2) an inhaler technique assessment to measure level of competency by participants in using their inhaler device(s); and (3) an allergic rhinitis assessment to identify extent of any allergic rhinitis symptoms, as effective treatment of allergic rhinitis is associated with improved asthma control. Details of the clinical management algorithms supporting each intervention are presented in Section A6.

Differences in the Delivery of the Proposed Medical Service and the Comparator

In the intervention arm that received the Pharmacy Asthma Service, support mechanisms to improve medication adherence, correct inhaler technique and provide a review of allergic rhinitis and management advice were applied and followed up in subsequent visits over the 12 months of the trial.

In the comparator arm, participants completed relevant questionnaires to enable comparative analyses with those who received the Pharmacy Asthma Service; however, they did not receive the pharmacist's ongoing assessment and support in relation to inhaler use, medications or allergic rhinitis. Instead, at the end of the baseline visit, these participants received a referral to their GP for review, and additional referrals in subsequent phone calls if required.

Clinical Claim

The interventions used in the Pharmacy Asthma Service have been shown to improve asthma control and asthma-related quality of life. The benefits to the health system would be cost savings (better asthma control incurs less utilisation of health care) and maximising asthma care capacity using the privately funded infrastructure of pharmacy.

Given the high prevalence of asthma nationally, it is envisaged that the Pharmacy Asthma Service will be of similar benefit to all Australian adults with poorly controlled asthma. Taking into account the current population with asthma in Australia is 2.7 million (1) the number of patients with poorly controlled asthma (50% = 1.35 million) (2)

and the proportion who are adults (~80%= 1.08 million) (3) and excluding those who might also have COPD (20%) (4) a potential 864,000 adults could access the service. With the assumption that only half of these would use the service, it is estimated that 432,000 people with asthma would benefit from the implementation of the service. If implemented in rural and remote pharmacies, the Pharmacy Asthma Service has potential to be of significant benefit to Aboriginal and Torres Strait Islander peoples and consumers in these areas, whose health care is compromised by limited access to standard services.

Approach Taken to the Evidence Assessment

Direct evidence in the form of a randomised clinical trial has been undertaken to assess the comparative clinical efficacy and cost effectiveness of the proposed Pharmacy Asthma Service. In this trial, statistical analyses and an economic evaluation were conducted independently to assess the clinical outcomes and cost savings (direct and indirect) to the health care system.

Characteristics of the Evidence Base

The overall prevalence of asthma in Australia increased from 9.9% in 2007-2008 (1) to 11.2% in 2017-2018, with higher rates being recorded in regional and remote Australia, in areas of lower socioeconomic status, and in Aboriginal and Torres Strait Islanders (3). In 2016-2017, there were 41,871 hospitalisations and 389 deaths where asthma was recorded as the principal diagnosis. Thirty-four percent of people living with asthma report that asthma affects their ability to carry out daily activities (5). People with asthma also report comorbid respiratory and other conditions that may exacerbate their asthma, e.g., in Australia, at least 75% of people with asthma reported having allergic rhinitis (6, 7).

The proposed Pharmacy Asthma Service identified possible causes for poor asthma control and used evidence-based practices to address the need to improve clinical and quality of life outcomes, by extending the role of community pharmacists in the delivery of this service. On average, Australians visit a pharmacy 18 times per year, and pharmacies are the most frequented healthcare venue for people with asthma (8). This provides an opportunity for pharmacists when dispensing preventer inhaler prescriptions or responding to a request for an over-the-counter reliever inhaler or topical anti-inflammatory/antihistamines for allergic rhinitis, to apply their therapeutic expertise and understanding of evidence-based medication to improve asthma management.

Previous studies have shown that even when prescribed guideline-based therapy, many people with asthma do not adhere to daily use of preventers, relying instead on over-the-counter relievers (2, 9). A vast majority of people do not follow the correct steps in using their inhalers, leading to suboptimal dosing, unnecessary side effects and lack of asthma control (10-13). Comorbid conditions, such as allergic rhinitis, often go unnoticed and untreated, placing patients at greater risk of poorly controlled asthma and detrimental effects on their clinical trajectory (14). Therefore, with correct medication, appropriate dosing, competent inhaler technique and improved allergic rhinitis management, asthma can be well controlled.

Asthma is associated with significant morbidity and mortality, with the net effect comprising burden at the individual, societal and economic level. Approximately 50% of adults with asthma are poorly controlled, and this has been shown to impact patient quality of life as well as resulting in a higher risk for exacerbations, emergency department visits and hospitalisation. The costs associated with asthma management are significant. In 2015, it was estimated that the cost of asthma in Australia was AU$28 billion or AU$11,740 per individual with asthma (15).

Effectiveness

The Pharmacy Asthma Service had positive effects on the participants' asthma in terms of symptom control, quality of life, allergic rhinitis control and reliever use. At the same time, the comparator arm also demonstrated

improvements in these key indicators, although for quality of life, this improvement was significantly less than in the intervention arm.

There was a significant improvement in the proportion of the population with good asthma control from 0% at baseline (due to the inclusion criteria) to 62% at the end of the Pharmacy Asthma Service. This was the primary outcome of the study. At the same time, there was also an improvement in the comparator arm. Although the improvement was not as great, it was still significant (0 to 53%). Asthma control was measured using the ACQ, a validated measure of asthma control.

A follow-up was conducted to explore the involvement of pharmacists in the comparator arm. It was found that at least 38% of the 20 comparator pharmacists interviewed were non-adherent to the research protocol and performed extra interventions with their patients which potentially influenced the subsequent improvement in participant clinical outcomes. Thus, a structured intervention by pharmacists when compared to pharmacist-plus-GP interventions provided comparable improvements in asthma control, with the pharmacy intervention providing a greater improvement in quality of life.

Improvements in asthma control reduced reliance on reliever overuse (3-4 puffs or more each day). Inappropriate reliever use in the intervention arm reduced from 75% at baseline to 26% at the final follow-up. Inappropriate use in the comparator arm reduced from 63% at baseline to 43% at the final follow-up. Surprisingly, despite participant self-reported preventer adherence increasing significantly in the intervention arm from baseline to month 12, there was no significant difference in participants' adherence to preventer medications in the intervention versus comparator arm according to pharmacy dispensing records and PBS data.

Improvements were evident in inhaler technique for participants receiving the intervention, and improvements were sustained at the one month and 12-month visit for more than half of the participants using pressurised metered dose inhalers (pMDI) with or without a spacer, and dry powder inhalers (DPIs). The proportion of patients within the intervention arm who were competent in all their prescribed device types increased significantly between baseline and month 12.

Improvement in participant-perceived mental and physical health was recorded in both intervention and comparator arms over the 12-month period. However, the negative impact of asthma on day-to-day life for comparator participants was significantly greater than for the intervention participants at month 12.

Similarly, improvement in allergic rhinitis control over time was recorded in both intervention and comparator arms.

The Pharmacy Asthma Service also had positive effects on health care utilisation. Participants in the intervention arm reported a significant reduction in the mean number of Emergency Department presentations and GP visits during the trial when compared with the 12 months prior to the trial. There was no significant reduction in the comparator arm.

There were no significant differences between the intervention and comparator arms in their mean annual MBS and PBS costs, or their mean annual total costs (MBS and PBS) per person per year for the 12 months in which they were engaged in the trial.

TRANSLATION ISSUES

There were several enablers and barriers that affected the delivery of the Pharmacy Asthma Service.

Key barriers to service translation were the withdrawal rate of pharmacists, software issues, engaging participants, understanding of research versus service elements and remuneration for the time taken. In the future, further refining and streamlining the software, the inclusion of training for pharmacists regarding overcoming participant barriers and joining in a partnership around their health, removal of research-based data collection such as extensive quality of life questionnaires, and readdressing estimated time frames for service delivery and adjusting

remuneration accordingly, should assist in overcoming these barriers. Additionally, the investigative team explored reasons for withdrawal of pharmacies at the recruitment phase and published the work (Appendix A).

Enablers for translation included the positive response from participants who completed the service, and positive responses from pharmacists who completed the online training and skills assessment and delivered the service. Participants who received the Pharmacy Asthma Service expressed a high degree of satisfaction, and most participants interviewed post-service (n=101) identified positive health impacts, especially relating to understanding of asthma and approaches to management. The service improved their confidence in managing their asthma, 93% said they would recommend it to others, and 77% would participate in the service if it were offered in the future. Thus, the uptake of the Pharmacy Asthma Service is likely to be high. Pharmacists thought the service would assist them and complement their professional services, and they could envisage how it would benefit their patients.

The availability of a private consulting area and the availability of more than one pharmacist on-site, a requirement for this project, had enabled the delivery of the service. Additionally, the training was well received, and the availability of online training and skills assessment enabled the upskilling of both metropolitan, regional and rural pharmacists. This enhanced their confidence in the delivery of the service.

Interprofessional barriers did not arise in this study. This could be because it was clear that pharmacists were primarily managing medication issues. Pharmacists who were referring participants to the GP reported that this had improved their relationship. It would be important to stress this in future.

ECONOMIC EVALUATION

In this study, the annualised intervention cost was $349 per participant in the intervention arm. The intervention costs were estimated from training materials development, payments to pharmacists and costs associated with items such as software licenses, tool development and hardware.

Outcome variables were defined as the annual MBS and PBS costs, and the sum of these two formed the annual total costs per person per year. Overall, there were differences in the mean annual costs of MBS (intervention, $2,436 and comparator, $2,496), PBS (intervention, $1599 and comparator, $1448) and the mean annual total costs (intervention, $4,035 and comparator, $3,943) between the two trial arms, although these differences were not statistically significant.

There was, however, a significant decrease in mean annual total costs for the intervention participants before compared with during the trial. Over the same time period, the total costs for comparator participants increased, and the difference between the two arms was not statistically significant.

This study has shown that substantial direct healthcare costs and cost burden are associated with asthma in the Australian population, and this highlights the importance of asthma control and prevention. Although there was no significant difference in costs between the intervention and comparator groups during the trial, there was a significant reduction in costs for the intervention arm during the trial compared to the previous 12 months. Although we cannot establish causality, we suggest that the intervention may have had an effect on asthma-related costs.

ESTIMATED EXTENT OF USE AND FINANCIAL IMPLICATIONS

The cost of delivering the Pharmacy Asthma Service was calculated as $349 per participant. Taking into consideration earlier estimates that the Pharmacy Asthma Service would be of benefit to 432,000 Australians with asthma, initially it is estimated that the cost to deliver the 12-month service would be $151M.

CONSUMER IMPACT SUMMARY

The Pharmacy Asthma Service had an impact on the daily lives of participants, i.e., people with asthma in the community. Asthma, as a chronic disease, is known to have a significant impact on a person's quality of life. The Pharmacy Asthma Service significantly improved the quality of life of those who received it. This improvement was seen one month after delivery of the service and was maintained at 12 months.

In terms of symptoms, the asthma control questionnaire (ACQ) score is an evidence-based assessment of control of asthma symptoms and is based on participant self-report of the severity of their symptoms. It has been shown that a score of lower than 1.5 (termed 'controlled asthma') is associated with lower risk for exacerbations and worsening health. The Pharmacy Asthma Service resulted in 62% of the cohort recruited (all not controlled and therefore at risk) becoming controlled.

Fewer symptoms, fewer exacerbations and better reported quality of life not only will have an impact on the person with asthma, but also on their family. The burden of asthma affects the entire family, with lost productivity, cancellation of events, the potential for emergency hospital visits and admissions, and care responsibilities for members of the family. If asthma is controlled, the risk of these impacts on the family is significantly reduced.

The impact in the community is also likely to be lower if more people were to benefit from the Pharmacy Asthma Service. The cost of exacerbations for the public health system, the cost of lost days of productive work/education will be reduced.

In addition, asthma affects the mental health and wellbeing of people with asthma. This burden of poorer mental health and subsequent need for treatment and/or support will be reduced if people feel that they are controlling their disease rather than the disease controlling them. In post-service consultation with those who had participated in the Pharmacy Asthma Service, being confident about managing asthma, regaining a feeling of 'control' over asthma and satisfaction with the 'time' devoted to them by provider pharmacists were key messages offered.

> *"The information I received, and advice has changed my life, I now control my asthma and hay fever instead of it controlling me." (19175239)*

OTHER RELEVANT CONSIDERATIONS

The primary role of a community pharmacist is to optimise medication use. The Pharmacy Asthma Service falls within the scope of professional practice for community pharmacists as it focused on three elements of better medication use:

1. Regular use of an inhaled preventer medication
2. Using inhaled medications correctly
3. Identifying and managing allergic rhinitis symptoms.

Community pharmacies are convenient and easily accessible to most people in all areas of Australia including regional and remote communities where people with asthma may not have the same healthcare opportunities as those in metropolitan areas. By creating a structured pharmacy service that can promote and educate on the better use of medications, pharmacists can add to the value chain in the healthcare community.

Additionally, in the future, the Pharmacy Asthma Service could become a mechanism through which changes in asthma management recommendations could be relayed to participants and their prescribing GPs. An example of such a change, after our service, was the recent change to the PBS to subsidise as-needed low-dose Symbicort® (budesonide/formoterol) for patients with mild asthma.

ACRONYMS AND ABBREVIATIONS

Allergic Rhinitis in Asthma (ARIA)

Asthma Control Questionnaire (ACQ)

Australian Bureau of Statistics (ABS)

Australian Health Practitioner Registration Authority (AHPRA)

Chronic obstructive pulmonary disease (COPD)

Consumer Medicines Information (CMI)

Disease state management (DSM)

Dose administration aid (DAA)

Dry Powder Inhalers (DPIs)

Epidemic Thunderstorm Asthma (ETSA)

Expression of interest (EOI)

Gastro-oesophageal reflux disease (GORD)

General practitioner (GP)

Global Initiative for Asthma (GINA)

Health Collaboration Model (HCM)

Impact of Asthma on Quality of Life Questionnaire (IAQLQ)

Inhaled corticosteroid(s) (ICS)

Interquartile range (IQR)

Long-acting β2 agonists (LABA)

Maximum (Max)

Medicare Benefits Schedule (MBS)

Minimum (Min)

Multiple choice questions (MCQs)

National Asthma Council Australia (NAC)

New South Wales (NSW)

Patient, Intervention, Comparator and Outcome (PICO)

Pharmaceutical Benefits Scheme (PBS)

Pharmaceutical Society of Australia (PSA)

Pharmacy Access/Remoteness Index of Australia (PhARIA)

Pharmacy Asthma Care Program (PACP)

Pressured metered-dose inhaler (pMDI),

Proportion of days covered (PDC)

Quality-adjusted life years (QALY)

Quartile – first (Q1)

Quartile – third (Q3)

Randomised controlled trial (RCT)

Rhinitis Control Assessment Test (RCAT)

Short-Form 12 – Generic Quality of Life (SF-12)

Soft-mist inhaler (SMI)

Standard deviation (SD)

Visual analogue scale (VAS)

Western Australia (WA)

SECTION A: CONTEXT

This submission-based assessment of a pharmacy-based clinical service for the management of asthma is intended for the Medical Services Advisory Committee (MSAC). MSAC evaluates new and existing health technologies and procedures for which funding is sought under the MBS in terms of their safety, effectiveness and cost-effectiveness, while considering other issues such as access and equity. MSAC adopts an evidence-based approach to its assessments, based on reviews of the scientific literature and other information sources, including clinical expertise.

The Woolcock Institute of Medical Research has conducted a randomised controlled trial (RCT) and an economic evaluation of the proposed pharmacy-based asthma management service in order to inform MSAC's decision-making regarding whether the proposed medical service should be publicly funded.

ASTHMA IN AUSTRALIA

Asthma is a significant chronic lung disease that can be controlled but not cured, and can affect Australians of all ages (6). In clinical practice, asthma is defined as *"a heterogeneous disease, usually characterised 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"* (16).

PREVALENCE

In 2017-2018, approximately 2.7 million Australians had asthma (one in nine persons of all ages) (1). In the space of a decade, the prevalence of Asthma increased from 9.9% in 2007-2008 to 11.2% in 2017-2018 (1). According to the Australian Bureau of Statistics (ABS), females had higher rates of asthma than males in 2017-2018 (12.3% compared with 10.2%) (1). Prevalence is higher in inner regional (12.9%) and outer regional and remote Australia (12.7%), compared to those living in metropolitan cities (10.6%). Similarly, the prevalence of asthma is significantly higher among people living in areas of lower socioeconomic status compared to those in areas of higher socioeconomic status, and this disparity has been increasing over the past five years (1). Data released in 2013 showed that the prevalence of asthma in Aboriginal and Torres Strait Islander Australians was almost twice that of the general population (18.9%) (3).

BURDEN OF DISEASE

Asthma is associated with significant morbidity and mortality, with the net effect comprising burden at the individual, societal and economic level.

MORBIDITY AND MORTALITY

People with asthma report worse health and a poorer quality of life than people without asthma, and this can impact participation in everyday life (5, 17). Thirty-four percent of people living with asthma report that asthma interferes with their daily living, and 22% of people aged 15-25 years required some amount of time off work, school or study due to their asthma (5). In addition, it was found that in comparison to people without asthma, people with asthma were more likely to report themselves as having fair (9.9% vs 16.2%, respectively) or poor (3.0% vs 7.4%, respectively) health rather than reporting excellent health (22.7% vs 10.8%, respectively) (3).

In 2016-2017, there were 41,871 hospitalisations in which asthma was the principal diagnosis (174 per 100,000 population), and it was previously shown that the hospitalisation rate, in adults, was higher in Indigenous Australians, people living in rural/remote versus metropolitan areas and those living in areas of lower socioeconomic status (3, 17). In addition to morbidity, in 2018 asthma was responsible for the deaths of 389 Australians (139 males and 250 females), which is high in comparison to other developed countries (18).

People with asthma also report comorbid respiratory and other conditions. For example, in Australia, at least 75% of people with asthma report having allergic rhinitis (6, 7). It is also important to note within the multicultural context of Australia, a relationship between ethnicity and asthma has been

demonstrated, with associated impact on health behaviours; however, the needs of culturally and linguistically diverse people within Australia have not yet been addressed (19-21).

Costs

The costs associated with asthma management are significant. In 2015, it was estimated that the cost of asthma in Australia was $28 billion or $11,740 per individual with asthma (15). Direct health system expenditure accounted for $1.2 billion of this total; this included the cost of prescription medications, in-patient hospital care and out of hospital primary care where most asthma management occurs (15). In 2011-2012, 57.1% of people with asthma reported consulting a GP about their condition in the previous 12 months (22).

At the individual level, rising costs of therapeutic management, even in Australia where the government subsidises a proportion of patient medications, has been shown to play a role in decision making regarding adherence to treatment (23-25). Expenses and financial burden associated with prescription preventer medications (inhaled corticosteroids; ICS) for asthma can deter adherence, with people relying primarily on less-expensive reliever-based medication that can be purchased without a prescription in Australian pharmacies (23). This can lead to deterioration in asthma control; as such, the pharmacist has a crucial role in ensuring appropriateness of therapy (23).

Impact of Climate on Asthma in Australia

Increased climactic variability experienced globally and in Australia has increased the number of extreme heat days, altered and lengthened pollen seasons, and increased the presence of particulate matter and air pollutants (26-28). Erratic weather patterns such as thunderstorms, dust storms and bushfires have led to negative health outcomes and new phenomena that affect those with asthma (26-28). The emerging number of Epidemic Thunderstorm Asthma (ETSA) cases, in which people with asthma experience acute cases of bronchospasm following thunderstorm activity, have not only led to loss of life and pressures placed on health systems due to hospitalisations, but have also been associated with continued loss of asthma control (28). Suboptimal behaviours regarding asthma management, including poor adherence and lack of asthma action plan ownership, can further increase future exacerbation and ETSA episode risk (28).

The Centre for Air pollution, energy and health Research have reported that over a 12-year period between 2001-2013 smoke from 184 bushfire occurrences was associated with 197 premature deaths, 436 cardiovascular hospitalisations and 787 respiratory hospitalisations (27). The increased presence of fine particulate matter ($PM_{2.5}$) from bush-fire smoke has been implicated in the increased intensity and frequency of disease symptoms and heightened burden on the health system (27). The long-term effects of exposure are yet to be determined (27). Primary care can assist in helping people with asthma adapt and manage their risks to this environmental issue (28).

Natural History and Pathophysiology

Asthma is a heterogeneous disease, and its inception and persistence are driven by gene–environment interactions (29). Inflammatory responses to inhaled allergens within the lung drive constriction of the airway smooth muscle, excessive mucus production and damage to the airway lining, all of which lead

to the hallmark symptoms of cough, wheeze and shortness of breath. Although classically thought to be a variable response with resolution to normal function once the triggering event was absent or in response to medications, the concept of airway remodelling now suggests that ongoing unmanaged asthma symptoms may lead to a basal level of ongoing inflammation and anatomical changes in the airway structure (29, 30). Understanding of asthma is evolving, and in recent years, there is also evidence to suggest that asthma occurs in phenotypic patterns, which can be used to define treatment targets (31, 32).

Asthma Management in Australia

The *Australian Asthma Handbook* is revised by the National Asthma Council Australia (NAC) using current evidence and expert review (6). These guidelines are widely disseminated and describe best-practice management for asthma. The pivotal decision making in asthma treatment is a person's ongoing level of symptom control, as described in Table 1 (6).

Table 1: Definition of asthma control

GOOD CONTROL – If all the following apply:	PARTIAL CONTROL – If one or two of the following apply:	POOR CONTROL – If three or more of the following apply:
• Daytime symptoms ≤2 days per week[α]	• Daytime symptoms >2 days per week[α]	• Daytime symptoms >2 days per week[α]
• Need for reliever ≤2 days per week[†]	• Need for reliever >2 days per week[†]	• Need for reliever >2 days per week[†]
• No limitation of activities[α]	• Any limitation of activities[α]	• Any limitation of activities[α]
• No symptoms during night or on waking[α]	• Any symptoms during night or on waking[α]	• Any symptoms during night or on waking[α]

Note: Adapted from Australian Asthma Handbook by the NAC (2019)(6).

[†] Not including doses taken prophylactically before exercise.

[α] Recent asthma control is based on symptoms over the previous four weeks.

The current guidelines recommend that a clinical history of level of control should direct treatment level. When defining therapeutic management, asthma medications are typically divided into two classes:

1. Relievers, which mainly act to relax tightened or constricted airway smooth muscle (6),
2. Preventers, which are anti-inflammatory medications (6).

Reliever medications mostly include short-acting β2 agonists, e.g. salbutamol inhalers, available in Australia as Pharmacist Only Medicines (i.e. Schedule 3). Preventers mostly include ICS, leukotriene receptor antagonists and cromones. Combinations of ICS with long-acting β2 agonists (ICS/LABA) are also recommended as step-up therapy when asthma is not controlled by lower-dose ICS alone (6).

With the increasing recognition of 'airway remodelling', the current Australian guidelines recommend that most adults with symptoms occurring at least twice a month should be on low-dose ICS (6). The idea is that treatment level can be intensified to medium-dose ICS or low-medium dose ICS/LABA combinations if symptoms are poorly controlled, with the recommendation that a 'step-down' must occur to lower the risk of long-term exposure to preventer medications. All people with asthma are always recommended to carry a reliever. The stepped guide to prescribing in asthma is displayed in Figure 1 (6).

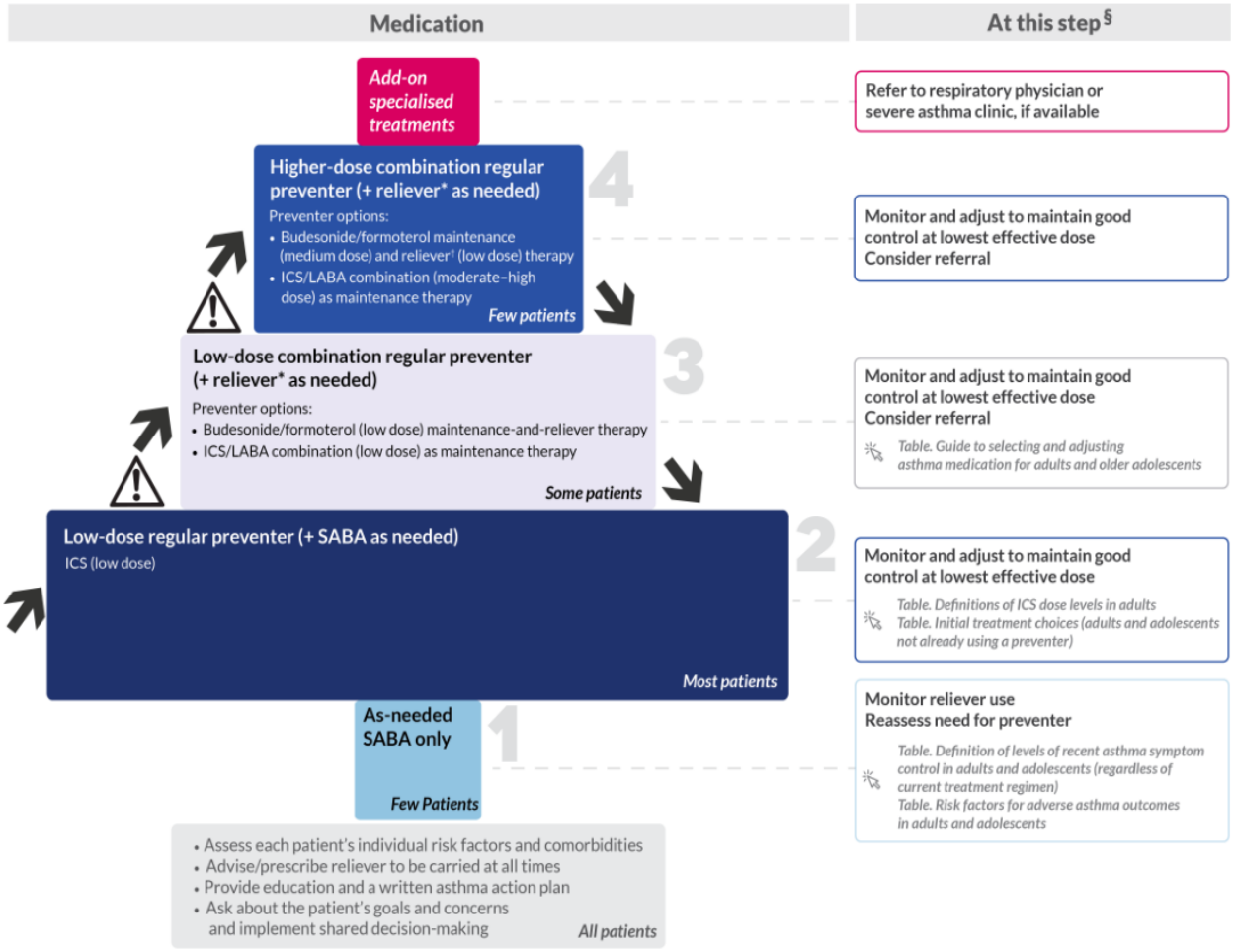


Figure 1: Asthma management guidelines for adults

Note: Reproduced from Australian Asthma Handbook with permission from National Asthma Council Australia (2019) (6).

It should be noted that the Global Initiative for Asthma (GINA) released their *Global Strategy for Asthma Prevention and Management* in 2019, from which new recommendations are yet to be integrated into the *Australian Asthma Management Guidelines* (16). These new recommendations include the fact that GINA no longer recommends sole SABA therapy, due to evidence that regular and frequent use can increase risk of exacerbations, and to avoid patient reliance on short-term solutions. Rather, GINA recommends that all adults with mild cases of asthma receive symptom-driven low-dose ICS-formoterol, or that a low-dose ICS be taken whenever a SABA is used (16, 33).

Additionally, due to the growing knowledge surrounding the phenotypic classification of asthma, it is suggested that the phenotype needs to be determined before treatment in order to isolate and focus on traits that are "identifiable and treatable" and thus could be used as targets for management (31, 32). This is still research based and not instituted widely yet.

In addition to monitoring asthma control, identifying causes and optimising medication management, asthma management guidelines highlight the need for people with asthma to self-manage with appropriate behaviours and medication use. This is facilitated using self-management plans (Asthma Action Plans) and education (34). Written Asthma Action Plans direct the person with asthma to self-titrate therapy in response to current symptoms, including directions in the case of emergency. Asthma education is another important component of the guidelines in order to address perceptions that can lead to suboptimal asthma management (35, 36). In a survey conducted across 11 European countries, more than 80% of the 8,000 people with asthma considered their asthma to be controlled, despite 45% being clinically uncontrolled according to the GINA Criteria (37). Additionally, despite experiencing exacerbations requiring oral corticosteroids in the preceding year, over two-thirds of people with asthma regarded their asthma as not serious (37). This study was mirrored across eight countries in Asia; of the 2,467 participants, about 90% reported that their asthma was under control, and 82% considered their condition not serious, despite 38% having visited an Emergency Department, 33% having been hospitalised and 73% having at least one course of oral corticosteroids in the preceding year (38).

One of the factors that may contribute towards suboptimal asthma control is comorbid conditions. Conditions such as AR, gastro-oesophageal reflux disease (GORD), obesity and depression may occur more frequently in people with asthma. Besides impacting control, these comorbidities may also increase health care utilisation and incur costs. The systematic identification and mapping of these comorbid conditions may lead to customised, targeted treatment, which has the potential to substantially improve outcomes in people with asthma (16, 39, 40).

Allergic rhinitis is suggested by GINA guidelines as a key complication, as post-nasal drip resulting from nasal site inflammation in response to allergens exacerbates underlying asthma symptoms (16, 40). Allergic rhinitis and asthma are linked epidemiologically, pathophysiologically and therapeutically, and can be considered different manifestations of a single inflammatory airway syndrome (41). Asthma is present in about 40% of adults with rhinitis, while allergic rhinitis occurs in up to 80% of people with asthma (41). In a study in primary care, people with concomitant allergic rhinitis had more GP visits (5.2 vs. 4.2; $p<0.0001$) than those with asthma alone, and more people with rhinitis were hospitalised for asthma (0.76% vs. 0.45%; $p<0.01$) (42). allergic rhinitis was predictive of hospitalisation for asthma (odds ratio 1.52, 95% confidence interval (CI) 1.03-2.24), and was associated with an increase in the

annual number of asthma-related GP visits (mean increase per patient 0.42, 95% CI 0.42-0.43) and annual asthma-related drug costs (10).

THE EVIDENCE-PRACTICE GAP

With correct medication, appropriate dosing and appropriate inhaler technique asthma can be well controlled. Evidence clearly indicates that even when prescribed guideline-based therapy, many adults do not adhere to daily use of preventers, relying instead on over-the-counter relievers (2, 9). A vast majority of people do not follow the correct steps in using their inhalers, leading to suboptimal dosing, unnecessary side effects and lack of asthma control (10-13). Comorbid conditions such as allergic rhinitis often go un-noticed and untreated, adding to poorly controlled asthma symptoms (14).

In a recent cross-sectional web-based national survey conducted by Reddel *et al*. (2015), 2,686 Australian people with asthma aged 16 years or older were surveyed and their self-reported level of asthma control and adherence mapped using validated measures (2). Asthma was 'not well controlled' or 'very poorly controlled' for 45.6% of people surveyed, and 25.4% of poorly controlled patients reported using their ICS containing preventer infrequently (less than five times per week) (2). Within their sample, 23.4% had made at least one urgent visit to a GP concerning their asthma, and 10.0% at least one Emergency Department visit in the previous 12 months (2). Urgent consultations were more common for 'very poorly controlled' than 'well controlled' asthma (adjusted odds ratio, urgent GP visits 5.98 [95% CI 4.75-7.54] and Emergency Department visits 2.59 [95% CI 1.91-3.53], respectively) (2).

Despite the availability of effective medications, quality use of such medications is compromised due to both patient and health profession-related reasons. Our team previously explored 'at-risk' asthma populations in a community setting, and found that incorrect inhaler use and inappropriate use of medications by people with asthma were highly prevalent and related to poor disease control (10). The deviations away from the guideline-based objective that most adults should be on regular low-dose ICS daily to limit airway remodelling and maintain ongoing asthma control (30) is evident in 2017-2018 data from the ABS, which highlighted the extent of poor adherence, where 41.0% of people with asthma had not taken medication in the previous two weeks, 17.3% were using their medications a few times in the preceding two weeks, and only 32.8% of people were using asthma medication daily (1). Prescribing aberrations are also evident in Australian primary care; over 80% of ICS are supplied in combination with a LABA, despite recommendations stating these are only to be used in people with asthma when control is not achieved from ICS alone (5).

Suboptimal medication management is also apparent in the treatment of AR, which impacts asthma control in people who concurrently suffer from allergic rhinitis and asthma. Topical anti-inflammatory and oral antihistamines for allergic rhinitis treatment can be purchased directly from Australian pharmacies; consequently, people with allergic rhinitis often self-select medications in the pharmacy without consulting a healthcare professional (43, 44), and make their decisions based on experimentation and their own experience (45). The result is that only 16.5% leave the pharmacy with an appropriate medication (44), with overuse of oral antihistamines and underuse of intranasal corticosteroids. People with asthma usually require more frequent use of asthma medications for their poorly controlled asthma when not taking allergic rhinitis treatments (45). Therefore, the treatment of

allergic rhinitis is vital for the effective management of asthma, and intranasal corticosteroids are first-line treatment for people with allergic rhinitis and coexisting asthma (46).

The Community Pharmacist's Role in Asthma Care

Asthma management occurs primarily within primary care. Community pharmacists have a significant role to play in asthma and allergic rhinitis care. When dispensing preventer inhaler prescriptions and responding to a request for an over-the-counter reliever inhaler or topical anti-inflammatory/antihistamines for AR, there is an opportunity to apply therapeutic expertise and understanding of evidence-based medication to improve asthma management. On average, Australians visit a pharmacy 18 times per year, and pharmacies are the most frequented healthcare venue for people with asthma, enabling pharmacists an opportunity to be involved in asthma management (47). Upskilling the pharmacist workforce regarding asthma has been shown to have a significant positive impact on the clinical trajectory of people with asthma (48). Research conducted by members of the investigation team within Australia has demonstrated that structured pharmacy-based, pharmacist-delivered, patient-centred asthma management services can cost-effectively improve a range of outcomes, including self-management, adherence, inhaler technique, symptom control, asthma awareness and asthma-related quality of life (47, 49, 50). Research conducted by the investigation team over the past decade in this field of research is outlined in Appendix B.

International studies within this field indicate Australia is lagging behind other developed countries. An example includes the success achieved by the Finnish National Asthma Programme, which reduced the number of people with severe or poorly controlled asthma from 20.0% in 2001 to 2.5% in 2016, and reduced healthcare expenditure from 330 million euros per annum in 1993 to 191 million euros per annum in 2013 using a multi-pronged asthma management approach spanning all levels of primary healthcare, including community pharmacy (51). Greater effort is required in Australia to accept well-trained pharmacists as a resource that can be effectively utilised to help mitigate current and future predicted asthma risk, improve therapeutic outcomes, and alleviate economic pressures.

Trial Governance and Funding

The trial protocol was approved by the Human Research Ethics Committees of the University of Sydney, Curtin University, and the University of Tasmania. All participant pharmacists and patients provided written or electronic informed consent. The trial was initiated in July 2018 and completed in December 2019.

The *Getting Asthma under Control using the Skills of the Community Pharmacist* trial was administered and funded by the Australian Government Department of Health.

The service being trialled was designed and implemented by a consortium led by the Woolcock Institute of Medical Research. Members of the implementation team included University of Sydney, Curtin University, University of Tasmania, Pharmacy Guild of Australia (Guild), Pharmaceutical Society of Australia (PSA), the NAC and The George Institute. The roles of each organisation are detailed in Appendix C.

In total, $2,074,099.95 (GST exclusive) was budgeted for the implementation of the trial. This included funds for all participating contractors and trial participants.

A1 ITEMS IN THE AGREED PICO CONFIRMATION

The following PICO summary presented in Table 2 reflects the delivered protocol. The originally approved PICO summary is presented in Appendix D. Departures in methods from the original PICO have been made under the guidance and approval of the Department of Health.

Table 2: PICO Summary of Getting Asthma under Control using the Skills of the Community Pharmacist

Component	Description
Patients	The following eligibility criteria applied to patients entering the trial: • Current diagnosis of asthma (symptoms of asthma plus use of asthma medication in the past 12 months) • Aged ≥18 years • Asthma Control Questionnaire (ACQ) score ≥ 1.5, indicative of poor control (52-54) • Able to communicate with the pharmacist in English • Regular client of the pharmacy providing the service (receiving asthma medications from that pharmacy for the previous 12 months) • Managing their own medications (as judged by the pharmacist). The following criteria excluded patients from entering the trial: • High dependence on medical care (five or more morbidities with specialist care) • Unable to manage their own medication • A confirmed diagnosis of chronic obstructive pulmonary disease (COPD) (as reported by the patient) • Terminal illness. Eligible patients recruited into the trial were allocated to either the intervention or comparator arm.
Intervention	The Pharmacy Asthma Service targeted three key factors associated with poorly controlled asthma: • Suboptimal adherence characterised by underuse of preventer medication and/or overuse of reliever medication (6) • Suboptimal inhaler technique and/or • Uncontrolled allergic rhinitis. **Note:** For all other possible causes of poorly controlled asthma, the patient was referred to their GP and did not receive the intervention. The Pharmacy Asthma Service was a pharmacist-led 12-month program conducted in the regular pharmacy of an eligible asthma patient. To deliver the intervention, the pharmacist undertook three private face-to-face

Component	Description
	consultations with the individual over a period of 12 months: at baseline, one month and 12 months, with one additional telephone follow-up at six months to monitor progress and identify potential risks. At the initial consultation (in person), the pharmacist: • Assessed asthma control using the ACQ (52, 53) • Assessed asthma-related quality of life using *the Impact of Asthma on Quality of Life Questionnaire* (IAQLQ) (55) • Reviewed short-acting β2 agonists use • Assessed asthma medication adherence and addressed any issues identified • Assessed and corrected inhaler technique • Assessed allergic rhinitis control using the *Rhinitis Control Assessment Test* (RCAT) (56) and recommended appropriate therapy and/or referred to the GP as appropriate. **At the one-month follow-up (in person), the pharmacist:** • Reassessed asthma control using the ACQ (52, 53) • Remeasured asthma-related quality of life using the IAQLQ (55) • Reassessed inhaler technique • Reassessed allergic rhinitis control if appropriate using the RCAT (56) **At six months, the pharmacist contacted the patient by telephone and:** • Reassessed asthma control using the ACQ (52, 53) • Asked if there were any issues to address. **At the 12-month follow-up (in person), the pharmacist:** • Reassessed asthma control using the ACQ (52, 53) • Remeasured asthma-related quality of life using the IAQLQ (55) • Reviewed short-acting β2 agonists use • Reassessed asthma medication adherence • Reassessed inhaler technique • Asked about asthma action plan ownership and prompted the patient to obtain an asthma action plan from their GP (if the individual did not already have one) • Assessed allergic rhinitis control (if appropriate) using the RCAT (56) In addition to these interventions/assessments, the *Short-Form 12* (SF-12) Generic Quality of Life (57) instrument was administered by pharmacists at baseline and 12 months for all patients. Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) data and dispensed records were

Component	Description
	also collected for each participant at their respective baseline and 12-month consultations. This was undertaken for those who provided consent for these data to be collected, to enable economic evaluation of the intervention. The project utilised an online platform in order to integrate data collection into routine pharmacy practice. *GuildPath* is web-based data collection software designed and developed specifically for this trial to guide pharmacists through each session and interventions, facilitating review of patients' adherence assessment, inhaler technique and allergic rhinitis. *GuildPath* was integrated with *GuildCareNG*, professional services software operating in over 5000 pharmacies in Australia (58).
Comparator	There was one comparator arm in the assessment of this medical service: the minimal-intervention pharmacy arm. Patients identified as having poorly controlled asthma (ACQ score ≥ 1.5) (52-54) and fulfilling the eligibility criteria above were invited to participate in the comparator arm by pharmacies (pharmacy staff) randomised to this arm. Patients within the comparator arm were requested to attend three interactions with their pharmacist, including one in-person initial consultation where asthma and allergic rhinitis questionnaires were administered after which they were given a referral to their GP. They were then contacted by the pharmacist by telephone one month and 12 months after their initial consultation to collect comparative date (no interventions were made). At the initial consultation (in person), the pharmacist: • Assessed asthma control using the ACQ (52, 53) • Measured asthma-related quality of life using the IAQLQ (55) • Assessed allergic rhinitis control using the RCAT (56) • Provided a referral to their GP. **At one month, the pharmacist contacted the patient by telephone and:** • Reassessed asthma control using the ACQ (52, 53) • Remeasured asthma-related quality of life using the IAQLQ (55) • Assessed allergic rhinitis control (if appropriate) using the RCAT (56) **At 12 months, the pharmacist contacted the patient by telephone and:** • Reassessed asthma control using the ACQ (52, 53) • Remeasured asthma-related quality of life using the IAQLQ (55) • Assessed allergic rhinitis control (if appropriate) using the RCAT (56)

Component	Description
	• Asked about asthma action plan ownership and prompted the patient to obtain an asthma action plan from their GP if the individual did not already have one. In addition to these interventions/assessments, the SF-12 (57) was administered by the pharmacist at baseline and 12 months for all participating patients. MBS/PBS data and dispensed records were also collected for each participant at their respective baseline and 12-month consultations. This was undertaken for those who provided consent for these data to be collected, to facilitate economic evaluation.
Outcomes	A summary of evaluation components is provided in Appendix E. **Primary** The change in proportion (from baseline to post-intervention at 12 months) of patients in each arm who had good asthma control. **Secondary** • Mean change in asthma control (ACQ score) between baseline and 12 months post-intervention (intervention and comparator) • Mean change in asthma-related quality of life (IAQLQ score) between baseline and 12 months post-intervention (intervention and comparator) • Mean change in adherence between baseline and six months, and baseline and 12 months post-intervention (intervention and comparator) • Mean change in inhaler technique (inhaler technique scores) between baseline and 12 months post-intervention (intervention) • Patient and pharmacist satisfaction with the intervention (intervention) • Cost effectiveness and cost utility over the trial period (12 months) (intervention and comparator).

A2 PROPOSED MEDICAL SERVICE

The proposed Pharmacy Asthma Service addressed the need to improve clinical outcomes for the population at risk of poorly controlled asthma, by extending the role of pharmacists in the delivery of primary healthcare services through community pharmacy.The proposed pharmacy service targeted patients with poorly controlled asthma, as poor asthma control is a risk for exacerbations, Emergency Department visits and hospitalisation. These patients represent approximately 50% of adults with asthma, have the highest burden of disease, self-manage poorly (2) and frequent the pharmacy on a regular basis (59).

The service was based on pharmacists:

1. Identifying patients with poorly controlled asthma.

2. Assessing possible causes of poor control (poor adherence, poor inhaler technique, poor allergic rhinitis control).
3. Referring patients with poorly controlled asthma with unknown causes/complex issues to their GP or delivering a targeted intervention to the remaining patients.

Complex issues refer to poorly controlled asthma not due to issues with medication adherence, inhaler technique or lack of allergic rhinitis control, hence warranting referral to their GP.

Once patients were identified, the Pharmacy Asthma Service targeted three key factors associated with poorly controlled asthma:

- Suboptimal adherence characterised by underuse of preventer medication and/or over use of reliever medication (6),
- Suboptimal inhaler technique and/or
- Uncontrolled allergic rhinitis.

The proposed intervention involved a simpler version of a previously established evidence-based pharmacist-delivered service for patients with poorly controlled asthma (47, 49, 50), which could easily be integrated into pharmacists' workflow.

A cluster randomised controlled trial design was used, with pharmacies the unit of cluster and patients as the unit of analysis, to compare the effectiveness (increase in proportion of patients with controlled asthma) and cost effectiveness of a pharmacist-delivered asthma service. The service comprised consultations with the pharmacist over a 12-month period for people with poorly controlled asthma (intervention) compared with a low-level pharmacy intervention comprising identification of poorly controlled asthma with referral to the GP (comparator). The primary hypothesis was that a pharmacist-delivered asthma service comprising three private face-to-face consultations and one telephone check with the pharmacist over a 12-month period for people with poorly controlled asthma will be more effective and cost effective than a low-level pharmacy intervention comprising identification of poorly controlled asthma with referral to the GP.

To deliver the intervention, the pharmacists randomised to the intervention arm undertook three private consultations with the patient over a period of 12 months (at baseline, one month and 12 months), with one additional six-month telephone check-up mid-program. In our previous work, we provided evidence that three visits over six months (baseline, one month and six months) resulted in improved health outcomes (47, 50). The number of visits and the time taken for each visit has been streamlined from our previous evidence-based interventions to increase feasibility and sustainability.

At the initial consultation (in person), the pharmacist:

- Assessed asthma control using the ACQ (52, 53)
- Assessed asthma-related quality of life using the IAQLQ (55)
- Reviewed SABA use
- Assessed asthma medication adherence and addressed any issues identified
- Assessed and corrected inhaler technique
- Assessed allergic rhinitis control using the RCAT (56) and recommended appropriate therapy/referred to the GP as appropriate.

At the one-month follow-up (in person), the pharmacist:

- Reassessed asthma control using the ACQ (52, 53)
- Remeasured asthma-related quality of life using IAQLQ (55)
- Reassessed inhaler technique
- Reassessed allergic rhinitis control if appropriate using the RCAT (56)

At six months, the pharmacist contacted the patient by telephone and:

- Reassessed asthma control using the ACQ (52, 53)
- Asked if there are any issues to address.

At the 12-month follow-up (in person), the pharmacist:

- Reassessed asthma control using the ACQ (52, 53)
- Remeasured asthma-related quality of life using IAQLQ (55)
- Reviewed short-acting β2 agonists use
- Reassessed asthma medication adherence
- Reassessed inhaler technique
- Asked about asthma action plan ownership and prompted the patient to obtain an asthma action plan from their GP (if the individual did not already have one)
- Assessed allergic rhinitis control if appropriate using the RCAT (56)

In addition to these interventions/assessments, the *Short-Form 12* (SF-12) Generic Quality of Life (57) instrument was administered by pharmacists at baseline and 12 months for all patients. MBS and PBS data and dispensed records were also collected for each participant at their respective baseline and 12-month consultations. This was undertaken for those who provided consent for these data to be collected, to enable economic evaluation of the intervention. We acknowledge Services Australia (formerly the Department of Human Services) for supplying the MBS and PBS information.

The project utilised an online platform to integrate data collection into routine pharmacy practice. *GuildPath* is web-based data collection software designed and developed specifically for this trial to guide pharmacists through each session and interventions, facilitating review of patients' adherence assessment, inhaler technique and allergic rhinitis. *GuildPath* was integrated with *GuildCareNG*, professional services software operating in over 5000 pharmacies in Australia (58).

A3 PROPOSAL FOR PUBLIC FUNDING

Not applicable

A4 PROPOSED POPULATION

TRIAL PHARMACISTS

Pharmacists from regional and metropolitan areas in New South Wales (NSW), Western Australia (WA) and Tasmania were invited to participate in the asthma service by the Pharmacy Guild of Australia. Pharmacists were eligible to participate in the trial if the pharmacy fulfilled the following criteria:

- The pharmacy was approved to dispense PBS medicines as part of the National Health Scheme defined in Section 90 of the National Health Act 1953 (Cth) (Section 90 pharmacy)
- The pharmacy had an area of the community pharmacy that was physically separated from the retail trading floor so that the privacy and confidentiality of the patient was protected
- The pharmacy had a minimum of two pharmacists on duty at times when the service was to be delivered.

Pharmacists registered for the trial online. To approximate the geographical distribution of pharmacies in NSW, Tasmania and WA, randomisation was stratified by metropolitan/urban/rural residential areas and matched to the distribution of the Australian population using the Pharmacy Access/Remoteness Index of Australia (PhARIA) (60-62). Pharmacies were classified as:

1. Highly Accessible (PhARIA Cat 1)
2. Accessible (PhARIA Cat 2 and 3)
3. Moderately accessible, remote, and very remote (PhARIA Cat 4, 5 and 6).

Pharmacies were randomly selected to participate within the trial and randomly assigned to intervention and comparator arms using random number generation. Pharmacists were offered remuneration for their participation on a per-completed-patient basis. Intervention pharmacists received AU$120 per completed patient, and comparator pharmacists received AU$35 per completed patient.

The Pharmacy Asthma Service falls within the scope of professional practice for pharmacists, as covered by the Australian Health Practitioner Registration Authority (AHPRA) (Appendix F).

Sample Size

It was assumed that no more than 30% of patients from the comparator arm would have controlled asthma by 12 months, and around 50% with controlled asthma in the intervention arm (a 20% absolute increase between comparator and intervention arms). A total of 68 pharmacies (34 pharmacies each in intervention versus comparator) each recruiting a minimum of five patients would provide 90% power to test a difference in proportions with an intra-cluster correlation of 0.10. Allowing for a 20% patient dropout and a 15% pharmacy dropout, the requisite sample was 80 pharmacies (40 each in intervention and comparator arms), with seven patients per cluster, giving a total of 280 per arm (560 in total).

Specialised Pharmacist Training

Prior to implementation, pharmacists in the intervention arm underwent both theoretical and skills-based training to ensure they had the necessary skills and knowledge to recruit patients and deliver the intervention consistently as shown in Figure 2. Pharmacists were required to pass both components of training to deliver the service. Pharmacists in the comparator arm required protocol training only.

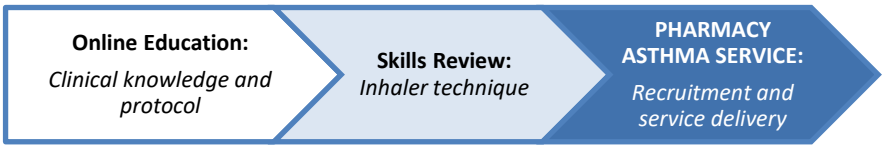


Figure 2: Specialised intervention training and implementation pathway

ONLINE EDUCATION

The online education modules comprised of content and videos and were developed by the PSA and the research team based on current guidelines. The PSA is a peak national professional pharmacy organisation committed to providing high-quality practitioner development and practice support via their online education platform (63). The use of the online modality allowed for easy access to training for all pharmacists in the trial, no matter where they were located.

The content was organised into five online modules:

1. Background to asthma, trial background and plan
2. Medication and adherence
3. Inhaler devices and technique
4. Management of allergic rhinitis
5. Protocol pathway and case study.

The training modules covered a range of topics including service protocol, patient eligibility and clinical pathway, asthma pathophysiology, risk assessment, medications, and current best practice in asthma management. The modules focussed on the importance of adherence, optimal inhaler technique, allergic rhinitis and other co-morbidities and their role in maintaining good asthma control. To illustrate correct implementation of the trial protocol, a case study was filmed and included in Module 5. Pharmacists were thus able to observe knowledge and skills application in an exemplar scenario typically experienced in community pharmacy.

Module descriptions and learning objectives are detailed in Appendix G. The five modules were accredited by the PSA for Continuing Professional Development, and took approximately 5.5 hours to complete.

For each module, a lead researcher produced the initial outline of the required content and resources to support the knowledge delivery as well as the competence level required. This was reviewed by the project team and the PSA, who were responsible for the final module composition and delivery. Once the content of each module was considered appropriate by the research team, the PSA designed the online format of the modules in line with adult learning principles.

KNOWLEDGE ASSESSMENT

Each module was designed so that each section was to be completed before a pharmacist could proceed to the following section, ensuring that pharmacists navigated their way through all the content. Each module was followed by an assessment using multiple choice questions (MCQs). Each module comprised five multiple-choice questions (MCQs), except for Module Four, which had eight questions. A pass was defined as scoring at least 75% for MCQs in each module assessment.

Pharmacists were allowed two attempts to pass each module. If further attempts were required, pharmacists were contacted by a member of the project team, visited, and provided with individual assistance.

Skills Review

Each pharmacist also received an in-person or remote (via video upload) skills review of inhaler technique, on five of the most common inhaler devices, by a trained inhaler technique assessor. The method of review was determined depending on the pharmacy's proximity to the research sites and available trainers. Devices assessed were the pressured metered-dose inhaler (pMDI), pMDI with spacer (both tidal and single breath method), Turbuhaler®, Accuhaler® and Ellipta®. Pharmacists were required to demonstrate that they could use each device in accordance with the device specific inhaler technique checklists created by the NAC (64). In addition to correct technique, pharmacists were offered advice on motivational techniques to be able to better engage with and correct their patients' technique when assessed in the intervention. At each review, a video of the pharmacist baseline skillset was captured, which was followed by feedback and further education tailored to any gaps in technique and device knowledge. The pharmacists were asked to re-demonstrate, and this cycle of demonstrating and review was continued until the trainer was satisfied with the pharmacist's competency (see Figure 3) (65).

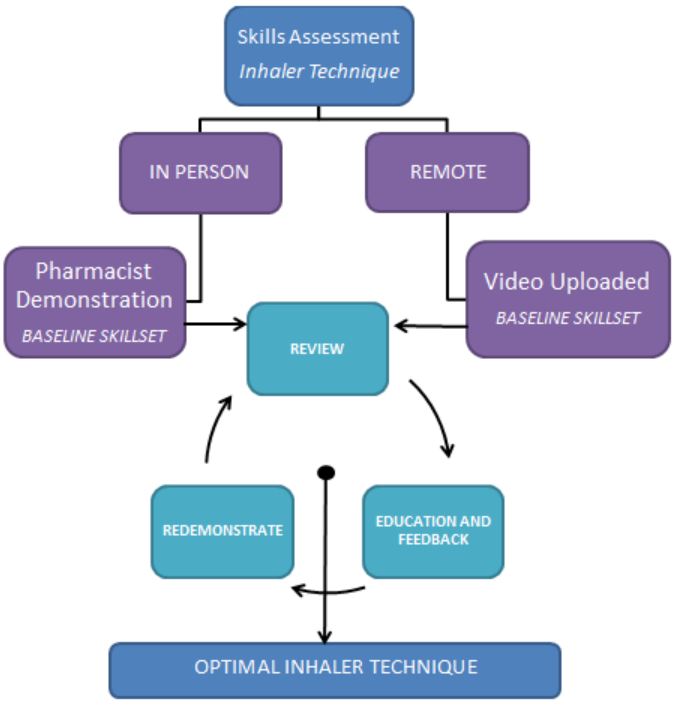


Figure 3: Skills-based assessment pathway

Trial Patients

Upon completion of pharmacist training, pharmacies were asked to recruit a minimum of seven patients each between August 2018 and February 2019.

Patient Inclusion Criteria

The target population for the trial comprised individuals ≥18 years of age with poorly controlled asthma, as determined by a ACQ score ≥1.5, who were able to communicate with the pharmacist in English, a regular patient of the pharmacy (receiving medications from that pharmacy for the previous 12 months) and managing their own medications (as determined by the pharmacist).

Patient Exclusion Criteria

Patients were excluded from the trial if they had a high dependence on medical care (more than five morbidities and specialist care), were unable to manage their own medications (as determined by the pharmacist), and/or had a confirmed diagnosis of COPD (as reported by the patient), or a terminal illness.

The feasibility of patient recruitment using these criteria had been demonstrated by investigators CA, BS, SBA, LE and IK as well as BB and LB in previous trials (47, 49, 50, 54, 66, 67).

A5 Comparator Details

The comparator arm used in the assessment of this medical service formed a 'minimal intervention' pharmacy arm.

A group of patients with asthma (inclusion and exclusion criteria above) had their asthma control assessed by the pharmacist via the ACQ, and those identified with poorly controlled asthma (ACQ score ≥1.5) (52-54) were invited to participate in the service.

Patients within the comparator arm underwent three interactions with their pharmacist, including the initial in-person consultation, at which they were given a referral to their GP. They were then contacted one month and 12 months after this initial consultation via telephone.

At the initial consultation (in person), the pharmacist:

- Assessed asthma control using the ACQ (52, 53)
- Measured asthma related quality of life using IAQLQ (55)
- Assessed allergic rhinitis control (RCAT) (56)
- Provided a referral to the patient's GP.

At one month, the pharmacist contacted the patient by telephone and:

- Reassessed asthma control using the ACQ (52, 53)
- Remeasured asthma-related quality of life using IAQLQ (55)
- Assessed allergic rhinitis control if appropriate using the RCAT (56)

At 12 months, the pharmacist contacted the patient by telephone and:

- Reassessed asthma control using the ACQ (52, 53)
- Remeasured asthma-related quality of life using IAQLQ (55)
- Assessed allergic rhinitis control if appropriate using the RCAT (56)
- Asked about asthma action plan ownership, and prompted the patient to obtain an asthma action plan from their GP (if the individual did not already have one).

In addition to these interventions/assessments, the SF-12 (57) was administered by the pharmacist at baseline and 12 months for all participating patients. MBS/PBS data and dispensed records were also collected for each participant at their respective baseline and 12-month consultations. This was undertaken for those who provided consent for these data to be collected, to facilitate economic evaluation.

A6 CLINICAL MANAGEMENT ALGORITHM(S)

The Pharmacy Asthma Service was based on a clinical management algorithm, which pharmacists used to guide evidence-based care. The clinical management algorithm details essential steps in the process of care delivery, allowing for the management of individual patient needs, supporting referral to GPs and allows documentation, monitoring and evaluation of variations between individual patients.

Prior to delivery of the Pharmacy Asthma Service, pharmacies were required to proactively identify patients who might be eligible to receive the Pharmacy Asthma Service. The pathway required to identify eligible patients is described below and diagrammatically presented in Figure 4.

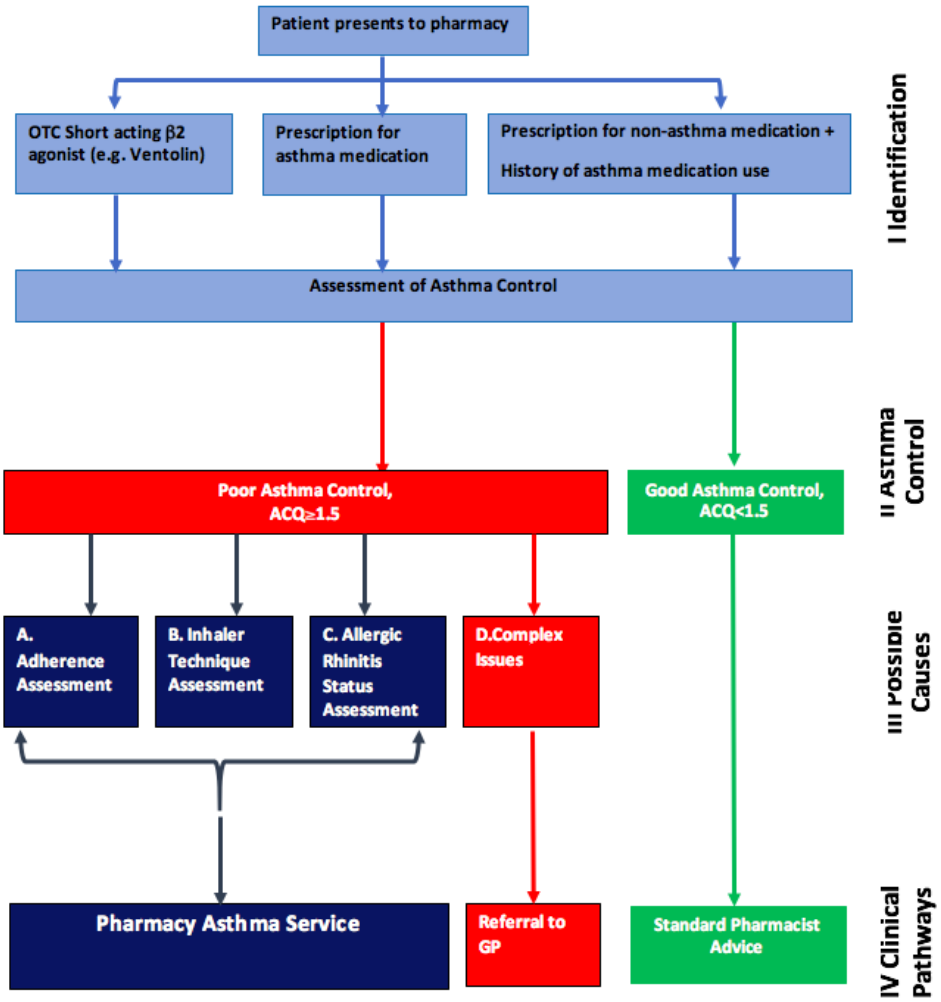


Figure 4: Identification of patients suitable for the Pharmacy Asthma Service in Intervention pharmacies

Note:

- *After screening, the patient was assessed for asthma control. If good control (ACQ <1.5), the patient was reassured, and standard practice followed (no intervention). If they had poor asthma control (ACQ ≥1.5), their adherence, inhaler technique and allergic rhinitis were checked. If any of these were not optimal, the patient was offered the Pharmacy Asthma Service. If they had any other issue that could not be addressed by the pharmacist, they were referred to the GP.*
- *This figure does not include the recruitment and data collection for the comparator arm.*
- *Complex issues = any other outstanding issue that cannot be identified or addressed by the pharmacist.*

I. PATIENT IDENTIFICATION

Individuals were assessed for eligibility for the Pharmacy Asthma Service:

1. When making a request to purchase an over-the-counter short-acting β2 agonists (e.g. Ventolin®).
2. When presenting a prescription for asthma medication.
3. During dispensing of any prescription, reviewing patient dispensary to identify patients prescribed asthma medications within the previous 12 months.

II. ASSESSING ASTHMA CONTROL

Asthma status/control (based on the validated ACQ) (52) was assessed by the pharmacist using the tablet device provided to the pharmacy for the duration of the trial. The ACQ comprises six questions relating to their asthma in the past seven days:

1. On average, during the past week, how often were you woken by your asthma during the night?
2. On average, during the past week, how bad are your asthma symptoms when you wake up in the morning?
3. In general, during the past week, how limited were you in your activities because of your asthma?
4. In general, during the past week, how much shortness of breath did you experience because of your asthma?
5. In general, during the past week, how much time did you wheeze?
6. On average, during the past week, how many puffs/inhalations of short-acting bronchodilator (e.g. Ventolin®) have you used each day?

Following completion of these six questions, an ACQ score was computed on the tablet device. Patients with an ACQ score ≥1.5, considered to have poorly-controlled asthma (53, 54), then proceeded to further assessment of the possible causes. Patients with an ACQ score <1.5 were considered to have well-controlled asthma. They were not considered for the Pharmacy Asthma Service on this occasion, and received standard care.

III. EVALUATING POSSIBLE CAUSES FOR POOR ASTHMA CONTROL

Once patients had been identified as eligible (ACQ ≥1.5), the pharmacist delivered the Pharmacy Asthma Service to determine possible causes for poor asthma control. Patients in the service received

at least one of three support interventions, based on the pharmacist's assessment of the possible cause of their poor asthma control:

a. Adherence assessment and support
b. Inhaler technique assessment and education and/or
c. Allergic rhinitis assessment and management optimisation

Figure 5 summarises the clinical management algorithm underpinning the Pharmacy Asthma Service.

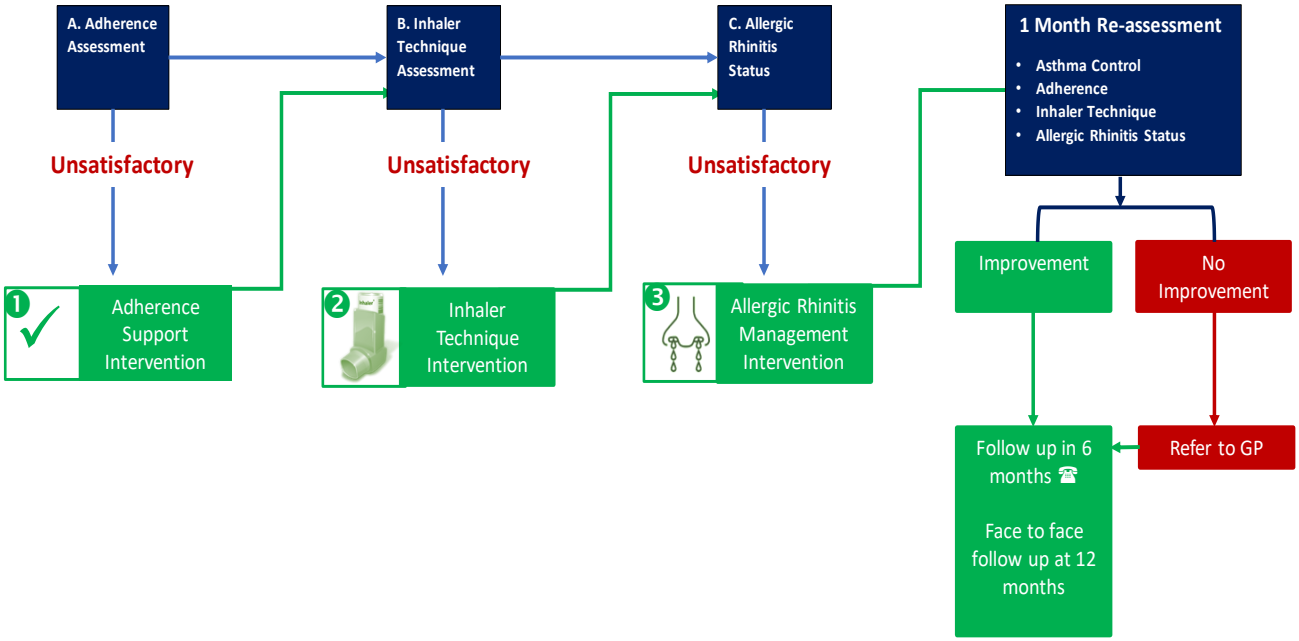


Figure 5: Pharmacy Asthma Service clinical management algorithm

Note: Adapted from Basheti et al. (2008), Bousquet et al. (2009) and Svarstad et al. (2000) (65, 68, 69)

a. Adherence assessment and support was based on the Health Collaboration Model (HCM), which identifies five core adherence barriers amenable to change. These core barriers include regimen knowledge barriers (poor understanding of the drug regimen and its elements such as dosage schedule, treatment duration, purpose), recall barriers (difficulty remembering multiple drugs and doses), motivational barriers (doubts regarding drug efficacy, benefits, or need for therapy), side effect barriers (bothersome side effects or concerns about long-term effects), and access barriers (difficulty paying or obtaining prescription refills) (Figure 6) (69, 70). This was explored using a series of guided questioning and information provision and the use of visual analogue scales (VAS) to determine whether adherence was an issue and identified which of the multiple factors underpinning poor adherence was likely. Patients identified with these core barriers were managed as follows:

1. Patients who lacked sufficient knowledge about their asthma received education on the disease itself, as well as education about the role of medications. NAC resources provided to pharmacists at the start of the trial were utilised to support the education as appropriate.

2. Patients who lacked understanding about the role of medications received specific education around the role and use of asthma medications. This was supported with relevant Consumer Medicines Information (CMI).
3. Patients who indicated uncertainty about the efficacy or the need for medication had their expectations discussed and received further explanation about how the medications work to improve asthma control and prevent long-term complications.
4. Patients who had concerns about any negative effects of their medication received further education and explanation about side effects, why they occur, how they can be monitored and minimised.
5. Patients who indicated that they forgot to take their medications received specific counselling and support that reinforced their medication regimen, as well as strategies to assist them to remember when to take their medication and refill their medication prescriptions (e.g. mobile text message, or alarm reminders, or subscriptions to apps).

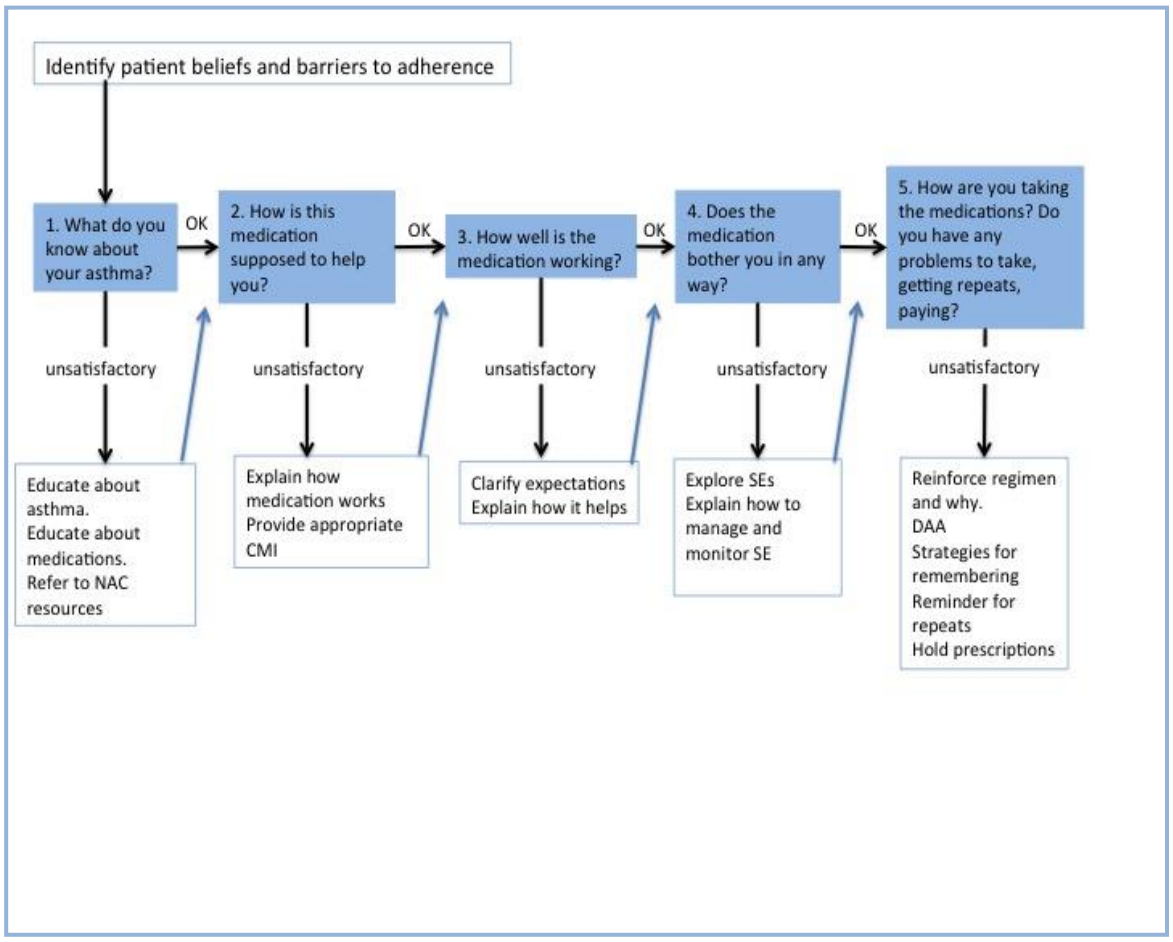


Figure 6: Adherence assessment and intervention algorithm

Note: DAA – Dose administration aid

Adherence and participant preventer use were measured from multiple sources:

1) **PBS data (intervention and comparator arms)** – This formed the primary adherence indicator. A complete PBS dispensing history for all participants who provided consent was collected.

This dataset includes both below-co-payment medicines and above-co-payments medicines (excluding items dispensed as 'private' or those not on the PBS List) for each participant from all pharmacies where they had medications dispensed. This included 24 months of data (12 months before baseline and the full 12-month duration of the trial).

2) **Pharmacy Dispensing data (intervention and comparator arms)** – Pharmacy-specific data extracted from pharmacy dispensed medication reports for each participant were manually entered by the research team. There was an assumption, based on the participant having to be a regular patient of that pharmacy (this was part of the criteria for inclusion), that the participant collected the majority of his/her/their medicines from that pharmacy. Reports generated included 24 months of data (12 months before baseline and the full 12-month duration of the trial) for each participant.

3) **Participant self-reported adherence using a VAS (intervention arm only) –** Intervention participants were asked to self-complete an adherence assessment using a sliding scale on an electronic tablet during the baseline and month 12 visits. Details of all VAS within the Pharmacy Asthma Service are depicted in Appendix H.

The proportion of patients who had at least one preventer medication dispensed in the 12 months prior to baseline (*baseline*) and during the trial (*month 12*) was estimated for participants in which a medication history was available.

Proportion of Days Covered (PDC) was used to calculate Global Baseline Adherence and Global 12-Month Adherence Scores from both the Pharmacy Dispensing data and the PBS data for each participant who was using at least one preventer medication (71). PDC refers to the proportion of days covered by at least one preventer medication, and was calculated using either the PBS data or Pharmacy Dispensing data to determine participant adherence to preventer medication. A participant with a PDC of 80% or higher was considered adherent (72).

PDC calculations using Pharmacy Dispensing data were based on prescribed dosages for each individual. In cases where the prescribed dose was not able to be accessed or dose variability occurred, standard dosage was used. Standard dosage is based on the minimum effective adult dose required for each formulation/product, as recommended by the *Australia Medicines Handbook* (AMH), *Therapeutic Guidelines* (eTG) and the *Australian Asthma Handbook* (AAH) (73-75). Prescribed dosage information for each individual is not available in PBS data, so PDC calculations using this source were based on standard dose.

Data on reliever use were only available for patients holding a government concession card (which reduces the patient co-payment for Pharmacist Only Medicines as well as Prescription Only Medicines if prescribed by their GP), since short-acting β2-agonists are available without prescription in Australia. Therefore, reliever use for intervention patients was collected via self-report.

b. Inhaler technique assessment and education was conducted by observing the patient demonstrate use of their inhaler(s)/asthma devices, then comparing this to NAC developed device-specific checklists (64). Based on the proportion of steps correctly performed, an inhaler technique score was generated by the software. Patients who were not able to correctly use their inhaler(s) on their first attempt received education on the correct use of their inhaler(s). This education took the form of a

physical demonstration by the pharmacist with a placebo inhaler, and was repeated (up to a maximum of three times) until the patient was able to use their inhaler without performing any errors, i.e. device mastery was achieved. Once device mastery had been achieved, the pharmacist produced an inhaler-specific label, highlighted the errors performed by the patient and attached the label to the inhaler. The proportion of patients leaving the session with correct inhaler technique and the number of attempts required to achieve mastery was recorded. This element of the clinical management algorithm is based on the evidence-based pharmacist-delivered inhaler technique education developed by Basheti et al. (65, 66). This intervention has been shown to be effective in improving inhaler technique (i.e. achieving mastery of inhaler use) and maintaining it over time.

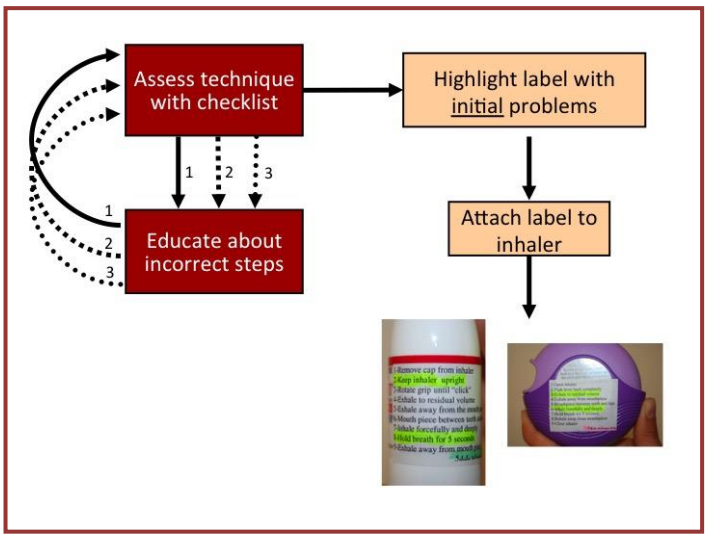


Figure 7: Inhaler technique assessment and review

c. Allergic rhinitis assessment and management optimisation (if* allergic rhinitis *is was present) was undertaken through patient questioning regarding diagnosis and symptoms. Patients with current or suspected co-existing rhinitis were asked to determine their level of allergic rhinitis control based on the RCAT (56) which consists of six questions:

1. During the past week, how often did you have nasal congestion?
2. During the past week, how often did you sneeze?
3. During the past week, how often did you have watery eyes?
4. During the past week, to what extent did your nasal or other allergy symptoms interfere with your sleep?
5. During the last week, how often did you avoid any activities (for example, visiting a house with a dog or cat, gardening) because of your nasal or other allergy symptoms?
6. During the past week, how well was your nasal or other allergy symptoms controlled?

Two VASs (for nasal and ocular symptoms) were administered to determine the burden of allergic rhinitis symptoms and to guide allergic rhinitis medication management utilising the evidence-based Allergic Rhinitis in Asthma (ARIA) clinical management algorithm (68) (Table 3). Based on this algorithm, patients were recommended an over-the-counter allergic rhinitis medicine, or in some cases, were referred to the GP for prescription and allergic rhinitis treatment.

Table 3: Allergic rhinitis recommendation algorithm used

Session	Symptom Type	VAS Score	Recommendation
Baseline	Nasal	1	No treatment required
		>1	1st line: intranasal corticosteroid Can be used in conjunction with the following for symptomatic relief: • Oral antihistamine (conditional recommendation, with very low certainty of evidence) • Intranasal antihistamine • Intranasal saline
	Eye	1	No treatment required
		1<Vas <5	1st line: oral antihistamine *(If no nasal symptoms)* Can be used in conjunction with the following for symptomatic relief: • Intraocular saline 1st Line: Intranasal corticosteroid *(if combined with nasal symptoms)* Can be used in conjunction with the following for symptomatic relief: • Intranasal saline • Intraocular saline • Oral antihistamine
		≥5	1st line: intraocular antihistamine Can be used in conjunction with the following for symptomatic relief: • Intranasal saline (If nasal symptoms present) • Intraocular saline • Oral antihistamine
Month 1	Nasal	1	No treatment required if patient recorded a 1 at baseline visit. Otherwise, outside allergy season consider stopping recommended treatment; if within allergy season continue treatment.

Session	Symptom Type	VAS Score	Recommendation
		2≤Vas≤5	Continue recommended treatment. Recommended 1st line: intranasal corticosteroid Can be used in conjunction with the following for symptomatic relief: • Oral antihistamine • Intranasal antihistamine • Intranasal saline
		>5	Refer to GP Recommended 1st line: intranasal corticosteroid + intranasal antihistamine Can be used in conjunction with the following for symptomatic relief: • Oral antihistamine • Intranasal antihistamine • Intranasal saline
	Eye	1	No treatment required if patient recorded a 1 at baseline visit. Otherwise, outside allergy season consider stopping recommended treatment; if within allergy season continue treatment.
		1<Vas<5	Continue recommended treatment. 1st line: oral antihistamine *(If no nasal symptoms)* Can be used in conjunction with the following for symptomatic relief: • Intraocular saline 1st Line: Intranasal corticosteroid *(if combined with nasal symptoms)* Can be used in conjunction with the following for symptomatic relief: • Intranasal saline • Intraocular saline • Oral antihistamine

Session	Symptom Type	VAS Score	Recommendation
		≥5	Refer to GP.

Note: Based on Allergic Rhinitis in Asthma (ARIA) clinical management algorithm

IV. Clinical Pathways

Based on the outcome of patient screening and initial consultation (if applicable), patients proceeding in the clinical management pathway took on one of the following routes:

1. Patient continued with either the Pharmacy Asthma Service or minimal intervention comparator arm.
2. Patients with poorly controlled asthma due to complex issues (issues not related to medication adherence, inhaler technique or allergic rhinitis control) were referred to their GP were considered ineligible for the Pharmacy Asthma Service.
3. Patients with an ACQ score <1.5 were considered to have well-controlled asthma. They were not considered for the Pharmacy Asthma Service on this occasion and received standard care.

Follow-up and Referral to the GP

The Pharmacy Asthma Service was embedded within a framework of review, referral and follow-up; therefore, the first follow-up was in one month, at which time, asthma control (measured using the ACQ) and the relevant issues previously identified (i.e., adherence, inhaler technique or poorly managed allergic rhinitis) were re-assessed. If an improvement in patient clinical outcomes was determined, no further intervention was delivered. However, if no improvement in clinical outcomes was determined, the patient was referred to the GP for assessment and review.

Note: It was expected that the patient-maintained consultations with GPs during the trial period to obtain prescriptions for asthma. Furthermore, the proposed intervention was conducted in a 'naturalistic' setting, and as such, patients may have consulted other information sources and health providers as they normally would.

Documentation

The project utilised an online approach to data collection to better streamline it into everyday pharmacy practice. A web-based data collection software named GuildPath, was designed specifically for this trial, by the investigative team, to guide pharmacists through each session. GuildPath was developed to be launched from GuildCareNG, a professional services platform operating in over 5,000 pharmacies in Australia (58). This purpose-designed trial software provided a system of documentation and enabled longitudinal assessment of pharmacist interventions and patient outcomes.

Use of customised software linked to an existing platform was considered more practical than hard-copy documentation, and enabled scores to be computed accurately and immediately. The data were uploaded securely through the Cloud to from the GuildCareNG platform. As required for institutional

ethical approval of this type of research, participants (patients, pharmacists) were made aware of the secure methods being used to transfer and store data. All validated questionnaires, VASs, checklists, demographic data, guided counselling and educational content were embedded into GuildPath. It was expected that pharmacists completed these questionnaires while engaging with the patient, on the tablet device provided for the trial. GuildCare was also able to generate and store records of each intervention, as well as GP referral letters when they were required. The data collected at each time point of the project is displayed in Figure 8 and Figure 9.

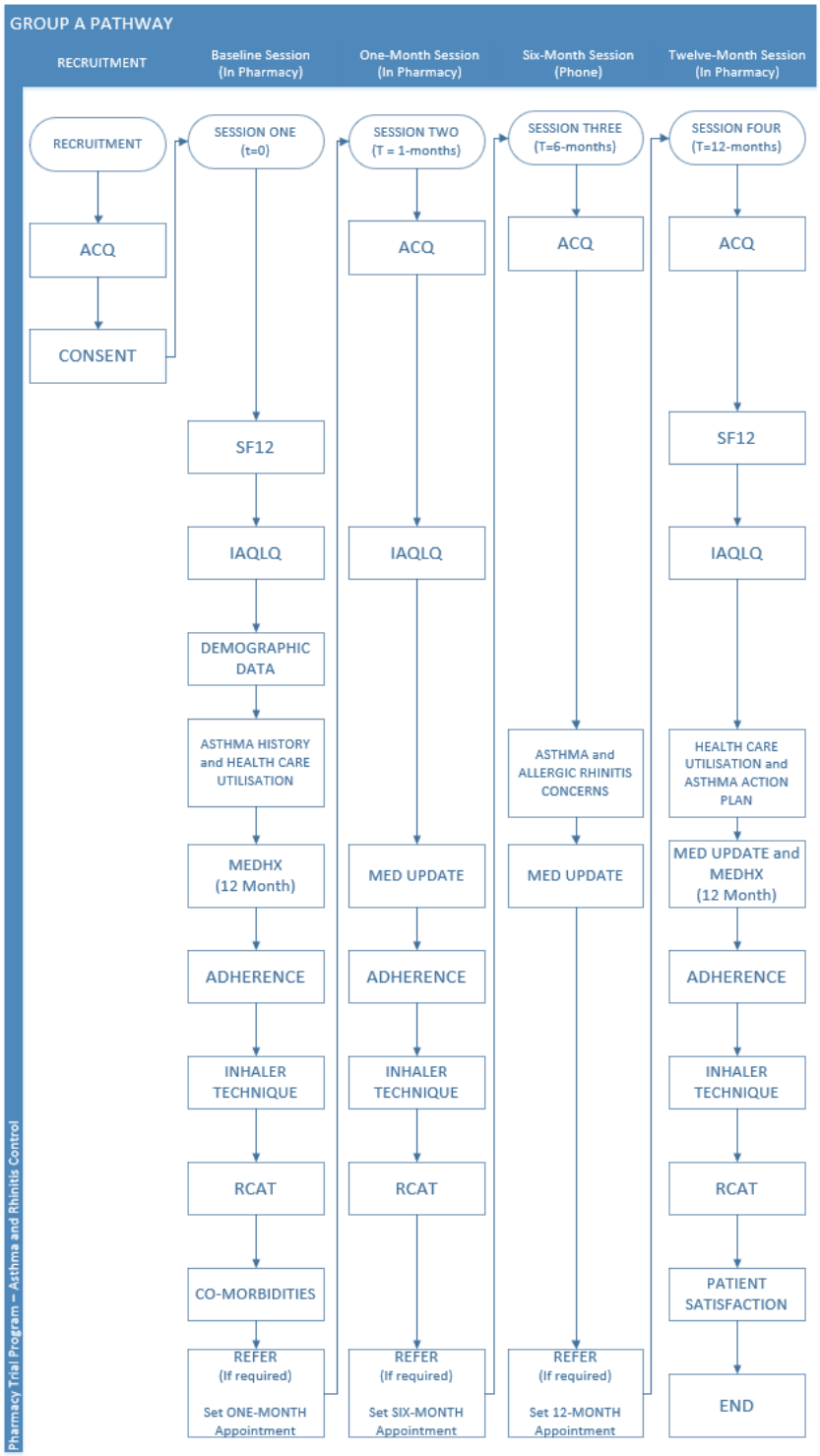


Figure 8: Intervention patient pathway

Note: ACQ = Asthma Control Questionnaire, SF12 = Short-Form 12, AQOL = The Impact of Asthma on Quality of Life Questionnaire

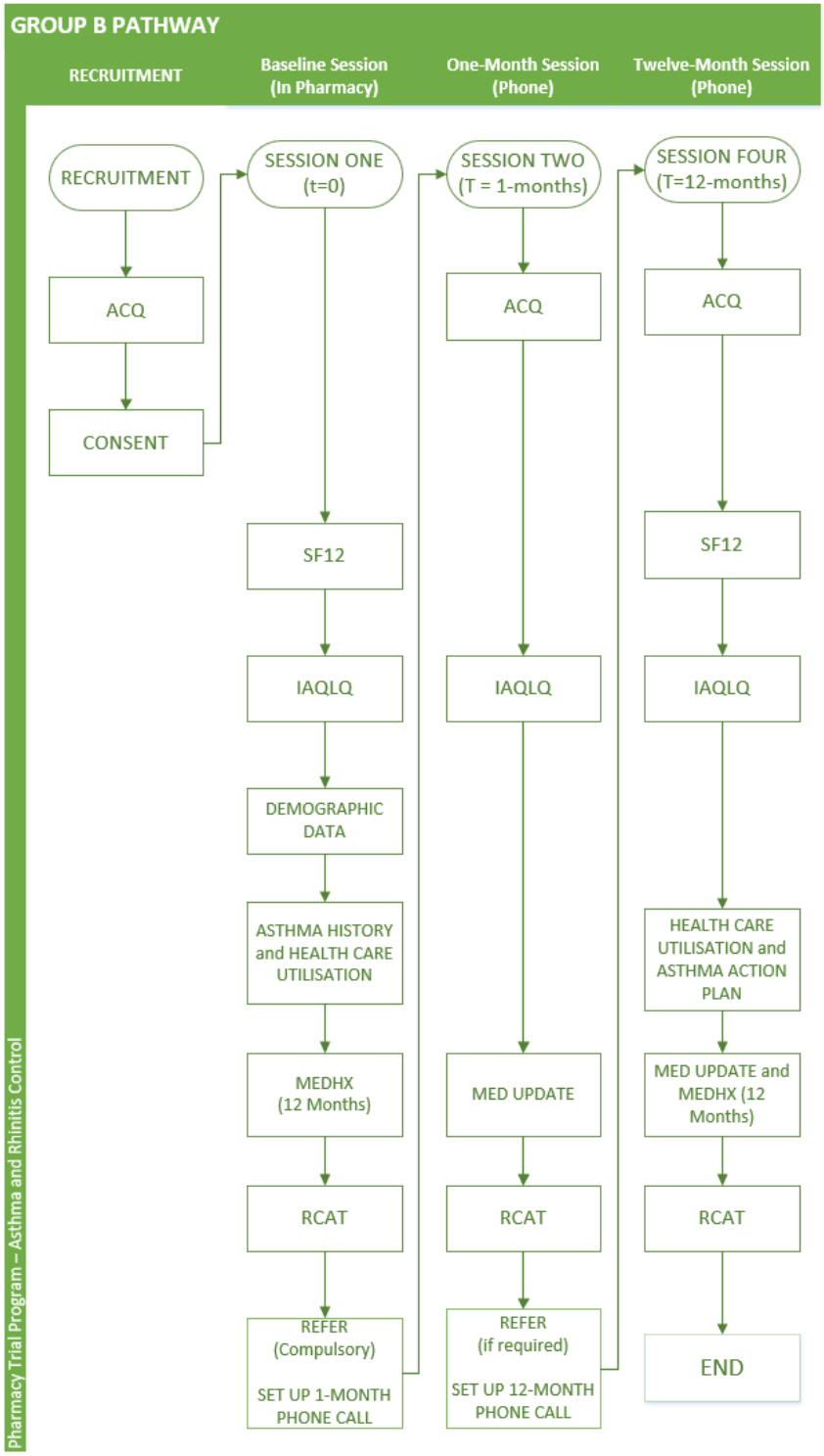


Figure 9: Comparator patient pathway

Note: ACQ = Asthma control Questionnaire, SF-12 = Short Form 12, IAQLQ = The Impact of Asthma on Quality of Life Questionnaire

Fidelity

Adherence to the trial protocol for the intervention arm was monitored and facilitated during visits of project staff to the pharmacies after each pharmacy had completed at least one patient's baseline visit. Audit visits enabled the research team to review trial progress, check that data were being collected appropriately, confirm that service delivery was in accordance with the trial protocol, ensure project resources were being used correctly and to provide feedback in order to optimise service delivery. Pharmacists in both arms were also contacted weekly/fortnightly by telephone depending on need, and were sent quarterly newsletters to keep them informed and motivated. Newsletters allowed us to provide uniform protocol assistance, motivational tips to encourage recruitment and follow-up and troubleshooting advice.

Program Evaluation Plan

In line with best practice for program evaluation, several forms of evaluation were undertaken in the trial: formative, process, outcome, and economic evaluation. A summary of the evaluation components of the trial and the statistical analysis plan were published online (https://osf.io/mjzrn) prior to the analysis and are detailed in Appendix E.

Firstly, pharmacy demographic data were collected at baseline to confirm the comparability of pharmacies randomised to the two different arms (intervention and comparator).

A formative evaluation was conducted with a 10% sample of participating pharmacies to gain feedback on barriers and facilitators experienced during the trial. This evaluation was carried using individual qualitative interviews with participating pharmacists, questions asked were in accordance to a guide created by the investigative team which is included in Appendix I. In addition, pharmacists who failed to recruit patients were interviewed to gain feedback on barriers and facilitators to the recruitment process specifically.

A process evaluation was used to assess the feasibility of implementing such a service in pharmacies in accordance with the trial protocol – it focused on the capacity of pharmacists to deliver the intervention as intended and identified issues in recruitment of eligible patients, and implementation and completion of the intervention. This included both objective measures of implementation including median number of services/pharmacy/week and total number of services per pharmacy and patient surveys to measure subjective assessment of the quality of the service treatment delivered by the pharmacist.

An outcome analysis was completed for the main outcomes of the trial, including change in asthma control, quality of life and changes in adherence, inhaler technique and allergic rhinitis control.

An economic analysis was conducted to determine the cost-effectiveness of the service. We determined the costs of providing the Pharmacy Asthma Service (including set-up costs, training of pharmacists, educational manual, pharmacist's time in providing consults/telephone follow-up) and costs of patients' healthcare utilisation (doctor visits, medication use, hospitalisations and emergency presentations). Information on healthcare use (intervention and usual care) was determined from linked MBS and PBS data.

A7 KEY DIFFERENCES IN THE PROPOSED MEDICAL SERVICE AND THE MAIN COMPARATOR

After the initial assessment of eligibility for patients and review of quality of life, the clinical trajectory of patients within the intervention and comparator arm differed. This is illustrated in Figure 8 and Figure 9. The Pharmacy Asthma Service identified possible causes for poor asthma control and used evidence-based practices shown to be effective in pharmacy settings (Figure 5) to help address these causes. Thus, the service involved the assessment of adherence and provision of support mechanisms to improve adherence, the assessment and correction of inhaler technique, the review of allergic rhinitis and management advice. The comparator arm identified patients by assessing asthma control, asthma quality of life and allergic rhinitis control, but rather than intervening at the pharmacy, patients were referred to the GP for review. The comparator arm was then followed up two more times via telephone to assess the same parameters, and additional referrals made if necessary. Patients in the intervention arm were met twice more in person and had one additional telephone check-in.

A8 CLINICAL CLAIM

Participating intervention pharmacists were trained about evidence-based asthma management interventions to improve asthma patients' inhaler use and medication adherence as well as allergic rhinitis management. These interventions have been shown to improve asthma control and asthma-related quality of life in the literature (65, 68, 69). The benefit to the health system would be cost savings (better asthma control involves lower healthcare utilisation) and maximising asthma care capacity (using the privately funded infrastructure of pharmacy). Some of the costs of sub optimally controlled asthma may stem from undermanaged rhinitis.

Given the high prevalence of asthma nationally, it is envisaged that this asthma intervention will be of similar benefit to all Australian adults with poorly controlled asthma. Taking into account the population with asthma in Australia is 2.7 million (1) the number of patients with poorly controlled asthma (50% = 1.35 million) (2) those who are adults (~80%= 1.08 million) (3) excluding those who might also have COPD (20%) (4) and the likelihood that only half of these would be estimated to undertake the service, we estimate 432,000 people with asthma would benefit immediately. If implemented in rural and remote pharmacies, the service has the potential to be of significant benefit to Aboriginal and Torres Strait Islander peoples and consumers in these areas, who often suffer from lack of access to standard care.

A9 PICO CONFIRMATION

The guiding framework of the service and assessment of effectiveness has been presented in Sections A1-A8. Primary care physicians (GPs) are currently seen as the pivotal source of care and education for asthma patients. However, limited time and resources resulting from increased pressures in the Australian primary care sector possibly compromise the quality of asthma care (8). Additionally, in Australia, a proportion of the population with asthma are not already seeking GP or health professional care for their asthma. Efficient task shifting between health professions could be a

solution to improve the quality of care, and access to care for asthma patients. This service presents an alternate/adjunct pathway to keep people with asthma engaged with their condition and well. Subsequent benefits to the health system are cost-saving (better asthma control implies lower healthcare utilisation) and maximising asthma care capacity, using the privately funded infrastructure of pharmacy.

A10 CONSUMER IMPACT STATEMENT

Quality of life is an important overall measure of wellbeing of an individual measured across many aspects of life, such as the ability to function productively and socially, mood, emotional state, and mental health. Experts suggest that measuring quality of life is an important aspect when testing the effects of a drug, process or service, as it has been shown that even if asthma symptoms improve for a given patient, asthma-related quality of life may not (76). Asthma, as a chronic disease, is known to have a significant impact on a person's quality of life; indeed, this was the case for patients who choose to participate in the Pharmacy Asthma Service at study commencement. At the end of the study, data indicated that the Pharmacy Asthma Service significantly improved the quality of life of those who received it. This improvement emerged one month after the delivery of the service, and the effect was maintained at 12 months. The improvements were evident in all aspects of quality of life that were measured using a self-administered evidence-based questionnaire with 20 questions (IAQLQ). These questions included asking people with asthma about being troubled by symptoms, feeling restricted because of asthma, energy levels, sleep, mood, anxiety, and their feeling of being limited or controlled by asthma. Given the Pharmacy Asthma Service led to improvements in all these aspects over 12 months, i.e. over a full cycle of seasons and seasonal effects, implies that the services had a sustained impact on the daily lives of patients, i.e. people with asthma in the community. Indeed, in post-service consultation with those who had participated in the Pharmacy Asthma Service, being confident about managing asthma, regaining a feeling of 'control' over asthma and satisfaction with the 'time' devoted to them by provider pharmacists were key messages offered.

In terms of specific symptoms, the asthma control score (ACQ) is an evidence-based assessment of control of asthma symptoms, and is based on patient self-report of the severity of their symptoms. It has been shown that a score of lower than 1.5 (termed "controlled asthma") is associated with lower risk for exacerbations and worsening health, and an improvement of ≥ 0.5 on this score for an individual is clinically important (77). The ACQ has also been shown to be a more sensitive measure compared to a clinician's assessment of asthma control. The Pharmacy Asthma Service resulted in 62% of the cohort recruited (all not controlled and therefore at-risk) becoming controlled. The ACQ scores averaged across all people who received the Pharmacy Asthma Service changed by ≥ 0.5, implying clinical improvement. One of the questions in the ACQ pertains to the use of reliever medicines; it was clear that overuse of these medications decreased by more than half, from 75% of over-users at the study commencement, to only 26% of over-users at the end. Relievers are available from pharmacies without a prescription, and are overused by many people. Relievers provide a sense of immediate relief, making it difficult for people with asthma to understand the danger involved in over-using these inhalers, especially if no preventers are being used at the same time. Thus, the Pharmacy Asthma Service improved the safe use of asthma medicines.

Finally, evidence highlights a clear link between asthma control, productivity, and health-related costs (78). An improvement in asthma control, as brought about by the Pharmacy Asthma Service, thus has impact on the future health of these people with asthma.

Fewer symptoms, fewer exacerbations and better reported quality of life not only will have an impact on the person with asthma, but also on their family. The burden of asthma affects the entire family, with lost productivity, events cancelled, emergency hospital visits and admissions, and caring responsibilities for members of the family. Previous studies in Australia indicate that asthma does impose a cost on family functionality.

If asthma is controlled, the risk of this impacting the family is significantly reduced.

The impact in the community is also likely to be lower if more people were to benefit from the Pharmacy Asthma Service. The cost of exacerbations for the public health system and the cost of lost days of productive work/education will be reduced. In addition, asthma affects the mental health and wellbeing of those who have the condition. This burden of poorer mental health and subsequent need for treatment and/or support will be reduced if people feel that they are controlling their disease rather than it controlling them (as one participant said).

The ubiquitous presence of pharmacies, their opening hours and ready access suggest that as a venue of delivery of a standardised evidence-based service, pharmacies can and should be a key point of ongoing asthma management.

SECTION B: CLINICAL EVALUATION

OUTCOME MEASURES AND ANALYSIS

The results of the evaluation are divided into four sections – outcome, process, formative and economic – as per our approved evaluation framework detailed in Appendix E.

Data analysis was carried out in accordance to a statistical analysis plan created by the research team. The statistical analysis plan has been published online at https://osf.io/mjzrn.

OUTCOME EVALUATION

SUMMARY OF PRIMARY AND SECONDARY OUTCOMES

Statistically significant improvements occurred in both intervention and comparator arms with respect to asthma control, quality of life and allergic rhinitis control scores in the period between baseline and the 12-month follow-up. The improvement in mean quality of life scores of participants in the intervention arm was statistically significantly greater than in the comparator arm participants over the 12-month timeframe (adjusted mean difference and 95% CI: -0.52 (-0.89 to -0.14), p=0.0079). There was no significant difference between the two arms over the 12-month period for mean asthma control and rhinitis control scores with an odds ratio of 1.51 (95% CI 0.84 to 2.70, p=0.17) for asthma control at month 12.

As seen in Table 4, for binary (yes/no) outcomes such as the proportion of participants with an ACQ score <1.5, we report raw numbers and percentages (columns 2 and 3) together with the odds ratio and p-value obtained from the logistic model. For continuous outcomes such as the ACQ, IAQLQ and RCAT scores, we report means and standard errors together with the mean differences and a p-value, all obtained from a linear model adjusted for the baseline value of the outcome of interest. For the primary outcome, an ACQ score <1.5, the logistic model is adjusted for the baseline ACQ score. All models include a random effect of the pharmacy to account for correlations between participants from the same pharmacy.

Table 4: Primary and secondary outcomes

	Intervention Mean (SE) or n (%)	Comparator Mean (SE) or n (%)	Mean difference or Odds ratio (95% CI)	p-value
Proportion with ACQ Score[1] < 1.5 *(primary analysis)*				
Baseline	0 (0.0)	0 (0.0)	-	-
Month 1	85 (44.7)	72 (55.0)	0.67 (0.40 to 1.13)	0.1300
Month 12	88 (61.5)	59 (53.2)	1.51 (0.84 to 2.70)	0.1669
ACQ score[1]				
Month 1	1.58 (0.07)	1.58 (0.09)	0.00 (-0.22 to 0.23)	0.9736
Baseline to Month 1	-0.86 (0.07)	-0.86 (0.09)		
p-value	<.0001	<.0001		
Month 12	1.34 (0.08)	1.50 (0.09)	-0.16 (-0.41 to 0.08)	0.1960
Baseline to Month 12	-1.10 (0.08)	-0.94 (0.09)		
p-value	<.0001	<.0001		
Baseline	3.5 (1.9) #	3.2 (2.0) #		
Month 1	2.25 (0.11)	2.45 (0.14)	-0.20 (-0.55 to 0.15)	0.2667
Baseline to Month 1	-0.97 (0.11)	-0.77 (0.14)		
p-value	<.0001	<.0001		
Month 12	1.94 (0.13)	2.45 (0.14)	-0.52 (-0.89 to -0.14)	0.0079*
Baseline to Month 12	-1.28 (0.13)	-.077 (0.14)		
p-value	<0.0001	<0.0001		
RCAT score[3]				
Baseline	20.8 (5.4) #	19.9 (5.1) #		
Month 1	22.61 (0.40)	21.94 (0.48)	0.67 (-0.57 to 1.91)	0.2866
Baseline to Month 1	2.36 (0.40)	1.69 (0.48)		
p-value	<.0001	0.0006		
Month 12	22.04 (0.44)	21.54 (0.51)	0.50 (-0.84 to 1.83)	0.4640
Baseline to Month 12	1.79 (0.44)	1.30 (0.51)		
p-value	<.0001	0.0122		
Asthma Action Plan				
Month 12	56 (39.2%)	54 (48.6%)	0.71 (0.39 to 1.29)	0.2620

Note:

* significant result

1. Asthma Control Questionnaire (ACQ) score lies between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (79).
2. The Impact of Asthma on Quality of Life Questionnaire (IAQLQ) scores lie between 0 and 10. Higher scores represent a greater impact of asthma on quality of life (55).
3. Rhinitis Control Assessment Test (RCAT) scores lie between 6 and 30. The lower the score, the more severe the allergic rhinitis; the higher the score, the less severe the allergic rhinitis. Participants scoring ≤21 are considered clinically "symptom uncontrolled"; those scoring >21 are considered "symptom controlled" (56).

ASTHMA CONTROL

Asthma control improved over the 12-month period of the trial in both the intervention and comparator arms (Figure 10). The ACQ consists of six questions focussed on symptoms and reliever use. Responses to individual ACQ questions at each visit are detailed in Appendix J.

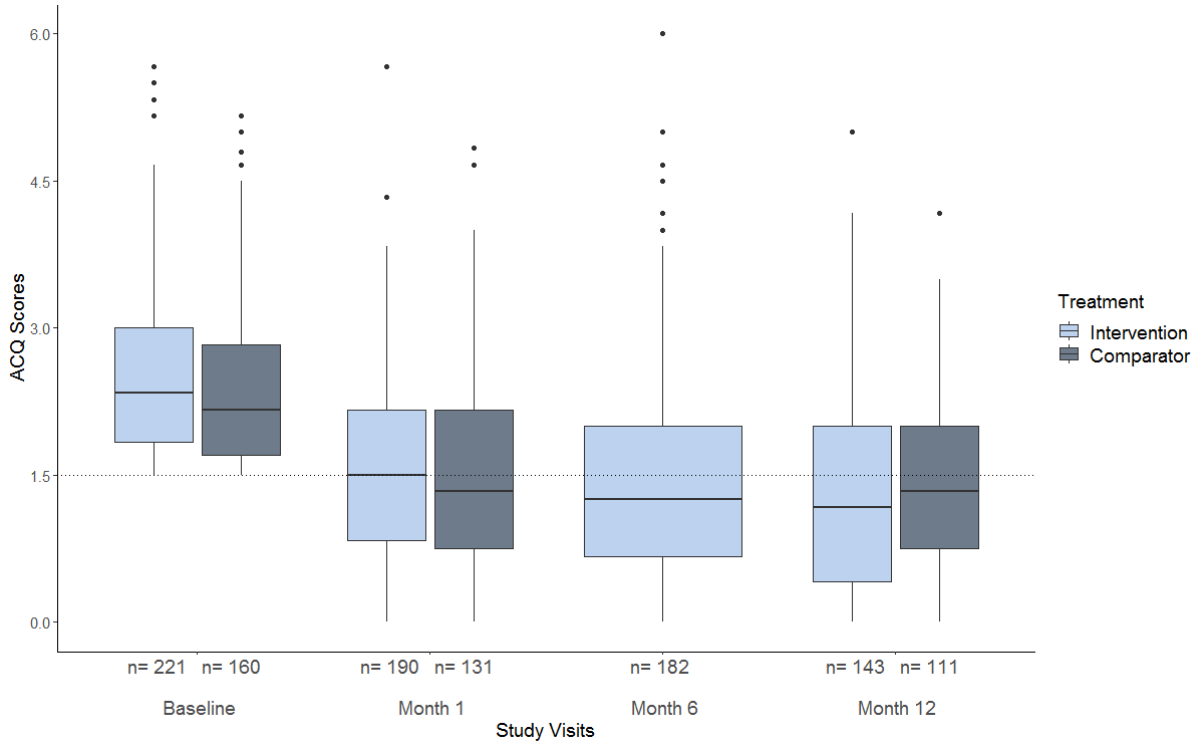


Figure 10: Asthma control by visit

Note: ACQ Score lies between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (2). A change in score of 0.5 is considered a clinically significant change. Note no assessment of ACQ at month 6 in comparator arm.

ADJUSTED ANALYSIS OF ASTHMA CONTROL, SUBGROUP ANALYSIS, TREATMENT OF MISSING DATA

We performed a range of sensitivity analyses to assess the robustness of the main findings. These additional analyses included:

1. Rerunning the analysis of the primary outcome (ACQ score <1.5) after adjusting for additional baseline covariates including age, lung function test, work status, smoking status and allergic rhinitis status.
2. Replacing missing ACQ scores using multiple imputations.
3. Removing data from visits that occurred outside of pre-specified windows.

All these sensitivity analyses lead to results that are consistent with the main analysis (Table 5), with odds ratios ranging between 1.40 and 1.53 in favour of the intervention arm but lacking statistical significance.

Table 5: Analysis of primary outcome (ACQ) on imputed data

	Intervention n (%)	Comparator n (%)	Odds ratio (95% CI)	p-value
ACQ Score < 1.5 (adjusted analysis)				
Month 1	85 (44.7%)	72 (55.0%)	0.63 (0.36 to 1.10)	0.1020
Month 12	88 (61.5%)	59 (53.2%)	1.48 (0.80 to 2.74)	0.2117
ACQ Score < 1.5 (multiple imputation)				
Month 1	n/a	n/a	0.70 (0.41 to 1.19)	0.1865
Month 12	n/a	n/a	1.53 (0.88 to 2.67)	0.1344
ACQ Score < 1.5 (restricted visit windows)				
Month 1	83 (44.6%)	62 (55.4%)	0.65 (0.38 to 1.13)	0.1294
Month 12	88 (62.0%)	54 (55.1%)	1.40 (0.77 to 2.57)	0.2730

Note:

* significant result

1. Asthma Control Questionnaire (ACQ) score lies between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (79).

- Missing data for ACQ Score at month 1 and month 12 has been imputed using a fully conditional specification with predictive mean matching (multiple imputation technique).
- The imputation model included the ACQ score at baseline, month 1 and month 12, a variable indicating the pharmacy (cluster), a variable indicating the intervention, as well as the following baseline variables: SF12 scores (Mental and Physical), IAQLQ score, age, sex, work status, education status, age since diagnosis, history of lung function test, smoking status and allergic rhinitis status.

FACTORS ASSOCIATED WITH WORSE ASTHMA CONTROL

A multiple linear regression was conducted to determine whether there were baseline characteristics of recruited participants associated with poor asthma control. The results (Appendix K) indicated that being an active smoker, lower levels of education and having at least one emergency room

presentation in the 12 months prior to entry into the trial were statistically significant determinants of poorer asthma control.

QUALITY OF LIFE

Asthma quality of life scores improved over time in both intervention and comparator arms (Figure 11). For those receiving the intervention, this difference in score over time was significantly greater than in the comparator arm. Responses to individual IAQLQ questions at each visit are detailed in Appendix K.

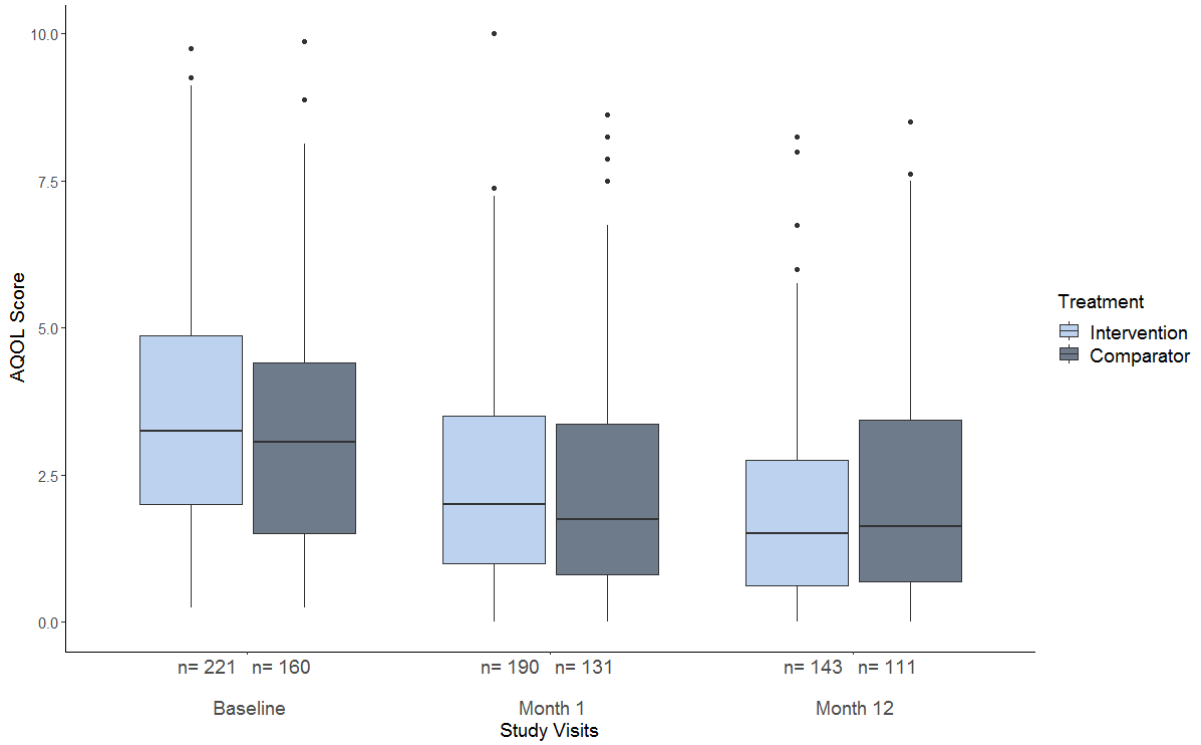


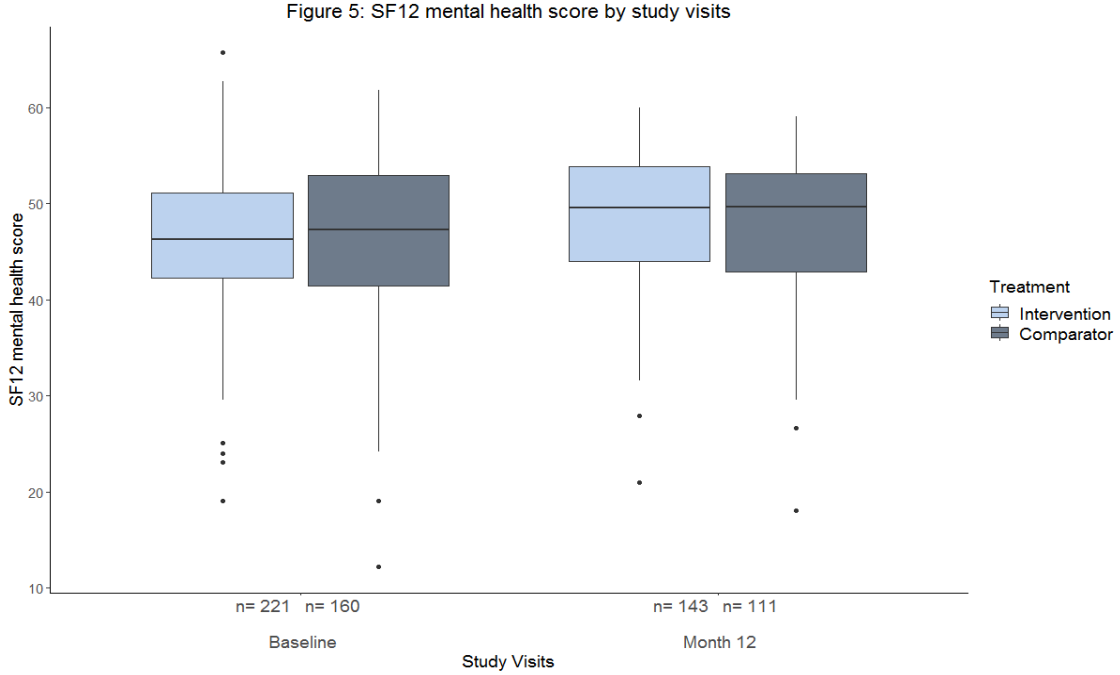
Figure 1: Impact of asthma on quality of life by visit

Note: The Impact of Asthma on Quality of Life Questionnaire (IAQLQ) scores lie between 0 and 10. Higher scores represent a greater impact of asthma on quality of life (55).

Improvement in participant-perceived mental and physical health was recorded in both intervention and comparator arms over the 12-month period (Figure 12). Responses to SF-12 survey questions at each visit are detailed in Appendix M.

a) Mental health

Figure 5: SF12 mental health score by study visits



b) Physical health

Figure 6: SF12 physical health score by study visits

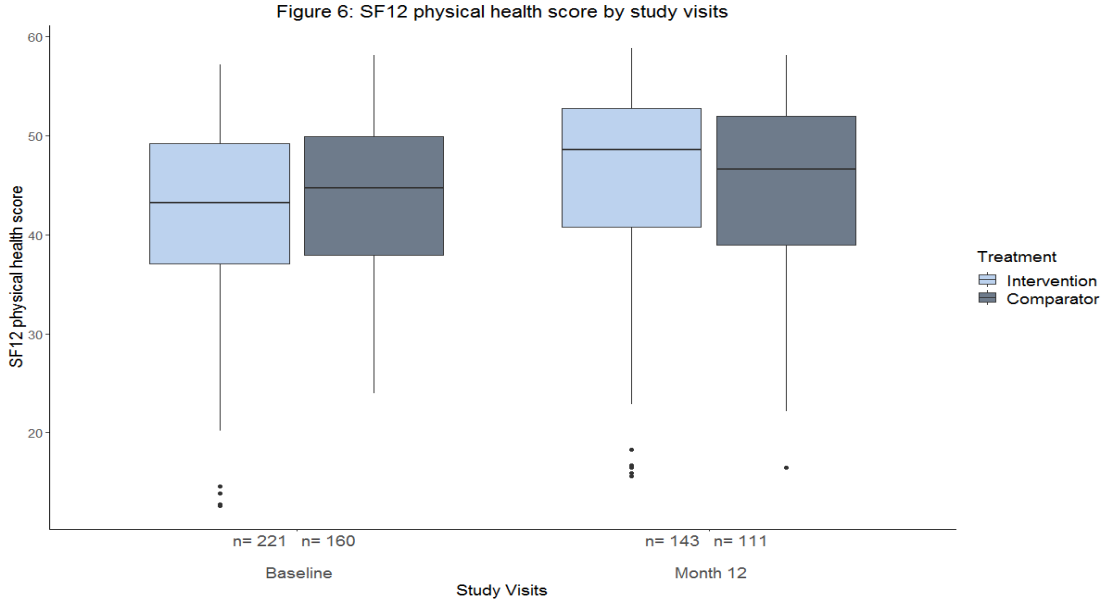


Figure 12: Quality of life by visit (SF-12)

Note: Short Form 12 Mental Health and Physical Health (SF-12) scores lie between 0 and 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health.

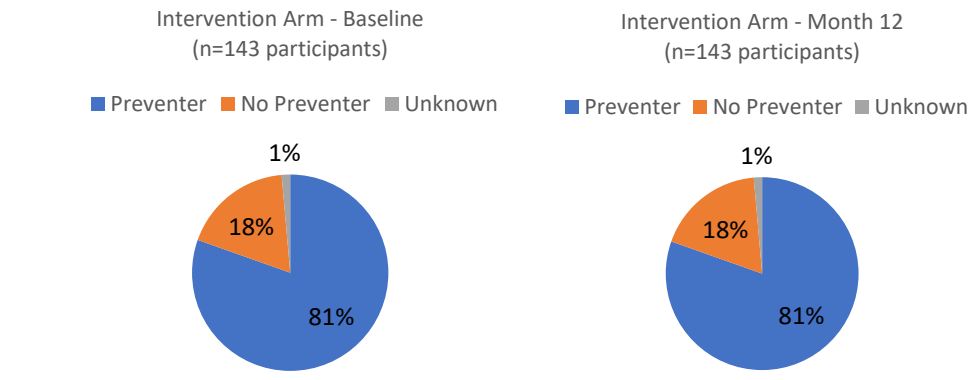
ADHERENCE – CHANGE IN PREVENTER AND RELIEVER THERAPY

PBS DATA (INTERVENTION AND COMPARATOR ARMS)

Of the total sample (n=381), 378 participants consented to the collection of their PBS data, and 345 were able to be linked to complete PBS data: 205 (93%) participants from the intervention arm and 140 (86%) from the comparator arm.

Preventer Use

There was a high proportion of participants who had at least one preventer dispensed in the 12 months prior to baseline and during the trial period. However according to PBS data, 18% of intervention participants and 19% of comparator participants did not have any preventer dispensed in the previous 12 months to the start of the trial. When looking only at participants who completed the full 12-month trial, the proportion that had at least one preventer dispensed slightly decreased in the comparator arm at month 12 but remained the same in the intervention arm (Figure 13). This analysis does not take into account whether there was a change in preventer or dose, or the number of times the preventer was collected from the pharmacy.



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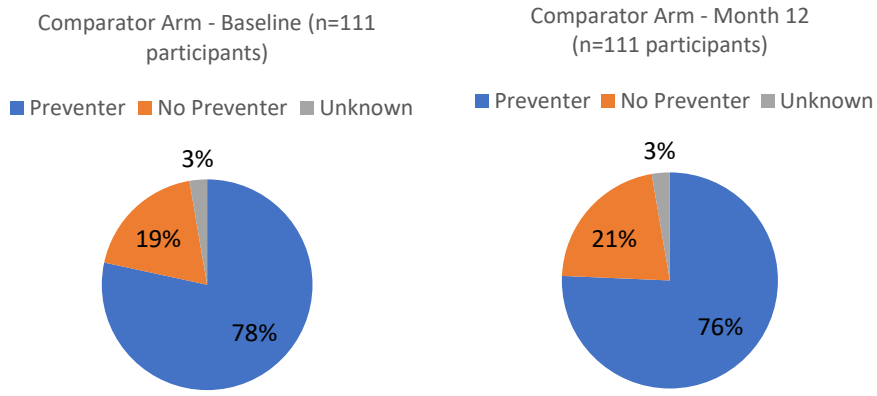


b)

Figure 13: Proportion of patients with at least one preventer dispensed (PBS data; participants who completed the 12-month trial). a) Intervention participants, b) Comparator participants.

Adherence

Using PBS data, it appears that adherence decreased in both arms over time; however, the change was not significant (Table 6, Figure 14). The paired analysis used a smaller sample, as paired data for all participants were not available. In this cohort of participants in neither arm of the trial was there any increase in adherence, in fact there was a trend to decreased adherence based on this data.

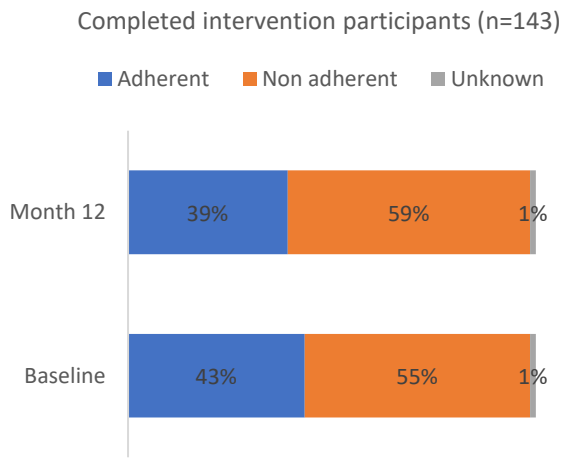
Table 6: Proportion of participants classified as adherent as determined via PBS data *

	Intervention Number adherent/total (%)	Comparator Number adherent/total (%)	Odds Ratio (95% C.I)[2]	p-value[2]
Participants who completed the full trial[3]				
Baseline (PDC[1] ≥ 80)	62/116 (53.4%)	55/86 (64.0%)		
Month-12 (PDC[1] ≥ 80)	56/115 (48.7%)	41/84 (48.8%)	1.04 (0.50, 2.16)	0.9087
Paired analysis[4]				
Baseline (PDC[1] ≥ 80)	58/108 (53.7%)	53/81 (65.4%)		
Month-12 (PDC[1] ≥ 80)	54/108 (50.0%)	41/81 (50.6%)	1.08 (0.52, 2.24)	0.8375

Note:

* Only participants for whom a PDC (proportion of days covered) score could be calculated were included in this analysis. We acknowledge Services Australia (formerly the Department of Human Services) for supplying PBS information.

1. *Proportion of Days Covered (PDC) by at least one preventer medication (71) was calculated. A participant with a PDC of 80% or higher was considered adherent (72).*
2. *Odds Ratios and p-values were obtained from a generalised linear mixed model with a fixed intervention effect and a random pharmacy effect.*
3. *Adherence was estimated from PBS data for all participants as a cohort of either intervention or comparator who were also represented in the 12-month follow-up dataset.*
4. *Paired PBS analysis (present at both pre-baseline and post-baseline periods from PBS data) – adherence was estimated for all participants who were also represented in the 12-month follow-up dataset in a paired comparison.*



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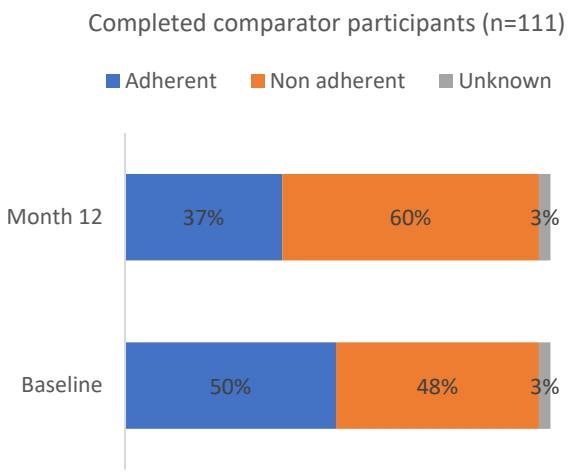


b)

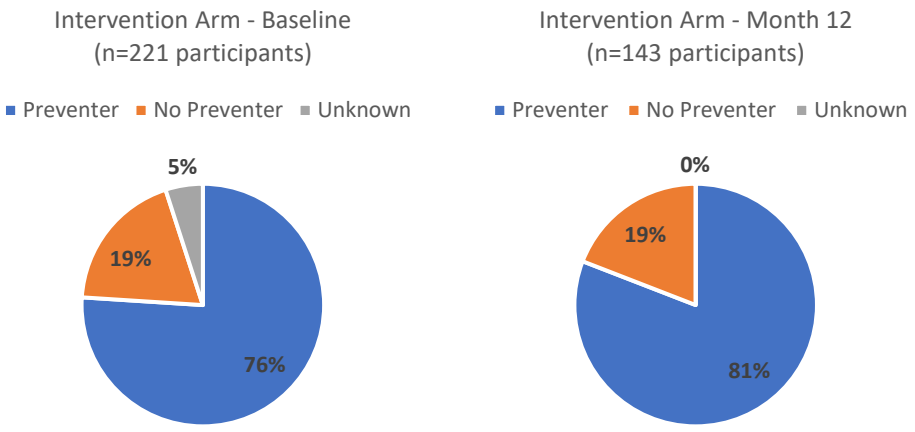
Figure 14: Adherence status for participants who completed the full 12-month trial via PBS data. ***a) Intervention participants, b) Comparator participants.***

Pharmacy Dispensing Data (Intervention and Comparator Arms)

Of the total sample (n=381), Pharmacy Dispensing Data was collected for 363 participants at baseline. 210 (95%) participants from the intervention arm and 153 (96%) from the comparator arm.

Preventer use

Data were entered from the dispensing records for the preceding 12 months for all participants who enrolled at baseline. At 12 months, we were only able to collect pharmacy dispensing data for those participants who completed the study. Thus, this comparison compares all those included at baseline with the smaller group at Month 12. Once again, as with the PBS data, 19% (intervention) and 18% (comparator) of participants did not have at least one preventer dispensed in the 12 months prior to the trial. This proportion stayed the same in the intervention group and slightly increased in the comparator group (Figure 15).



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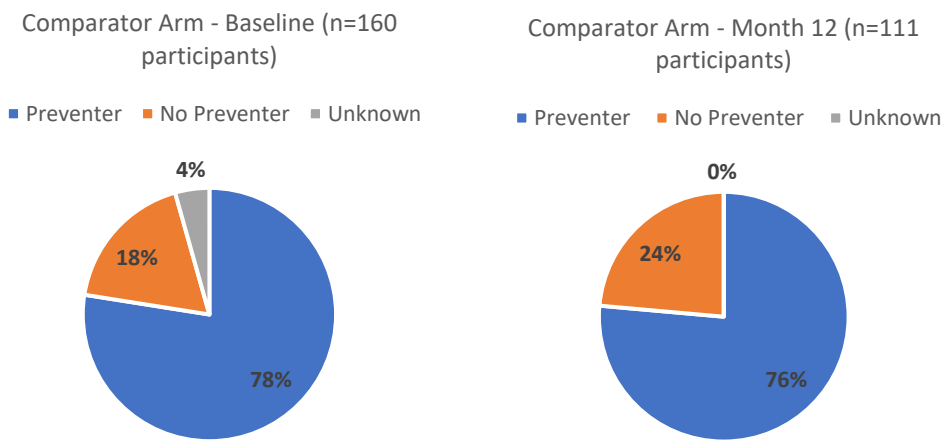


b)

Figure 15: Proportion of participants who had at least one preventer dispensed according to pharmacy dispensing data. *a) Intervention participants, b) Comparator participants. Unknown = participants in the trial who did not have pharmacy dispensing data available.*

Adherence

Using the pharmacy dispensing records, at baseline, 32% of the participants were adherent *(PDC ≥80)*. Although there was a slight increase in adherence in the intervention arm at 12 months, this was not significant. In the comparator arm, 40% of the participants were adherent at baseline and this decreased to 36*%* at the end of the trial; the difference was not statistically significant (Table 7). For this analysis, the proportion adherent is only representative of those participants who had at least one preventer dispensed.

Table 7: Participant adherence to preventer therapy based on Pharmacy Dispensing data *

Measure		Intervention n (%)	Comparator n (%)	Total n (%)	p-value
Adherent (PDC[1] ≥ 80)	Baseline	53/168 (31.5)	50/124 (40.3)	103/392 (35.2)	0.1438
	Month 12	39/110 (35.5)	28/81 (35.6)	67/191 (35.1)	0.4899
PDC Score					
	Mean (SD)	69.7 (28.1)	74.4 (26.4)	71.7 (27.4)	
	Min; Max	21.1; 100.0	24.7; 100.0	21.1; 100.0	
Baseline	Median	74.7	81.7	77.9	0.3048
	Q1; Q3	41.9; 100.0	51.4; 100.0	44.7; 100.0	
	(IQR)	(58.1)	(48.6)	(55.3)	
	Mean (SD)	68.1 (28.2)	66.6 (27.3)	67.4 (27.7)	
Month 12	Min; Max	15.6; 100.0	12.3; 100.0	12.3; 100.0	0.8892
	Median	74.9	67.0	68.9	

Measure		Intervention n (%)	Comparator n (%)	Total n (%)	p-value
	Q1; Q3 (IQR)	42.3; 100.0 (57.2)	39.3; 96.3 (57.0)	41.8; 99.5 (57.7)	

Note:

[1] PDC (proportion of days covered) only calculated for participants for whom medication history was available.

PARTICIPANT SELF-REPORTED ADHERENCE USING A VAS (INTERVENTION ARM ONLY)

Participants reported regular use of preventer in the seven days prior to the baseline and month 12 visits, and a range of reliever use (Table 8). Detailed issues raised by the participants regarding their medications and asthma as part of the intervention are described in Appendix N. Participants reported preventer usage increased, and reliever usage decreased significantly in the intervention arm (baseline vs 12 months) (Table 8). The range of reliever use reported by participants was from zero to 140 times in the previous 7 days.

Table 8: Participant self-reported adherence and reliever use

		Intervention		
		Baseline	Month 12	p-Value
		n = 221	n = 143	
Use of all of asthma preventer/controller medication as directed in the past 7 days[1]	Mean (SD)	6.9 (3.02)	7.6 (2.93)	0.0434
	Median (Q1; Q3)	7.8 (4.8; 9.8)	8.7 (6.3; 10.0)	
	Min Max	0 10	0 10	
Reliever use in past 7 days	Mean (SD)	15.1 (17.39)	9.2 (16.00)	0.0035
(how many times?)	Median (Q1; Q3)	12.0 (4.0; 20.0)	3.0 (1.0; 9.0)	
	Min Max	0 140	0 100	
Average number of puffs reported to obtain relief	Mean (SD)	3.0 (2.02)	2.1 (0.99)	<0.0001
	Median (Q1; Q3)	2.0 (2.0; 4.0)	2.0 (2.0; 2.0)	
	Min Max	0 14	0 6	

Note:

1. Adherence Visual Analogue Scale ("All things considered, how much of the time do you use ALL your asthma preventer/controller medications EXACTLY as directed?") Responses ranged from 1 (none of the time) to 10 (all the time).

Data collected from ACQ Question 6 were used to compare participant reliever use between baseline and month 12. The data were analysed using the binary comparison between up to 2 puffs (appropriate use) versus 3-4 puffs or greater (overuse). The reported use of reliever in this question was much higher than the participant reported use when asked directly by the pharmacist (Table 9). Reliever overuse decreased in the intervention arm from 75.1% at baseline to 26.4% (0.034) at the final follow-up. In the comparator arm, reliever overuse decreased from 63.1% at baseline to 43.2% at the final follow-up (0.009).

Table 9: Participant reliever use

		Intervention	Comparator	Total	
		n(%)	n (%)		p-value[1]
		n=221	n=160	n=381	
Baseline	≤ 1-2 puffs/inhalations most days	55 (24.9)	59 (36.9)	114 (29.9)	0.1646
	≥ 3-4 puffs/inhalations most days	166 (75.1)	101 (63.1)	267 (70.1)	
		n=143	n=111	n=254	
Month 12	≤ 1-2 puffs/inhalations most days	91 (63.6)	63 (56.8)	154 (60.6)	0.3872
	≥ 3-4 puffs/inhalations most days	52 (26.4)	48 (43.2)	100 (39.4)	
p-value		0.034*	0.009*		

Note:

* significant result

1. *Based on participant responses to Q6 of the Asthma Control Questionnaire (ACQ). Number of puffs of reliever medication each day on average.*

GP Referral

GP referrals made throughout the duration of the trial are presented in Table 10. A statistically higher amount of comparator participants visited the GP in the one month after baseline than intervention patients.

Table 10: General practitioner (GP) referrals and participant-reported GP visits

		Intervention n (%)	Comparator n (%)	Odds Ratio (95% CI)[1]	p-value[1]
BASELINE		n=221	n=160		
GP Referral given	No	186 (84.2)	0 (0.0)		
	Yes	35 (15.8)	160 (100.0)		
MONTH 1		n=190	n=131		
GP Referral given	No	174 (91.6)	131 (100.0)		
	Yes	16 (8.4)	0 (0.0)		
Seen doctor regarding your asthma since your last visit	No	140 (73.7)	74 (56.5)	0.40 (0.20, 0.77)	0.0062*
	Yes	50 (26.3)	57 (43.5)		
Updates regarding your asthma medications or therapy	No	163 (85.8)	115 (87.8)	1.19 (0.47, 3.03)	0.7191
	Yes	27 (14.2)	16 (12.2)		
MONTH 12		n=143	n=111		
GP Referral given	No	113 (79.0)	83 (74.8)	0.73 (0.34, 1.59)	0.4316
	Yes	30 (21.0)	28 (25.2)		
Seen doctor regarding your asthma since your last visit	No	48 (33.6)	40 (37.4)	1.18 (0.52, 2.68)	0.6960
	Yes	95 (66.4)	67 (62.6)		
Updates regarding your asthma medications or therapy	No	112 (78.3)	88 (82.2)	1.14 (0.49, 2.63)	0.7559
	Yes	31 (21.7)	19 (17.8)		

Inhaler Technique

Inhaler technique mastery and maintenance for participants receiving the intervention is summarised in Table 11.

In order to evaluate inhaler technique, the different inhalers used by participants were categorised based on inhaler type: pressurised metered dose inhalers (pMDI), including pMDI + spacer, dry powered inhalers (DPIs) and the soft mist inhaler (SMI).

At baseline, a similar mean technique score was observed for participants within each of the three categories of inhalers indicating that, on average between 80% and 90% of the steps required to use an inhaler correctly were achieved by participants at baseline. Exploration of the proportion of

participants who had device mastery at baseline indicated 33.5%, 39.7% and 45.5% of participants using pMDIs, DPIs and SMI, respectively had device mastery.

Almost all using a pMDI and a DPI achieved device mastery after training (baseline) and mastery was sustained by over half the participants over time (month 1 and month 12 follow ups).

For participants using a SMI, all achieved (baseline) and sustained device mastery for 1 month; this was not sustained for 12 months. It should be noted that the number of participants using a SMI was small, hence these results should be interpreted with caution.

Table 11: Participant inhaler technique assessment (Intervention arm only)

	Baseline	Month 1	Month 12
pMDI/pMDI spacer [1]	n=194	n=162	n=122
Technique score			
Mean (SD)	0.8 (0.20)	0.9 (0.14)	0.9 (0.21)
Median (Q1; Q3)	0.8 (0.7; 1.0)	1.0 (0.8; 1.0)	1.0 (0.8; 1.0)
min max	0 1	0 1	0 1
Patients who demonstrated device mastery (scored 100 percent) prior to training	65 (33.5%)	89 (54.9%)	63 (51.6%)
Patient who achieved device mastery following training	188 (96.9%)	157 (96.9%)	118 (96.7%)
Number of attempts required			
Mean (SD)	1.5 (0.65)	1.2 (0.51)	1.2 (0.49)
Median (Q1; Q3)	1.0 (1.0; 2.0)	1.0 (1.0; 1.0)	1.0 (1.0; 1.0)
min max	1 3	1 3	1 3
Dry powder inhaler [2]	n=116	n=107	n=64
Technique score			
Mean (SD)	0.8 (0.20)	0.9 (0.09)	0.9 (0.16)
Median (Q1; Q3)	0.9 (0.7; 1.0)	1.0 (0.9; 1.0)	1.0 (0.9; 1.0)
min max	0 1	1 1	0 1
Patients who demonstrated device mastery (scored 100 percent) prior to training	46 (39.7%)	70 (65.4%)	46 (71.9%)
Patient who achieved device mastery following training	112 (96.6%)	105 (98.1%)	64 (100.0%)
Number of attempts required			
Mean (SD)	1.3 (0.54)	1.2 (0.39)	1.2 (0.43)
Median (Q1; Q3)	1.0 (1.0; 2.0)	1.0 (1.0; 1.0)	1.0 (1.0; 1.0)
min max	1 3	1 3	1 3
Soft mist inhaler [3]	n=11	n=9	n=12
Technique score			

	Baseline	Month 1	Month 12
Mean (SD)	0.9 (0.18)	1.0 (0.00)	0.9 (0.13)
Median (Q1; Q3)	0.9 (0.8; 1.0)	1.0 (1.0; 1.0)	1.0 (0.9; 1.0)
min max	1 1	1 1	1 1
Patients who demonstrated device mastery (scored 100 percent) prior to training	5 (45.5%)	9 (100.0%)	8 (66.7%)
Patient who achieved device mastery following training	11 (100.0%)	9 (100.0%)	12 (100.0%)
Number of attempts required			
Mean (SD)	1.6 (0.81)	1.0 (0.00)	1.1 (0.29)
Median (Q1; Q3)	1.0 (1.0; 2.0)	1.0 (1.0; 1.0)	1.0 (1.0; 1.0)
min max	1 3	1 1	1 2

Note:

1. pMDI/pMDI spacer includes PMDI, PMDI Single spacer and PMDI Tidal breathing inhaler.
2. Dry powder inhalers include Accuhaler, Autohaler, Handihaler, Breezhaler, Ellipta, Turbuhaler and Spiromax
3. Soft mist inhaler includes Respimat inhaler.

Some patients were prescribed more than one inhaler device type. Thus, the proportion of patients that were competent in using all their inhaler device types was examined. For the purpose of this analysis competency is defined as an inhaler technique score of 100%. The proportion of participants that were competent in the use of all prescribed device types increased significantly in the intervention arm when comparing baseline and month 12 (Table 12).

Table 12: Overall inhaler technique competency (Intervention arm only)

	Baseline	Month 12	p-value[1]
Patients with 100% competency for all prescribed devices	62/221 (28.1%)	75/143 (52.4%)	<.0001

ALLERGIC RHINITIS CONTROL

In the intervention arm 72.9% of the participants had allergic rhinitis. Similarly, in the comparator arm 67.4% of participants had allergic rhinitis. At baseline, 85.7% of participants with allergic rhinitis in the intervention arm accepted a new recommendation by the pharmacist to help manage their allergic rhinitis.

Table 13: Baseline allergic rhinitis assessment and management

		Intervention Baseline (n=221)	Comparator Baseline (n=160)
Ever had hay fever	No	60 (27.1%)	62 (32.6%)
	Yes	161 (72.9%)	128 (67.4%)

		Intervention Baseline (n=221)	Comparator Baseline (n=160)
Presence of warning symptoms[1]	No	143 (64.7%)	-
	Yes	78 (35.3%)	-
Participant accepted recommendation for improvement	No	23 (14.3%)	-
	Yes	138 (85.7%)	-

Note:

1. *Proportion displaying warning symptoms or symptoms that may be indicative of another ailment – a yes response meant the participant should be referred to the doctor. Symptoms included unilateral symptoms, blocked nose only, thick nasal mucus, thin postnasal drip mucus, pain, recurrent bleeding nose, loss of sense of smell, burning eyes, conjunctivitis, photophobia.*

Improvement in allergic rhinitis control over time was recorded in both intervention and comparator arms (Figure 16). Responses to RCAT questions at each visit are detailed in Appendix O.

Changes in allergic rhinitis management between baseline and one month are presented in Appendix P. There was an improvement in participant-reported nasal and ocular symptom severity at the one-month mark. A larger proportion of participants were treating their symptoms at the one-month time point; however, suboptimal treatment was apparent in the intervention arm. Only 42.0% of participants were taking the first-line treatment recommended for participants with poor asthma control and co-morbid allergic rhinitis (intranasal corticosteroid) (80). This improved marginally at the one-month time point (not statistically significant).

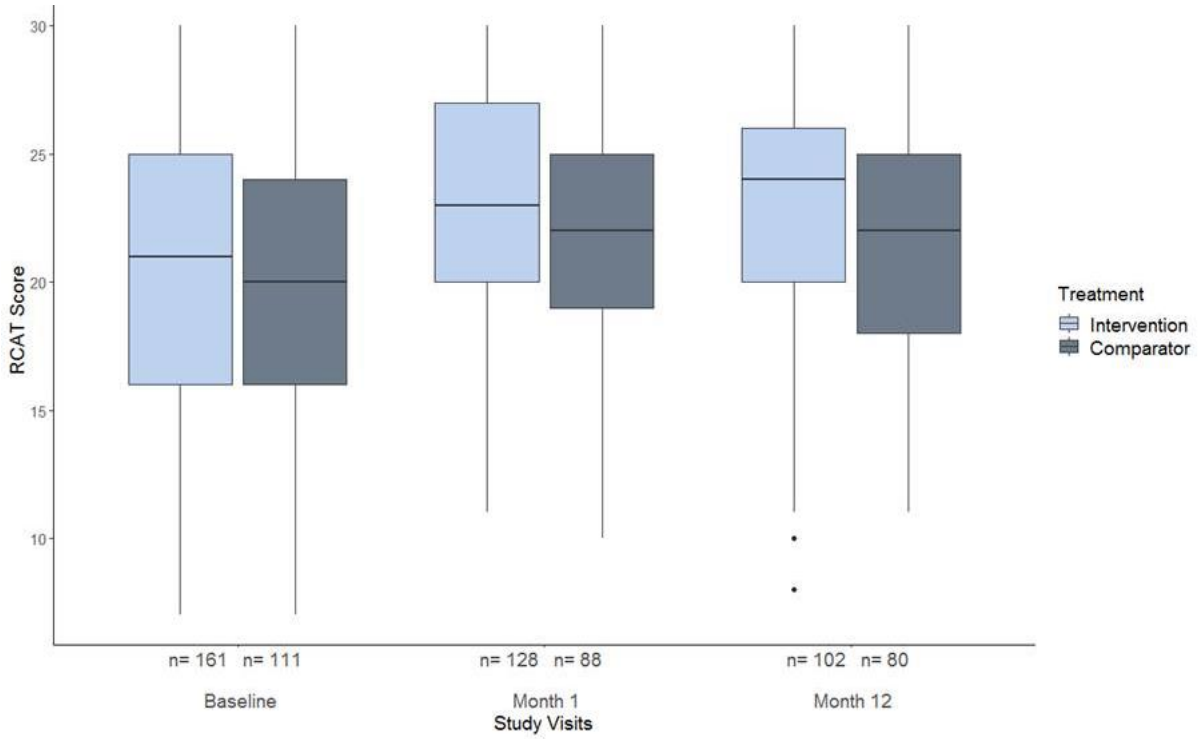


Figure 16: Participant allergic rhinitis control by visit (RCAT)

Note: Rhinitis Control Assessment Test (RCAT) Scores lie between 6 and 30. The lower the score, the more severe the allergic rhinitis; the higher the score, the less severe the allergic rhinitis. Participants scoring ≤21 are considered clinically "symptom uncontrolled"; those scoring >21 were considered "symptom controlled" (56).

CO-MORBIDITIES

Almost 50% of the intervention arm participants reported GORD, and more than one-third had sleep-related issues. Approximately 30% of the cohort reported anxiety or depression.

Table 14: Baseline co-morbidities (Intervention arm only)

Self-reported symptom or diagnosis	Intervention (n=221) *
Gastro-oesophageal reflux disease (GORD)	108 (48.9%)
Sleep-related issues	81 (36.7%)
Obesity	48 (21.7%)
Depression / anxiety	65 (29.4%)
Eczema	44 (19.9%)

*Participants could indicate more than one co-morbidity.

ASTHMA ACTION PLAN

Participants were only asked about their asthma action plan at the final follow up. At month 12, 56 (39%) intervention participants and 49 (50%) comparator participants had an asthma action plan (unadjusted odds ratio [95% CI]: 0.68 [0.37 to 1.23], p-value = 0.20).

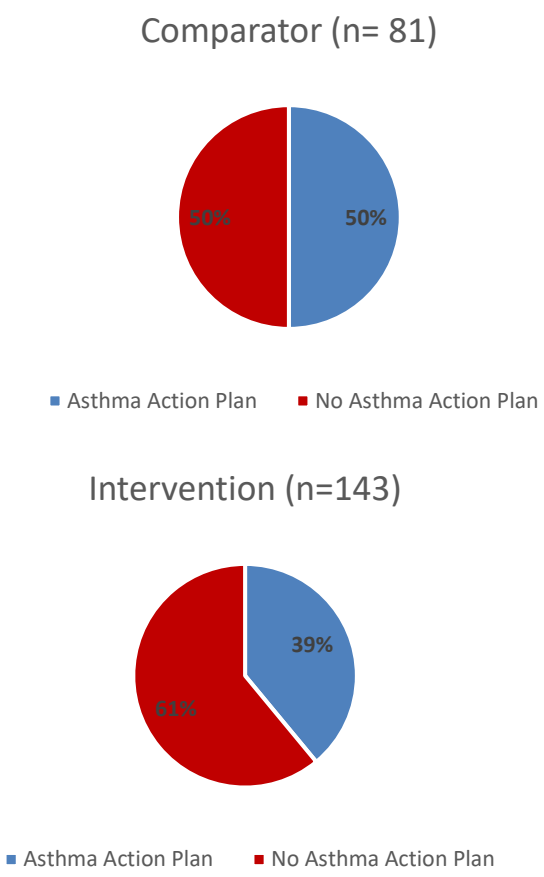


Figure 17: Proportion of participants with an asthma plan at final follow up

HEALTH CARE UTILISATION

There was a reduction in the mean number of self-reported Emergency Department presentations or hospital admissions for asthma during the 12 months of the trial compared with the 12 months prior to the trial in both the intervention and comparator arms (Table 15). For the intervention arm the reduction in participant Emergency Department presentations between the 12 months prior to the trial and 12 months during the trial was statistically significant. There was no significant reduction in Emergency Department presentations in the comparator arm, however they did experience a significant increase in GP visits during the trial.

Table 15: Participant hospital admissions and emergency department presentations

		Intervention	Comparator	Adjusted mean difference (95% CI) [1]	p-value [1]
BASELINE		n=221	n=160		
Number of Emergency Department visits for asthma	Mean (SD)	0.5 (2.21)	0.5 (1.36)		
	Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 1.0)		
	Min Max	0 30	0 14		

		Intervention	Comparator	Adjusted mean difference (95% CI) [1]	p-value [1]
Number of hospital admissions for asthma	Mean (SD)	0.3 (0.95)	0.4 (1.35)		
	Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)		
	Min Max	0 10	0 14		
Number of GP visits[2]	Mean (SD)	20.5 (20.87)	17.4 (14.84)		
	Median (Q1; Q3)	14.0 (7.0; 27.0)	16.0 (5.5; 26.5)		
	Min Max	0 158	0 76		
MONTH 12		n=143	n=111		
Number of r Emergency Department visits for asthma	Mean (SD)	0.1 (0.49)	0.3 (0.76)	0.18 (-0.01; 0.37)	0.0620
	Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)		
	Min Max	0 4	0 4		
Number of hospital admissions for asthma	Mean (SD)	0.1 (0.45)	0.3 (0.81)	0.20 (0.00; 0.404)	0.0532
	Median (Q1; Q3)	0.0 (0.0; 0.0)	0.0 (0.0; 0.0)		
	Min Max	0 4	0 5		
		n=143	n=111		
Number of GP visits[2,3]	Mean (SD)	22.3 (22.82)	24.2 (20.11)	2.56 (-1.17; 6.292)	0.1770
	Median (Q1; Q3)	16.0 (8.0; 28.0)	20.0 (10.0; 34.0)		
	Min Max	0 159	0 128		
P-value for change in AE admission		0.0115*	0.2470		
P-value for change in Hospital admission		0.0519	0.4585		
P-value for change in GP visits		0.1323	0.0110*		

Note: *significant result

1. *P-value from a random-effect analysis of covariance with the outcome at 12 months as the dependent variable and the following variables as independent variables: a fixed effect of the intervention, a fixed effect of the baseline value of the outcome and a random effect of the pharmacy to adjust for clustering.*
2. *GP visits for asthma were determined using Medicare Benefits Schedule data for each patient.*
3. *Including only those randomised patients who also have 12 months follow-up data.*

SENSITIVITY ANALYSIS

Some sessions were conducted outside of the predetermined windows for the visits (month 1, month6, month 12), e.g. they were conducted late. A sensitivity analysis which consisted of excluding data collected outside of pre-defined visit windows was performed on the primary and secondary

outcomes and led to similar results as an analysis including all data regardless of when the session was conducted (Table 5).

Process Evaluation

Pharmacy Participation and Retention

Figure 18 presents the process of pharmacy participation in the PTP-ARC Trial and reasons for pharmacy withdrawal from the trial at various time points.

The key stages of participation and withdrawal are described below:

Initially, pharmacies registered online in response to an Expression of Interest (EOI).

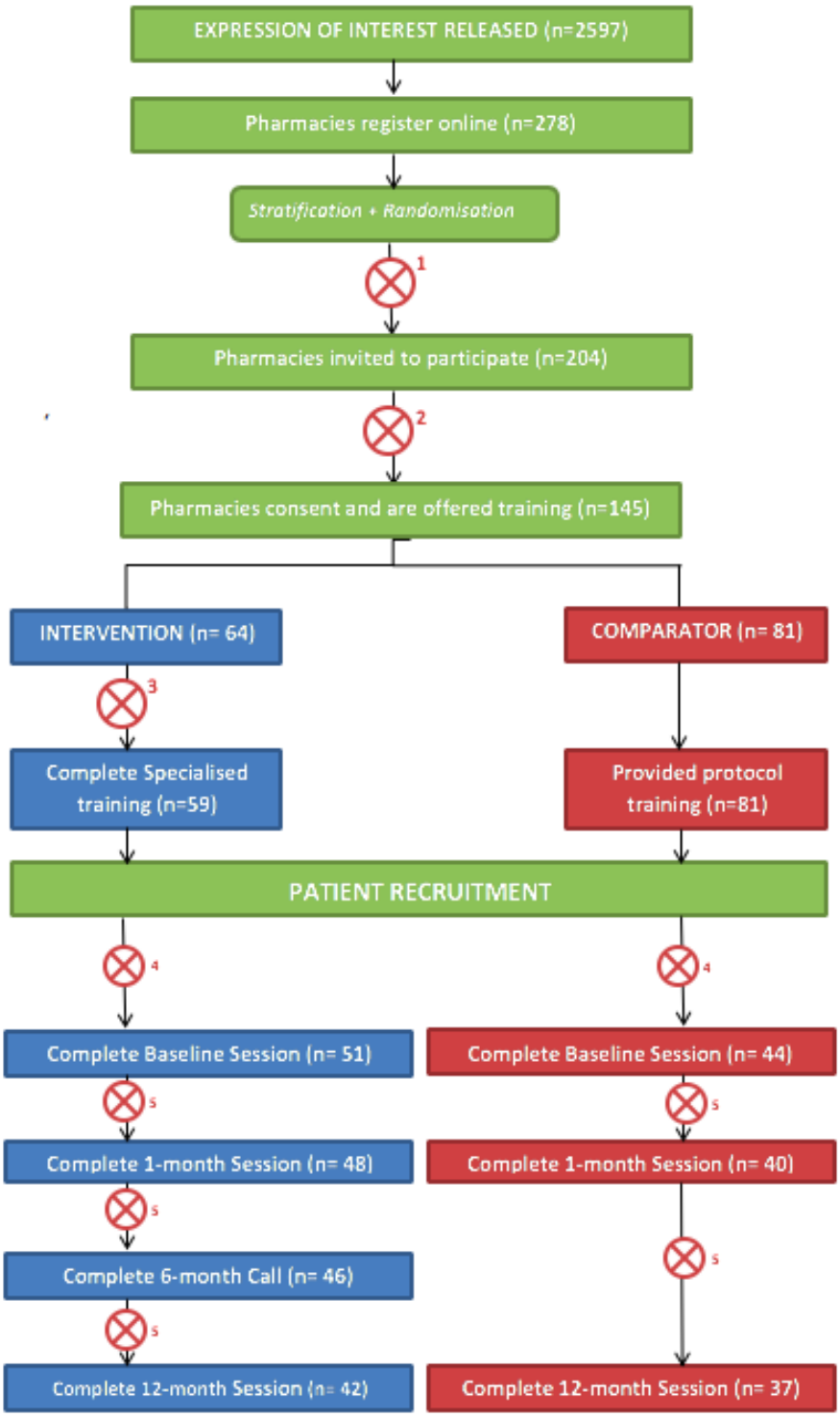
Registration of interest: Between July 2018 and January 2019, an EOI online registration form was sent out by the Pharmacy Guild of Australia to 2,597 Australian pharmacies in NSW, WA, and Tasmania. In response, 278 pharmacies registered to participate.

Invitations and pharmacist consent: Pharmacies were stratified based on national distribution and remoteness of the population as described in Section A and then randomly allocated into intervention and comparator arms. Two hundred and four pharmacies across NSW, WA and Tasmania were invited to participate, and 145 of these pharmacies provided consent. Of the consenting pharmacies, 64 were allocated to the intervention arm and 81 were allocated to the comparator arm.

Training participation: Intervention pharmacists were given access to specialised training modules, while comparator arm pharmacists received protocol training only. Fifty-nine pharmacies fulfilled all specialised training in the intervention arm. Eighty-one pharmacies received protocol only training in the comparator arm. More than one pharmacist could be trained in each participating pharmacy; pharmacist participation in the trial is presented in Appendix Q.

Participant recruitment: Fifty-one pharmacies went on to recruit participants and deliver the Pharmacy Asthma Service, while 44 pharmacies went on to deliver the comparator arm.

Pharmacy retention: Sixteen pharmacies from each arm withdrew from the program after commencing consultations. Forty-two pharmacies remained to deliver the full pharmacy asthma and rhinitis service in the intervention arm. The retention rate for intervention pharmacies based on the number that successfully completed training (n=59) is 71.2%. Thirty-seven pharmacies remained to deliver the complete comparator arm. The retention rate for comparator pharmacies based on those that received training (n=81) is 45.8%.


EXPRESSION OF INTEREST RELEASED (n=2597)
Pharmacies register online (n=278)
Stratification + Randomisation
1
Pharmacies invited to participate (n=204)
2
Pharmacies consent and are offered training (n=145)
INTERVENTION (n= 64)
COMPARATOR (n= 81)
3
Complete Specialised training (n=59)
Provided protocol training (n=81)
PATIENT RECRUITMENT
4
4
Complete Baseline Session (n= 51)
Complete Baseline Session (n= 44)
5
5
Complete 1-month Session (n= 48)
Complete 1-month Session (n= 40)
5
5
Complete 6-month Call (n= 46)
5
Complete 12-month Session (n= 42)
Complete 12-month Session (n= 37)

	Withdrawal point	Reason
⊗	1	Pharmacy not required– Intervention and Comparator (n=74) *Reasons: Cluster quota had been met for each state and remoteness category, proximity to other participants.*
⊗	2	Pharmacy declined – Intervention and Comparator (n=59) *Reasons: Inability to contact pharmacy manager, consent unreturned, inability to fulfil study requirements, no longer interested, too busy.*
⊗	3	Pharmacy did not attempt or complete training requirements – Intervention Only (n=5) *Reasons: Lack of time, personal reasons, change of mind.*
⊗	4	Pharmacy failed to recruit participants or complete at least one baseline session – Intervention and Comparator (n=45) *Reasons: Inability to recruit, participants not eligible or interested, no time/too busy, understaffed, technical difficulties, lack of interest, personal reasons, pharmacy sold, participants did not have time, short recruitment time, protocol too demanding.*
⊗	5	Pharmacy failed to follow up participants – Intervention and Comparator (n= 16) *Reasons: See Table 21: Reasons for participant loss to follow up.*

Figure 18: Pharmacy participation and retention

Note: *Invitations were sent out progressively in rounds from July 2018–January 2019 in response-to-response levels.

The state and remoteness distribution of pharmacies that were not required or withdrew post randomisation is presented in Table 16.

Table 16: State and remoteness distribution of pharmacies that were not required or withdrew (n=183)

		Intervention n (%)	Comparator n (%)	Total n (%)
Number of Pharmacies		87 (47.5)	96 (52.5)	183 (100.0)
State	NSW	44 (50.6)	48 (50.0)	92 (50.3)
	WA	36 (29.9)	37 (38.5)	73 (39.9)
	Tasmania	7 (8.2)	11 (11.5)	18 (9.8)
Remoteness	Highly Accessible	78 (89.7)	82 (85.4)	160 (87.4)
	Accessible	5 (5.8)	8 (8.3)	13 (7.1)
	Moderately Accessible, Remote, Very Remote	4 (4.6)	6 (6.3)	10 (5.5)

Interviews with pharmacists who did not recruit participants into the trial (n= 45) revealed a range of reasons for under-recruitment, largely consistent with previous studies. The findings of these interviews have been accepted for publication in the journal *Research in Social Administrative Pharmacy Journal* (Appendix A).

CHARACTERISTICS OF PARTICIPATING PHARMACIES – INTERVENTION AND COMPARATOR

Characteristics of participating pharmacies that were actively involved in the intervention and comparator arms (recruited at least one participant into the trial) are presented in Table 17. Relative to target numbers for state distribution (20 NSW, 10 Tasmania, and 10 WA for each arm), there was a slight under-representation of pharmacies in Tasmania, in particularly in the comparator arm, and an overrepresentation of NSW pharmacies in both intervention and comparator arms. Pharmacy distribution regarding target levels of remoteness is presented in Appendix R.

Table 17: Baseline state and remoteness distribution of participating pharmacies (n=95)

		Intervention n (%)	Comparator n (%)	Total n (%)
Number of pharmacies		51 (53.7)	44 (46.3)	95 (100)
State	New South Wales	32 (62.7)	31 (70.5)	63 (66.3)
	Western Australia	11 (21.6)	10 (22.7)	21 (22.1)
	Tasmania	8 (15.7)	3 (6.8)	11 (11.6)
Remoteness	Highly Accessible	35 (68.6)	33 (75.0)	68 (71.6)
	Accessible	11 (21.6)	7 (15.9)	18 (18.9)
	Moderately Accessible, Remote, Very Remote	5 (9.8)	4 (9.1)	9 (9.5)

Note: Pharmacies that recruited at least 1 participant into the trial.

Comparability data, including whether professional services had been provided prior to the trial, are presented in Appendix S. Comparability data were also collected from all pharmacists who aided the

delivery of the trial at their respective pharmacies in both intervention and comparator arms. Participating pharmacists represented a mix of proprietors and salaried pharmacists (Appendix T). The mean age of pharmacists in the intervention arm was 38.7 ± 10.6 years, and in the comparator arm, 36.9 ±10.7 years. Half (50%) of intervention pharmacies and 64% of comparator pharmacies were located in shopping strips, with the remainder located in shopping centres, isolated in a group of less than four shops or in a medical centre. Forty-eight percent of intervention and 45% of comparator pharmacies dispensed less than 200 prescriptions per day. The average number of pharmacists working at one time was two in both arms. Twenty-six percent of intervention and 23% of comparator pharmacies reported that they provided asthma services outside of this trial. More than half of the pharmacists in both arms had been involved in previous research studies.

Pharmacist Training and Evaluation – Intervention

Training was divided into two components – online knowledge/protocol training followed by assessment of inhaler skills (with feedback).

Online Module Performance

One hundred and thirteen pharmacists completed the online training modules. Performance of pharmacists on their first attempt of module assessment is presented in Figure 19. Pharmacists had the greatest difficulty with *Module 1 – Background to asthma, study background and plan* and *Module 5 – Protocol pathway and case study*, both of which were trial protocol-based modules. Theory-based asthma upskilling modules – *Module 2 – Medication and adherence*, *Module 3 – Inhaler devices and technique* and *Module 4 – Management of allergic rhinitis* – were passed with minimal difficulty by pharmacists. Pharmacists who failed received one-on-one feedback and protocol training. All pharmacists passed training before they administered the service.

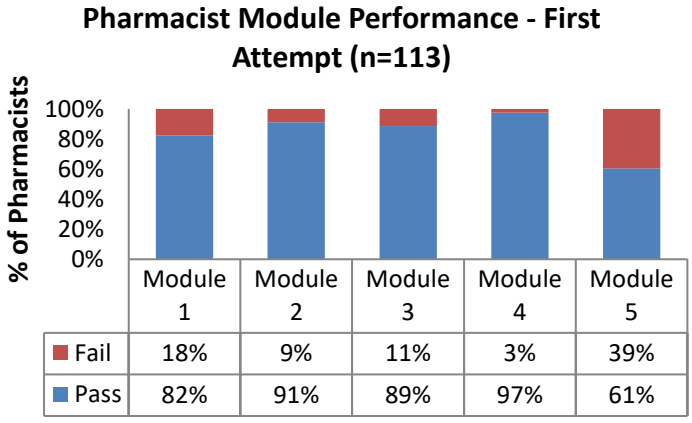


Figure 19: Pharmacists' performance on training modules – Intervention

Inhaler Technique Performance

One hundred and seven pharmacists completed inhaler technique assessment. Seventy-four assessments were in-person reviews and 33 were conducted remotely via video upload to Dropbox and videoconference feedback. In-person reviews took an average of 20-30 minutes with each

pharmacist. All 107 pharmacists were assessed as 100% competent in their demonstration of five inhalers/devices by the end of the review.

5BPharmacists' Evaluation of Training

Pharmacists' evaluation of online training modules, including content, efficacy and practical application, is explored in Appendix U. Pharmacists reported that the online modules and inhaler technique training achieved their learning objectives and improved their confidence in assisting participants with asthma, with a small number reporting that there was too much content. At the end of the training, pharmacists reported that regular evidence-based refresher training would further enhance their knowledge.

Participant Participation and Retention

Participant Recruitment

The target number for participant recruitment was a minimum of seven participants (adults with poorly controlled asthma) per pharmacy. In total, 381 participants were recruited to the program. Recruitment numbers varied between pharmacies, with an average of four participants per active pharmacy, ranging from one to 16. Ten intervention pharmacies and seven comparator pharmacies achieved the target.

Table 18: Number of participants recruited per participating pharmacy

	Participants recruited per pharmacy		
	Intervention (n=51)	Comparator (n=44)	Combined (n=95)
Total	221	160	381
Mean (± SD)	4.3 (± 3.7)	3.6 (± 2.4)	4.0 (± 3.1)
Median	3.0	3.0	3.0
Min Max	1.0 16.0	1.0 9.0	1.0 16.0
Q1; Q3 (IQR)	2.0; 5.5 (3.5)	1.8; 5.3 (3.5)	2.0; 5.5 (3.5)

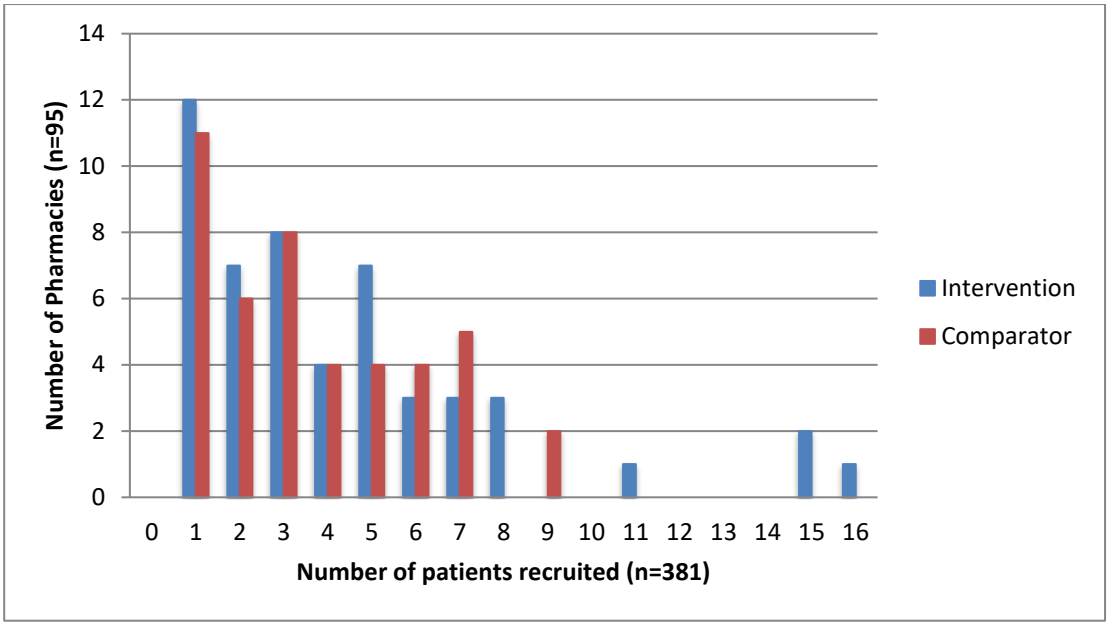


Figure 20: Number of participants recruited by participating pharmacies

Participant Baseline Characteristics

Participant baseline characteristics are presented in Table 19. Both intervention and comparator arms were comparable in all investigated variables. Most participants were female (69.6%), aged 56 years or over (53.8%), non-smokers (86.4%), and with self-reported hay fever (71%). Thirty-three percent of the cohort were retired, 48% had tertiary qualifications and 45% had had asthma as a child.

Table 19: Participant baseline characteristics

	Intervention	Comparator	Total	p-value
Pharmacy state	n=221	n=160	n=381	0.6502
NSW	159 (71.9%)	113 (70.6%)	272 (71.4%)	
WA	40 (18.1%)	25 (15.6%)	65 (17.1%)	
Tasmania	22 (10.0%)	22 (13.8%)	44 (11.5%)	
Pharmacy remoteness	n=221	n=160	n=381	0.2886
Highly Accessible	143 (64.7%)	110 (68.8%)	253 (66.4%)	
Accessible	59 (26.7%)	29 (18.1%)	88 (23.1%)	
Moderately Accessible, Remote, Very remote	19 (8.6%)	21 (13.1%)	40 (10.5%)	
Age (years)	n=221	n=160	n=381	0.2896
18 to 25	10 (4.5%)	14 (8.8%)	24 (6.3%)	
26 to 35	23 (10.4%)	12 (7.5%)	35 (9.2%)	
36 to 45	45 (20.4%)	13 (8.1%)	58 (15.2%)	
46 to 55	34 (15.4%)	25 (15.6%)	59 (15.5%)	
Above 56	109 (49.3%)	96 (60.0%)	205 (53.8%)	

	Intervention	Comparator	Total	p-value
Sex	n=221	n=160	n=381	0.6066
Male	65 (29.4%)	51 (31.9%)	116 (30.4%)	
Female	156 (70.6%)	109 (68.1%)	265 (69.6%)	
Work situation	n=221	n=160	n=381	0.2090
Full-time employed	56 (25.3%)	34 (21.3%)	90 (23.6%)	
Home duties	12 (5.4%)	21 (13.1%)	33 (8.7%)	
Part time or casually employed	53 (24.0%)	29 (18.1%)	82 (21.5%)	
Retired/Pensioner	75 (33.9%)	52 (32.5%)	127 (33.3%)	
Unemployed or seeking work	10 (4.5%)	13 (8.1%)	23 (6.0%)	
Full-time carer	5 (2.3%)	2 (1.3%)	7 (1.8%)	
Other	10 (4.5%)	9 (5.6%)	19 (5.0%)	
Level of education	n=221	n=160	n=381	0.9749
No formal education	3 (1.4%)	4 (2.5%)	7 (1.8%)	
Primary school	7 (3.2%)	4 (2.5%)	11 (2.9%)	
High school	101 (45.7%)	81 (50.6%)	182 (47.8%)	
Tertiary non-university (e.g. TAFE)	61 (27.6%)	35 (21.9%)	96 (25.2%)	
University	39 (17.6%)	31 (19.4%)	70 (18.4%)	
Postgraduate	10 (4.5%)	5 (3.1%)	15 (3.9%)	
Age at asthma onset	n=221	n=160	n=381	0.7374
0-5 years	49 (22.2%)	41 (25.6%)	90 (23.6%)	
6-15 years	52 (23.5%)	28 (17.5%)	80 (21.0%)	
16-34 years	57 (25.8%)	40 (25.0%)	97 (25.5%)	
35-55 years	36 (16.3%)	31 (19.4%)	67 (17.6%)	
above 55 years	27 (12.2%)	20 (12.5%)	47 (12.3%)	
Ever had a lung function test	n=221	n=160	n=381	0.0514
No	54 (24.4%)	54 (33.8%)	108 (28.3%)	
Yes	167 (75.6%)	106 (66.3%)	273 (71.7%)	
Last lung function test	n=167	n=106	n=273	0.4040
< 12 months ago	58 (34.7%)	41 (38.7%)	99 (36.3%)	
≥12 months ago	109 (65.3%)	65 (61.3%)	174 (63.7%)	
Active smoker	n=221	n=160	n=381	0.3812
No	194 (87.8%)	135 (84.4%)	329 (86.4%)	
Yes	27 (12.2%)	25 (15.6%)	52 (13.6%)	
History of hay fever	n=221	n=160	n=381	0.3121

	Intervention	Comparator	Total	p-value
No	60 (27.1%)	49 (30.6%)	109 (28.6%)	
Yes	161 (72.9%)	111 (69.4%)	272 (71.4%)	
RCAT score[1]	n=221	n=160	n=381	0.2360
Mean (SD)	20.8 (5.4)	19.9 (5.1)	20.4 (5.3)	
Median (Q1; Q3)	21.0 (16.0; 25.0)	20.0 (16.0; 24.0)	20.0 (16.0; 25.0)	
Min Max	7 30	7 30	7 30	
IAQLQ score[2]	n=221	n=160	n=381	0.3747
Mean (SD)	3.5 (1.9)	3.2 (2.0)	3.4 (2.0)	
Median (Q1; Q3)	3.3 (2.0; 4.9)	3.1 (1.5; 4.4)	3.1 (1.8; 4.8)	
Min Max	0 10	0 10	0 10	
ACQ score[3]	n=221	n=160	n=381	0.8105
Mean (SD)	2.5 (0.9)	2.4 (0.9)	2.5 (0.9)	
Median (Q1; Q3)	2.3 (1.8; 3.0)	2.2 (1.7; 2.8)	2.2 (1.7; 3.0)	
Min Max	2 6	2 5	2 6	
SF-12 mental health score[4]	n=221	n=160	n=381	0.8050
Mean (SD)	46.3 (7.1)	46.2 (8.8)	46.3 (7.8)	
Median (Q1; Q3)	46.3 (42.3; 51.1)	47.3 (41.5; 53.0)	46.7 (41.9; 52.3)	
Min Max	19 66	12 62	12 66	
SF-12 physical health score[4]	n=221	n=160	n=381	0.1782
Mean (SD)	42.2 (8.9)	43.5 (8.0)	42.7 (8.6)	
Median (Q1; Q3)	43.2 (37.1; 49.2)	44.7 (37.9; 49.9)	43.6 (37.2; 49.7)	
Min Max	13 57	24 58	13 58	

Note:

* significant result

1. *Rhinitis Control Assessment Test (RCAT) scores lie between 6 and 30. The lower the score, the more severe the allergic rhinitis; the higher the score, the less severe the allergic rhinitis. Participants scoring ≤21 are considered clinically "symptom uncontrolled"; those scoring >21 are considered "symptom controlled" (56).*
2. *The Impact of Asthma on Quality of Life Questionnaire (IAQLQ) scores lie between 0 and 10. Higher scores represent a greater impact of asthma on quality of life (55).*
3. *Asthma Control Questionnaire (ACQ) score lies between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (79).*
4. *SF-12 MH and SF-12 PH scores lie between 0 and 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health.*

PARTICIPANT COMPLETION

In total, 254 participants completed the 12-month trial. As indicated in Figure 21 and Table 20, there were similar completion rates in both arms of the study, ranging from 0 to 14 completed participants per pharmacy at the end of 12-months.

Table 20: Number of completed participants per active pharmacy

	Participants completed per pharmacy		
	Intervention (n=51)	**Comparator (n=44)**	**Combined (n=95)**
Total	143	111	254
Mean (± SD)	2.8 (±2.7)	2.52 (±2.1)	2.67 (±2.5)
Median	2.00	2.00	2.00
Min Max	0.0 14.0	0.0 7.0	0.0 14.0
Q1; Q3 (IQR)	1.0; 4.0 (3.0)	1.0; 4.0 (3.0)	1.0; 4.0 (3.0)

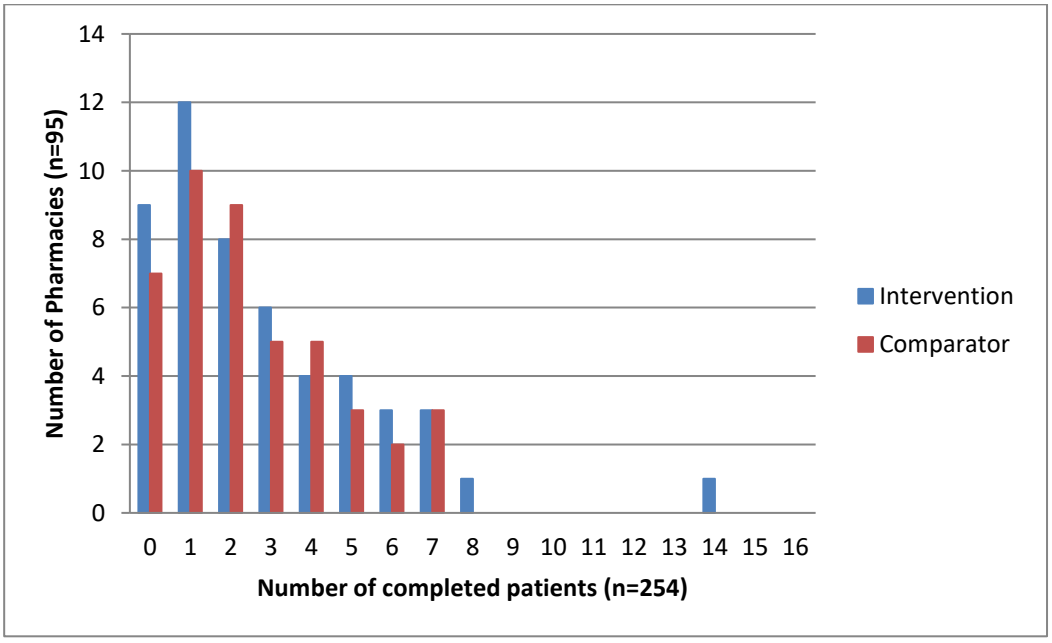


Figure 21: Number of completed participants by active pharmacies

PARTICIPANT LOSS TO FOLLOW-UP

Participant engagement throughout the trial is depicted in Figure 22.

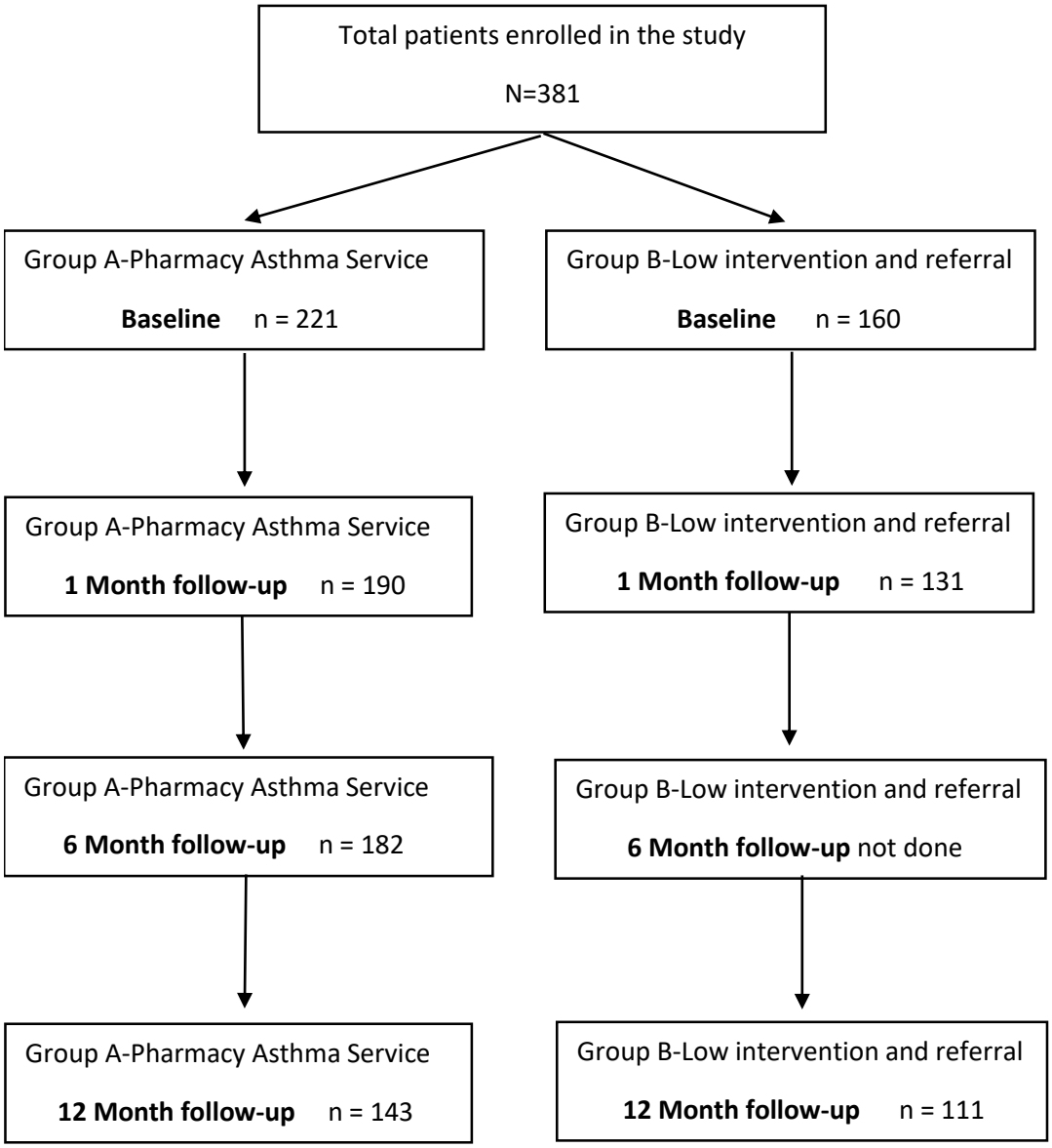


Figure 22: Participant consort diagram

A total of 127 participants did not complete the full 12-month trial. A slightly larger proportion of these participants were from the intervention arm. There were 78 participants who did not complete the intervention arm, ranging from zero to 16 participants per pharmacy. In the comparator arm, 49 participants did not complete; this ranged from zero to nine participants per pharmacy. Main reasons for loss to follow-up are presented in Table 21.

Table 21: Reasons for participant loss to follow-up

Reason	Frequency n (%)
Participant factors	

Reason	Frequency n (%)
Participant too busy	20 (15.7)
Participant not willing to participate/asked to withdraw	18 (14.2)
Participant unwell	12 (9.5)
Participant moved out of area	10 (7.9)
Pharmacy factors	
Participant uncontactable	55 (43.3)
Pharmacist unwilling or unable to complete	27 (21.3)

Note: * multiple responses possible (n=127)

Other less common reasons for loss to follow-up included the participant believing they did not need assistance as their asthma symptoms improved, the trained pharmacist leaving with no-one remaining to provide the service, or sale of the pharmacy.

Participants who did not complete the full service were contacted at the end of the trial (when their final follow up would have been due) to determine asthma control. Of the withdrawn participants, 41.7% of participants were successfully contacted. The mean ACQ score reported by these participants was 1.7 (±1.0) and 60.4% of the withdrawn participants contacted had poorly controlled asthma at that point in time, as indicated by their ACQ score.

Table 22 compares the baseline characteristics of participants who completed the full 12-month trial to those who did not. The two arms were overall quite comparable; however, those who did not complete were less likely to have history of allergic rhinitis, had a higher *IAQLQ* and ACQ scores and were recruited from highly accessible metropolitan pharmacies in NSW.

Table 22: Baseline characteristics according to study completion status

	Did not complete (n=127)	Completed (n=254)	P-Value
Pharmacy state			0.0089*
NSW	88 (69.3%)	184 (72.4%)	
WA	16 (12.6%)	49 (19.3%)	
Tasmania	23 (18.1%)	21 (8.3%)	
Pharmacy remoteness			<0.001*
Highly Accessible	103 (81.1%)	150 (59.1%)	
Accessible	12 (9.4%)	76 (29.9%)	
Moderately Accessible, Remote, Very remote	12 (9.4%)	28 (11.0%)	
Age (years)			0.1776
18 to 25	10 (7.9%)	14 (5.5%)	
26 to 35	11 (8.7%)	24 (9.4%)	
36 to 45	26 (20.5%)	32 (12.6%)	

	Did not complete (n=127)	Completed (n=254)	P-Value
46 to 55	21 (16.5%)	38 (15.0%)	
Above 56	59 (46.5%)	146 (57.5%)	
Sex			0.3865
Male	35 (27.6%)	81 (31.9%)	
Female	92 (72.4%)	173 (68.1%)	
Work situation			0.3195
Full-time employed	30 (23.6%)	60 (23.6%)	
Home duties	13 (10.2%)	20 (7.9%)	
Part time or casually employed	28 (22.0%)	54 (21.3%)	
Retired/Pensioner	38 (29.9%)	89 (35.0%)	
Unemployed or seeking work	11 (8.7%)	12 (4.7%)	
Full-time carer	0	7 (2.8%)	
Other (Please specify)	7 (5.5%)	12 (4.7%)	
Level of education			0.6618
No formal education	2 (1.6%)	5 (2.0%)	
Primary school	4 (3.1%)	7 (2.8%)	
High school	62 (48.8%)	120 (47.2%)	
Tertiary non-university (e.g. TAFE)	26 (20.5%)	70 (27.6%)	
University	28 (22.0%)	42 (16.5%)	
Post-graduate	5 (3.9%)	10 (3.9%)	
Age at asthma onset			0.3213
0-5 years of age	30 (23.6%)	60 (23.6%)	
6-15 years of age	34 (26.8%)	46 (18.1%)	
16-34 years of age	30 (23.6%)	67 (26.4%)	
35-55 years of age	21 (16.5%)	46 (18.1%)	
above 55 years	12 (9.4%)	35 (13.8%)	
Ever had a lung function test			0.6296
No	34 (26.8%)	74 (29.1%)	
Yes	93 (73.2%)	180 (70.9%)	
Last lung function test			0.0740
12 months ago	27 (29.0%)	72 (40.0%)	
>=12 months ago	66 (71.0%)	108 (60.0%)	
Active smoker			0.9160

	Did not complete (n=127)	Completed (n=254)	P-Value
No	110 (86.6%)	219 (86.2%)	
Yes	17 (13.4%)	35 (13.8%)	
History of hay fever			0.0050*
No	48 (37.8%)	61 (24.0%)	
Yes	79 (62.2%)	193 (76.0%)	
RCAT score			0.3250
Mean (SD)	19.9 (5.52)	20.6 (5.20)	
Median (Q1; Q3)	20.0 (15.0; 25.0)	20.0 (17.0; 25.0)	
min max	7 30	7 30	
IAQLQ score			0.0004*
Mean (SD)	3.9 (1.77)	3.1 (1.99)	
Median (Q1; Q3)	3.6 (2.5; 5.0)	2.8 (1.5; 4.5)	
min max	1 9	0 10	
ACQ score			0.0029*
Mean (SD)	2.7 (0.98)	2.4 (0.83)	
Median (Q1; Q3)	2.5 (1.8; 3.5)	2.2 (1.7; 2.8)	
min max	2 5	2 6	
SF-12 mental health score			0.0185*
Mean (SD)	44.9 (7.24)	46.9 (8.04)	
Median (Q1; Q3)	45.2 (40.1; 49.9)	47.4 (42.6; 53.0)	
min max	23 62	12 66	
SF-12 physical health score			0.4789
Mean (SD)	42.3 (8.22)	43.0 (8.76)	
Median (Q1; Q3)	43.1 (37.1; 48.7)	43.8 (37.5; 49.9)	
min max	13 57	13 58	

Note:

* significant result

SESSIONS PROVIDED

A total of 736 interventions sessions were conducted over the 12-month period, with a median number of 12 sessions conducted per pharmacy, ranging from 0 to 58. In total, the comparator pharmacies conducted 402 sessions over the 12-month period, with a median of 12 sessions per pharmacy ranging from 0 to 21. A summary of the numbers of sessions conducted by pharmacies is presented in Appendix V.

TIME TAKEN

The time taken to deliver the full 12-month service, as reported by the delivering pharmacists, is presented in Table 23. On average, it took intervention pharmacists just under 100 minutes to deliver the full 12-month intervention per participant; this ranged from 32 minutes to 225 minutes. For comparator pharmacies, it took on average 55 minutes to deliver the minimal intervention over 12 months per participant; this ranged from 18 minutes to 115 minutes.

Table 23: Time taken to deliver session – pharmacist reported (minutes)

	Baseline	Month-1	Month-6	Month-12	Full Service
Intervention					
Mean (± SD)	44.7 (±15.5)	27.8 (±10.4)	10.7 (±5.9)	29.2 (±11.2)	99 (± 30)
Median	35	20	10	25	96
Min Max	15 100	5 60	2 45	7 60	32 225
Q1; Q3 (IQR)	30; 45 (15)	17; 30 (13)	5; 10 (5)	20; 30 (10)	80; 115 (35)
Comparator					
Mean (± SD)	22.2	13.3	-	19.1	55 (± 17)
Median	20	10	-	20	53
Min Max	1 90	2 40	-	5 45	18 115
Q1; Q3 (IQR)	15; 30 (15)	10; 15 (5)		15; 20 (5)	44; 65 (21)

PARTICIPANT FEEDBACK

Participant feedback was collected from 71% (n=101) of intervention arm participants at the completion of their full 12-month service, the outcomes of which are presented below. This does not represent the views of participants who did not respond to the survey or withdrew from the service.

PARTICIPANT SATISFACTION

The results from the survey indicate widespread participant satisfaction among participants who completed the service:

- 86% of respondents were very satisfied with the service and 10% were somewhat satisfied (Figure 23).
- 78% indicated an interest in participating in an asthma service in the future (Figure 24).
- 94% said they would recommend the service to a friend (Figure 24).

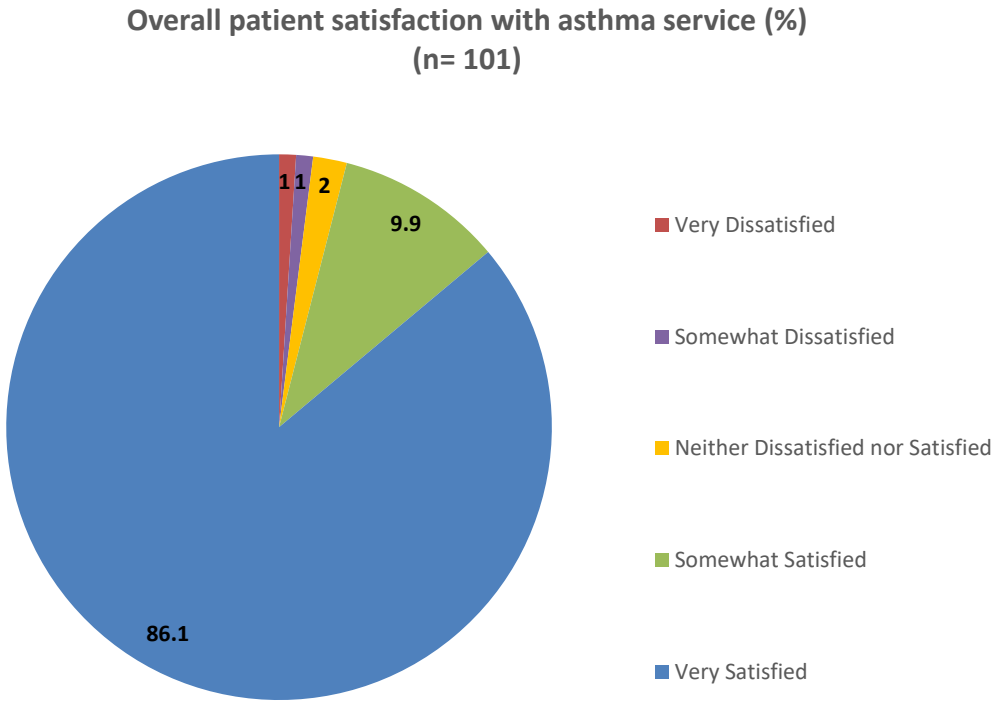


Figure 23: Overall participant satisfaction with the Pharmacy Asthma Service

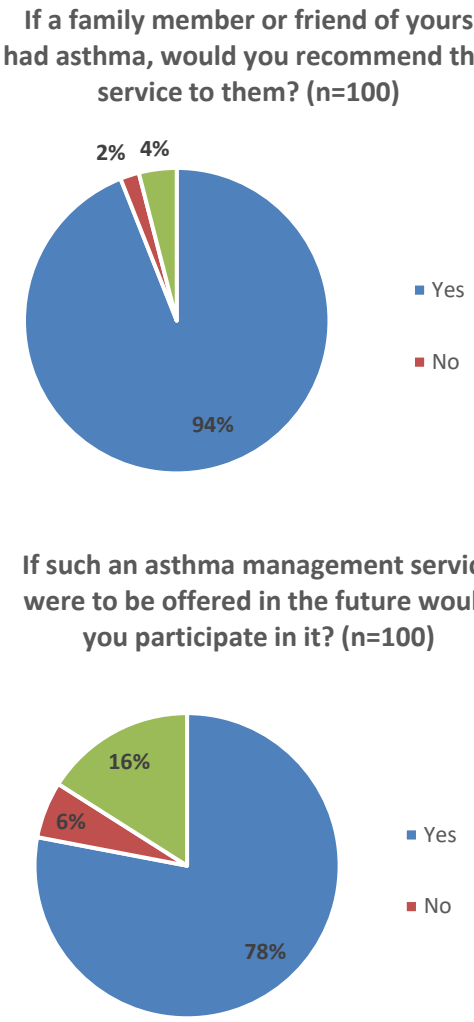


Figure 24: Future participant participation

Of those who were unsure if they would participate in the future (16%), 75% said they would participate if their symptoms worsened and they needed it again, they preferred to allow others to access the service, or they had learnt a lot already.

Participants had a very positive response to service delivery by the pharmacists (Figure 25). Eighty-eight percent were very satisfied with the information provided by their pharmacists, and 93% were very satisfied by their pharmacy's ability to respond to questions and concerns. 87% of participants were very satisfied by the time taken by pharmacists, and 85% of participants were very satisfied with the privacy and setting of the pharmacy.

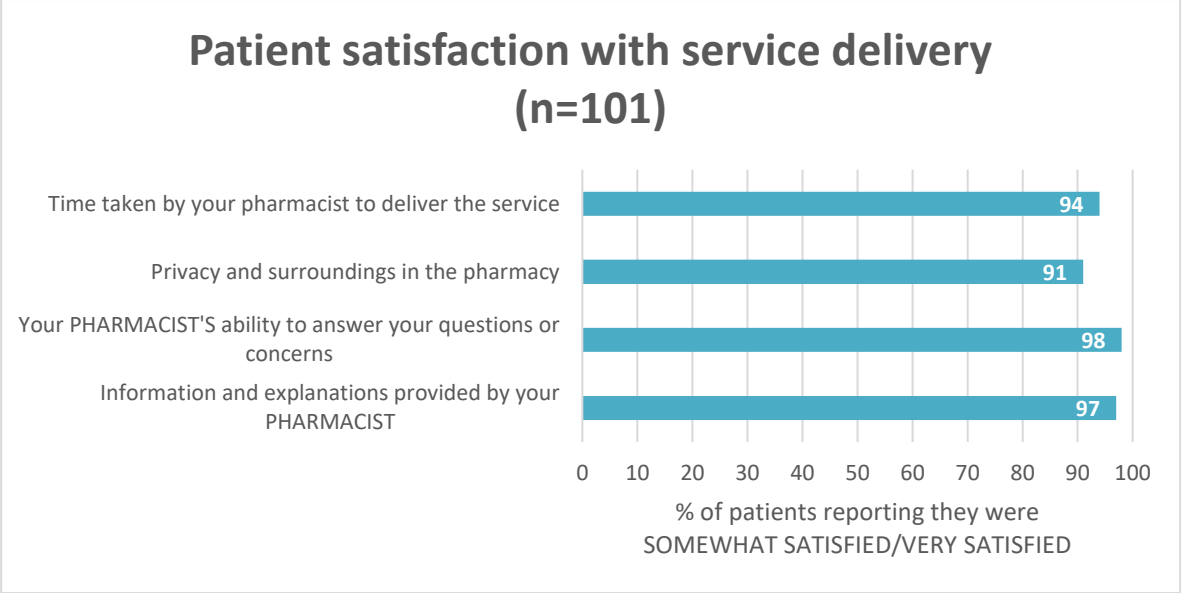


Figure 25: Participant satisfaction with pharmacy delivery

Participant Motivations

Participant feedback revealed that the main reasons for signing up to the study were a genuine interest in gaining more understanding and skills regarding their asthma, asthma management and medicines or because their pharmacist asked. Other reasons included the desire to take back control of their asthma and to help research. The main participant-reported motivations for entering the trial are summarised in Table 23. Other less commonly reported motivations to participate were that participants wished to have an asthma/medication review, confirmation they were managing their asthma, trust in the opinion and advice of the pharmacist, preference for the assistance of the pharmacist rather than the GP, and enabling them to help others in their family with asthma.

Table 24: Participant motivations to participate (n=94)

	Reason	Frequency n (%) *
Why did you decide to participate in the asthma management service?	Thought I would gain more understanding and skills regarding my asthma/management/medicines	29 (30.8)
	My pharmacist asked	25 (26.6)
	I wanted to take back control of my asthma	17 (18.1)
	To help research and the greater asthma population	17 (18.1)
	My asthma symptoms are impacting my daily life or worsening	12 (12.8)
	Believed it would be beneficial for me and my overall health	11 (11.7)

Note: *Multiple responses possible.

Participant Outcome Perceptions

Overall perceptions of the impact of the Pharmacy Asthma Service on participant health outcomes were very positive (Figure 26). Many pharmacists and participants identified positive health impacts, as well as positive impacts on understanding of asthma and approaches to management.

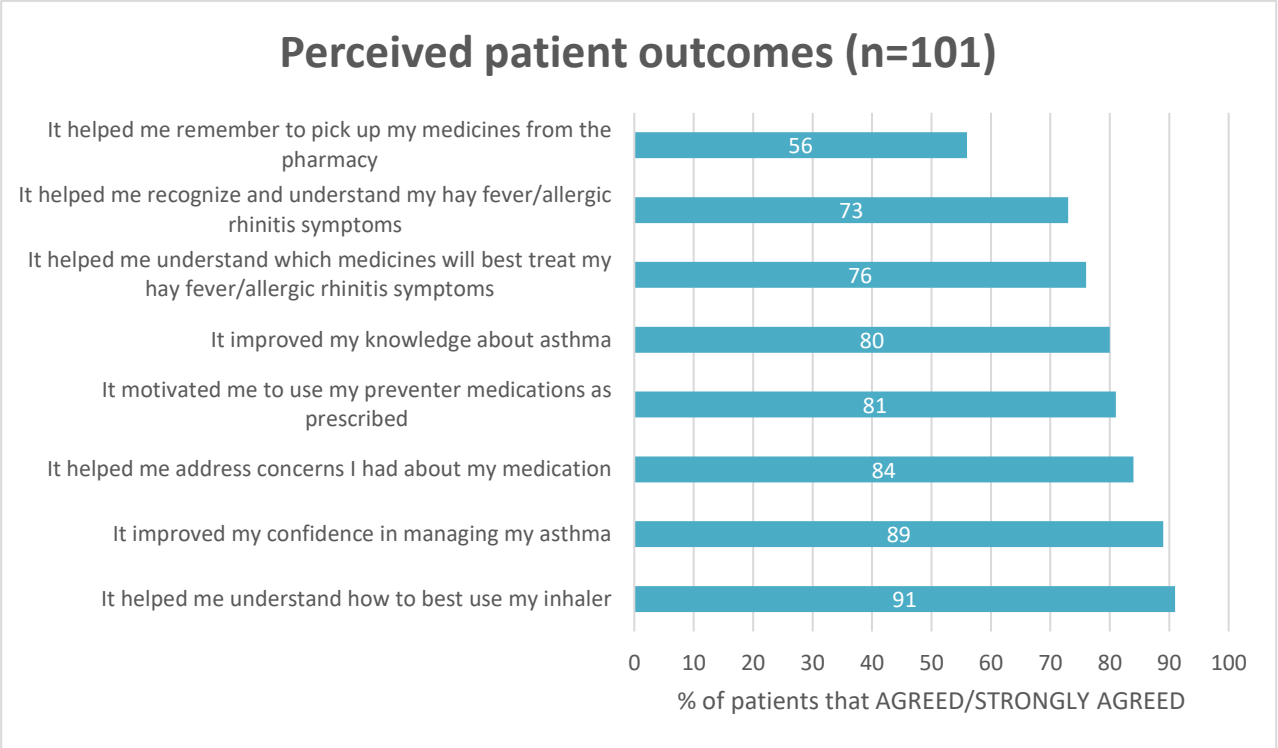


Figure 26: Proportion of participants that agreed/strongly agreed that the trial met clinical outcomes.

The most frequently reported health impacts identified by participants are presented in Table 25. No negative health impacts were reported by any participants.

Table 25: Participant reported impacts of the services (n=97)

	Impact	Frequency n (%) *
Impact of this service on your asthma management	Improved knowledge and/or understanding about asthma and medications	30 (30.9)
	Improved my asthma control	23 (23.7)
	Improved confidence and capacity to self-manage asthma	21 (21.6)
	Highlighted errors in my asthma management	18 (18.5)
	Improved inhaler technique	17 (17.5)
	Optimised use of my medicines – decreased reliance, improved compliance to preventer, reduced use of reliever	16 (16.5)
	Increased engagement with my condition and awareness of symptoms and changes	16 (16.5)

Note: *Multiple responses possible.

Participants were asked about what they liked most about the service; their most frequently reported responses are reported in Table 26. Many participants reported that the pharmacist's personal delivery of the service was the best component (39%). They also appreciated the advice and information obtained (26.1%), as well as the opportunity provided by the service to discuss their asthma (19%) and the one-on-one structure of the personal consultations (17%).

Table 26: What participants appreciated about the service (n=101)

	Response	Frequency n (%) *
What did you like best about the service?	The pharmacist's delivery (friendly, personal, kind, helpful, polite, thoughtful, professional, attentive, knowledgeable)	36 (39.1)
	Advice and information obtained	24 (26.1)
	Ability to discuss and ask questions about my asthma	17 (18.5)
	One-on-one, face-to-face, personal contact with the pharmacist in a private area	16 (17.4)
	Revision of inhaler technique, and how to use spacers and nasal sprays correctly	10 (10.9)
	The service was quick/efficient/thorough/clear	9 (9.8)
	Confidence in managing my condition	7 (7.6)
	All elements	5 (5.4)
	Regaining control of my asthma	4 (4.3)

Note: *Multiple responses possible.

Future Improvements

Most participants were not sure or had no suggestions about improving the service (75%). Of the 14 participants who did have a suggestion, the most frequently reported was to reduce the number and repetition of questions (n=6).

Future Service Funding

Nearly all surveyed participants (95%) reported that if the service were to be offered in the future, it should be government funded. A smaller proportion of participants proposed it should be funded by private health insurance (9.9%) or self-funded (4.0%).

Comparator (Control) Arm Evaluation

Key Findings

- Our randomised controlled trial (RCT) investigating a Pharmacy Asthma Service yielded positive clinical outcomes for both the intervention and comparator (control) arm participants. It was crucial that we understand why this occurred.
- Comparator arm pharmacists were interviewed and asked for feedback regarding the trial processes undertaken in their pharmacy to understand the services (if any) provided to people with asthma within and outside of the trial protocol.

- Interviews were conducted with a pharmacist from 20 of the 37 comparator arm pharmacies that completed the trial.
- Valuable feedback was obtained regarding expectations and motivations of pharmacists and participants, protocol delivery, including what actions the pharmacists undertook, and perceived benefits of the services to the pharmacist and the participant.
- Based on feedback received in the interviews, pharmacies were classified as adherent to the trial protocol (no interventions other than referral to GP) or non-adherent to the trial protocol, or inconclusive when unclear. Participant outcomes were then reviewed in these subgroups.
- Overall, 22% (n=8) of pharmacies were classified as adherent and 38% (n=14) as non-adherent, with the remaining inconclusive.
- While all participants commenced with uncontrolled asthma (ACQ >1.5), after 12 months the mean ACQ score for participants from adherent pharmacies (true control) was 1.8 (still uncontrolled asthma). This compares to an ACQ score of 1.4, (controlled asthma) in the non-adherent group (those offering extra interventions).
- Quality of life was unchanged in the adherent group, yet significantly improved in the non-adherent group over the 12 months of the trial.
- Pharmacists perceived that participants had high expectations of receiving asthma care from their pharmacist. This appears to have prompted many pharmacists not to adhere to the control protocol and offer care when it was required, with subsequent improvement in clinical outcomes.

BACKGROUND

PTP-ARC was designed to test a pharmacy asthma service that provided support mechanisms to participants to improve medication adherence, correct inhaler technique together with a review of allergic rhinitis and management advice through a series of one-on-one visits with their pharmacists over 12 months.

A minimal intervention pharmacy arm was used as the comparator (control) in the assessment of the Pharmacy Asthma Service. Participants within the comparator arm had three interactions with their pharmacist including the initial in-person consultation, at which they were to be given a referral to their GP. They were then contacted one month and 12 months after this initial consultation via telephone. In the comparator arm, the research protocol required participants to complete relevant questionnaires to enable comparative analyses with those who received the Pharmacy Asthma Service (intervention arm); however, there was no prescribed intervention, other than referral to their GP.

Forty-four pharmacies were involved in the comparator arm of the trial, of which 37 completed the full 12-month pathway for at least one participant.

The results of the trial indicated that there were significant improvements in outcomes for participants within the comparator arm as well as the intervention arm. Participant asthma control and allergic rhinitis control improved, there was a reduction in the impact of asthma on participant quality of life and a reduction in reliever usage. This positive result for both arms was an unexpected outcome.

As there was no difference in the rate of Asthma Control between intervention and comparator arms an additional analysis was suggested which consisted of analysing the entire cohort (Group A and B) together to estimate changes before versus after. A problem with that approach is that it is confounded with time and that it makes it difficult to establish causality, i.e., to know whether the changes occur as a result of the trial or if they would have occurred anyway, for example due to regression to the mean. A possible explanation for the lack of significant difference in intervention and comparator arms is the fact that some comparator arm pharmacies may have interacted with patients beyond usual care. To test that hypothesis, the investigative team undertook a supplementary mixed-methods analysis in order to determine the processes that had been undertaken by pharmacists within this comparator arm.

METHODS

Qualitative evaluation

Post-intervention qualitative interviews were conducted with 20 actively involved pharmacists from comparator pharmacies that had completed a full 12-month comparator pathway for at least two participants.

As some pharmacies had multiple pharmacists actively involved in the trial, the first pharmacist contacted and who agreed to be interviewed was included. Interviews were conducted from August to September 2020, which was 6-7 months after the conclusion of the trial. All interviews were conducted by telephone using a semi-structured interview guide. All interviews were conducted by the same member of the project team who has extensive experience in conducting qualitative interviews and who had minimal prior communication or contact with any participant pharmacists. Interviewer privacy was assured. Interviews varied in length from 6-25 minutes, and on average took 12 minutes. All interviews were audio-recorded and transcribed verbatim by an outsourced party external to the project team. Transcripts were then cross-checked against the original audio by a different team member to ensure accuracy of final transcripts and imported into NVivo software (QSR NUD*IST Vivo: version 12) to facilitate deductive thematic analysis. All transcripts were analysed on a line-by-line basis, through a method of constant comparison. Key concepts were identified and a coding frame developed, reviewed and subsequently applied to all transcripts. The codes were grouped into themes compared and discussed by the research team, and disagreements were resolved through discussion until agreement was reached.

Quantitative evaluation

A subgroup quantitative analysis was performed to compare participant outcomes between pharmacies found to adhere to the research protocol and those where additional interventions not described in the research protocol may have been conducted. Pharmacies were classified as either *adherent* or *non-adherent,* or *inconclusive* if unable to be classified. The decision for classification of each pharmacy was decided collaboratively by two members of the project team, based on review of the interview data. This process determined that 8 pharmacies were *adherent* and 14 were *non-adherent* to the research protocol. The remaining 15 pharmacies were listed as *inconclusive* if they

were not interviewed or if their interviews provided no clear indication of adherence or non-adherence.

An unadjusted analysis was conducted to explore asthma control, rhinitis control, asthma related quality of life and reliever usage between the recruited asthma participants of the two groups. P-values were calculated using the Chi-squared test for independent categorical variables and Student t-test for independent continuous variables.

RESULTS

Qualitative evaluation

A characteristic profile of interviewed comparator pharmacists is presented in Appendix Table X-1. A wealth of data was collected from interviewed pharmacists spanning insights into trial processes including recruitment, follow-up sessions and GP referrals, observations regarding protocol questions, problems presented by participants, clinical actions taken by the pharmacist and usual practice, as well as perceived benefits to participants and benefits for pharmacists. Data regarding the behaviours and performance of comparator pharmacists during the trial and their likely impact on participant outcomes are detailed in Appendix X.

Quantitative evaluation

A baseline comparison of participant characteristics is presented in Appendix Table X-2. The only characteristics significantly associated with adherence to the protocol were state (NSW) and location (Highly Accessible).

Participant outcomes

Changes in participant therapeutic outcomes over time are displayed in Table 27.

Table 27: Subgroup analysis of secondary continuous outcomes for comparator arm

	Adherent mean (SE)	Non-adherent mean (SE)	Mean differences (95% confidence intervals)	p-value[1]
ACQ score[2,5]				
Baseline[6]	2.6 (0.91)	2.6 (0.91)		
Month 1	1.44 (0.19)	1.42 (0.12)	0.02 (-0.43;0.47)	0.93
Month 1 – Baseline	-1.01 (0.19)	-1.03 (0.12)		
p-value	< 0.0001	< 0.0001		
Month 12	1.76 (0.20)	1.41 (0.13)	0.35 (-0.12;0.82)	0.14
Month 12 – Baseline	-0.69 (0.20)	-1.04 (0.13)		
p-value	0.0009	< 0.0001		
IAQLQ score[3,5]				
Baseline[6]	3.4 (1.90)	3.4 (1.90)		
Month 1	2.47 (0.31)	2.08 (0.21)	0.38 (-0.36;1.13)	0.31

	Adherent mean (SE)	Non-adherent mean (SE)	Mean differences (95% confidence intervals)	p-value[1]
Month 1 – Baseline	-0.60 (0.31)	-0.98 (0.21)		
p-value	0.0584	<.0001		
Month 12	2.55 (0.33)	2.13 (0.21)	0.42 (-0.36;1.21)	0.29
Month 12 – Baseline	-0.51 (0.33)	-0.94 (0.21)		
p-value	0.1257	< 0.0001		
RCAT score[4,5]				
Baseline[6]	18.7 (3.50)	18.7 (3.50)		
Month 1	22.80 (0.86)	21.90 (0.59)	0.90 (-1.19;3.00)	0.39
Month 1 – Baseline	3.41 (0.86)	2.51 (0.59)		
p-value	0.0003	0.0001		
Month 12	21.46 (0.94)	21.42 (0.58)	0.03 (-2.19;2.26)	0.97
Month 12 – Baseline	2.07 (0.94)	2.03 (0.58)		
p-value	0.0325	0.0012		

Note:

1. *All analyses were performed using generalised linear mixed models for repeated measures using binary distribution for categorical variables and gaussian distribution for continuous variables – with a fixed effect of the intervention, a fixed effect of the visit (month 1 or 12), a fixed intervention by visit interaction and a random intercept by pharmacy.*
2. *Asthma Control Questionnaire (ACQ) scores lie between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (79).*
3. *The Impact of Asthma on Quality of Life Questionnaire (IAQLQ) scores lie between 0 and 10. Higher scores represent a greater impact of asthma on quality of life (55).*
4. *Rhinitis Control Assessment Test (RCAT) scores lie between 6 and 30. The lower the score, the more severe the allergic rhinitis; the higher the score, the less severe the allergic rhinitis. Participants scoring ≤ 21 are considered clinically "symptom uncontrolled"; those scoring > 21 are considered "symptom controlled" (81).*
5. *Analysis type: unadjusted model with the baseline value of the outcome (continuous)*
6. *Raw estimates obtained from baseline visit.*

Asthma control

There were significant changes in asthma control within adherent and non-adherent groups, at both one month and 12 months after baseline. The mean ACQ score for participants belonging to adherent pharmacies at month 12 was 1.76, still indicative of poor control. The mean ACQ score for participants belonging to non-adherent pharmacies at 12 months was 1.41, indicative of controlled asthma. This is presented graphically in Figure 27.

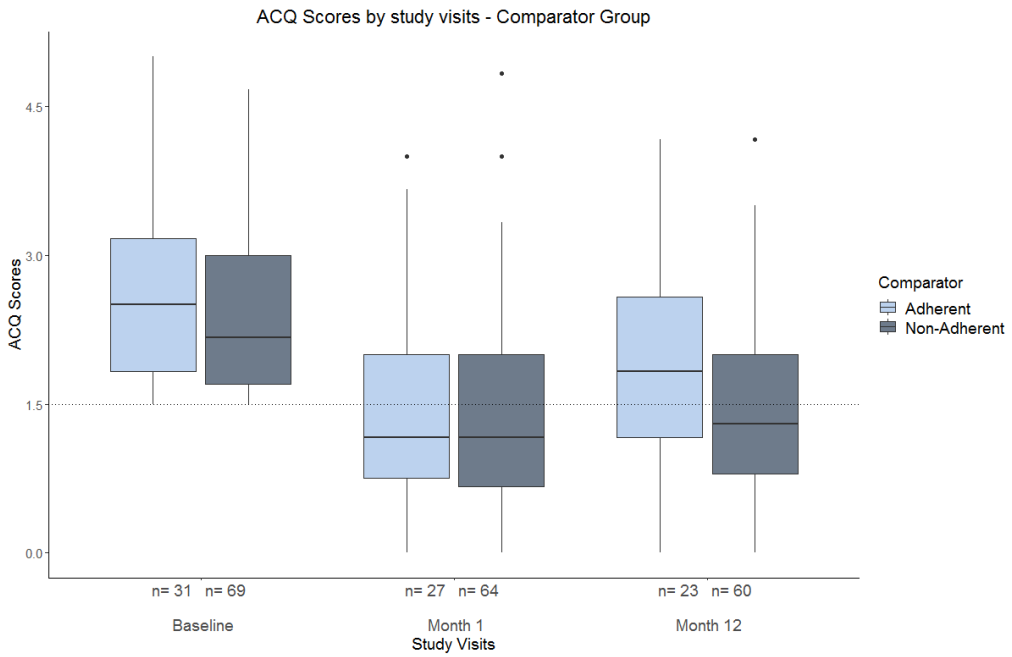


Figure 27: Asthma control over time for participants belonging to adherent and non-adherent comparator pharmacies.

Asthma-related quality of life

The impact of asthma on participant quality of life was significantly changed in participants from non-adherent pharmacies at both one month and 12 months after baseline. Participants belonging to adherent pharmacies had no significant change in asthma-related quality of life.

Allergic rhinitis control

Allergic rhinitis control significantly improved in adherent and non-adherent groups, both one month and 12 months after baseline.

Reliever use

Table 28: Participant reliever use

		Adherent	Non-Adherent	Overall	
		n=31	n=69	n=100	p-Value
Baseline	≤1-2 puffs/inhalations most days	7 (22.6)	30 (43.5)	37 (37.0)	0.14
	≥3-4 puffs/inhalations most days	24 (77.4)	39 (56.5)	63 (63.0)	0.14
		n=23	n=60	n=83	
Month 12	≤1-2 puffs/inhalations most days	10 (43.5)	37 (61.7)	47 (56.6)	0.14
	≥3-4 puffs/inhalations most days	13 (56.5)	23 (38.3)	36 (43.4)	0.14
p-Value		0.5351	0.0783		

Note:

* significant result

Based on participant responses to Q6 of the Asthma Control Questionnaire (ACQ). Number of puffs of reliever medication each day on average.

Interpretations of Findings

Our qualitative findings indicate that a large proportion of comparator pharmacists deviated from the research protocol by engaging in counselling practices with their recruited participants including review and corrections of inhaler technique; provision of education regarding asthma and its medications; and advice regarding allergic rhinitis and other comorbidities. Our quantitative analysis reveals that when comparator pharmacies were stratified in accordance with their adherence to the research protocol, participants reviewed in non-adherent pharmacies had a greater improvement in ACQ (mean difference 0.35) over time and a greater improvement in quality of life (mean difference 0.42). Although our sample size was small there appears to be a non-significant, but positive trend in the main outcome measure (ACQ) when we compare outcomes from adherent versus non-adherent pharmacies. Although this is an association rather than causation, this apparent difference in therapeutic outcomes is supportive of our hypothesis that the comparator arm was not a true control group within this trial but were active in their efforts to improve outcomes for their participants.

Considering the improvements made by participants and the greater improvements in the non-adherent pharmacy group, we cannot discount the effect that trial participation may have had on participant behaviours. The pharmacist had informed the participant their asthma is poorly controlled as a consequence of administering the ACQ, a tool and screening exercise not used in usual pharmacy practice. Most pharmacists also reported that the trial enabled them to identify asthma-related management issues among their participants including poor adherence to preventer medications, overuse of relievers, poor inhaler technique and the effects of other co-morbidities, which is interesting, as the protocol questions alone did not discuss preventer medication use, other co-morbidities or inhaler technique. Thus, it is evident that tangential conversations were occurring between participants and pharmacists. Pharmacists mentioned that the questionnaires were a stimulus for these discussions. In addition, a doctor referral was required in the protocol, which the majority of pharmacists recalled administering either verbally or via the written referral letter provided by the software, and the doctor was free to make changes to patient management. As such, the impetus for change could have been driven by the GP, the pharmacist or by participant self-motivation as a consequence of the new found understanding of their condition and ways it can be improved.

From the qualitative data and feedback, we can speculate on what may have driven pharmacists to perform additional interventions with their participants. They include the perception that participants had expectations of the pharmacist, a pharmacist's own duty of care and knowledge about asthma and allergic rhinitis. Whether or not these comparator pharmacies had a higher level of standard practice, insufficient understanding of research protocol and their place within the trial, or the fact that the study provided tools which facilitated deeper communication between the pharmacist and participant regarding their health is not clear.

Many of the interventions undertaken by comparator pharmacists have strong evidence in improving asthma management and control. Some pharmacists claimed these interventions were already part of their everyday practice, suggesting that although non-adherent to the research protocol they were adherent to their own standard of care for asthma patients. However, it should be noted that participants who were recruited into the study were regular patients of these pharmacies, as defined by the inclusion criteria, and all recruited participants had clinically uncontrolled asthma. Thus, for a majority of participants who achieved asthma control by the end of the trial, there were factors compromising their asthma management that had gone unnoticed or undetected by their pharmacists prior to entry into the trial. The degree of improvement in asthma symptoms during the trial suggests that the act of identifying people with poorly controlled asthma alone serves as an important trigger for community pharmacists to implement strategies to improve asthma control.

A simulated patient study conducted in Western Australia in 2009 attempted to profile usual community pharmacy practice in pharmacies when an asthma reliever medication is provided (82). The study found that patient assessment and medication counselling were suboptimal as only a quarter of the 160 pharmacies visited provided counselling and only 4 pharmacy staff members enquired about inhaler technique (82). This is in contrast to what we have experienced in this trial, with over three quarters of the comparator pharmacists interviewed providing further counselling to their participants and over half of the pharmacists reporting they reviewed and made recommendations regarding participant inhaler technique.

When comparing these outcomes to our prior experience with comparator groups within asthma research we have reason to speculate that there has been a shift over time in the expectations of pharmacists. This may be driven by the greater integration of research within pharmacy and the improvements and drive towards service based upskilling and professional development by the pharmacists that voluntarily enrol in pharmacy trial program initiatives. We have a pharmacist workforce that are now more trained and eager to participate in research to advance the profession. This must be taken into consideration, as there is an inherent bias in the selection of pharmacies within these trials, as the pharmacies that volunteer to participate may be more active and their efforts may not be representative of standard care. More work is required to understand what is now considered usual practice in asthma management in modern day pharmacies or whether what we have seen in the comparator arm is an expression of higher levels of usual care prompted by the tools provided in the protocol.

Our findings have the potential to impact future randomised controlled trial designs within pharmacy by asking the question of whether a control or comparator arm is feasible within a primary health care setting where a true control would mean withholding of required patient care. It may also suggest that further training and assessment is required for comparator participants as well as intervention pharmacists to ensure that optimal levels of research literacy as well as understanding of research protocol have been met, and to provide comparator pharmacies tools and pathways to deal with participant enquiries and concerns in a controlled environment.

It should be noted that there are some limitations to the analysis conducted. Interviews were conducted 6-7 months after the completion of the trial; for some pharmacists, this would have been up to one year and seven months after recruitment began and baseline visits were conducted. As

such, we cannot discount the effects of recall bias. Qualitative data presented on participant benefits and motivations for participation were the pharmacists' views and perspectives and not the direct views or opinions of the participant (asthma patient). Researchers engaged in the thematic analysis of the qualitative data were not blinded to the results of the trial and the purpose of this evaluation; however, data presented are a balanced representation of the information retrieved from the pharmacists. The allocation to the adherent or non-adherent subgroup was blinded in terms of the patient outcomes, and only inconsistencies/unsureness were discussed prior to final allocations and review of outcome data.

Formative Evaluation

Individual qualitative interviews were conducted with a sample of participating intervention pharmacists (n=10) to provide insights on the overall experience with service implementation. 'Participating pharmacists' refers to trained pharmacists in pharmacies that had recruited at least one participant into the study. The sample was selected to represent the distribution of states (NSW, WA, Tasmania), remoteness (Highly Accessible, Accessible, Moderately Accessible, Remote, Very Remote) and performance (the number of participants that successfully completed the full 12-month intervention) of the participating pharmacies. Questions asked were in accordance with a guide created by the investigative team which is included in Appendix H. The interviews ranged in length from 17 to 41 minutes each. The pharmacists' views are summarised below.

Motivation to Participate

All pharmacists saw an added benefit in offering the service, with most recognising the opportunity to help their patients better understand and manage asthma. Notably, all but one of the pharmacists indicated that they frequently encountered asthma patients, reflecting demand for this service. More than half of the pharmacists also had a general interest in asthma and indicated that the service appeared to complement their business model, which offered similar professional pharmacy services. The majority indicated that their participation would also benefit their professional practice by refreshing and/or improving their own awareness and knowledge of asthma management. In general, pharmacists also had a desire to contribute to national asthma research, with some indicating they had experience with previous involvement in similar chronic disease research trials. Some pharmacists also mentioned they were participating for personal interest reasons, with either a close friend, family member and/or themselves diagnosed with asthma. Additionally, one pharmacist was interested in participating to utilise their qualification as an asthma educator.

Overall Experience with Asthma Service

In general, pharmacists indicated a positive experience in conducting the service at their pharmacy, with the majority finding that the service protocol and operation were clear, streamlined, or easy to implement and sustain within their day-to-day practice. However, some also mentioned temporary technical issues with either the custom-designed software, computer device and/or their own internet connection or device. This appeared to cause some disruption to pharmacists but did not diminish the generally positive feelings about their overall experience in conducting the asthma service.

Additionally, nearly all pharmacists mentioned they had difficulty in recruiting and sometimes retaining participants for the service. Some reported that their participants saw involvement in the service as time consuming. Notably, many pharmacists also expressed the opinion that some participant attitudes were challenging, suspecting that participants did not accept or lacked the realisation that their asthma was poorly controlled, and that the service would be of considerable health benefit to them. One pharmacist also noted that costs associated with GP visits and new medications contributed to participant attitude:

> *"Definitely it's a cost thing for some. It is also the immediate – so you've got a breathing issue. You take the Ventolin and it goes away. So therefore, that is good. But the cost issue, in my area, is the fact that you might have to pay for a doctor visit and then the preventors are actually more – quite a bit more expensive than just say – so your Asmol or your Ventolin puffers, and I think that they [participants] don't sort of sit and think about the cost to their health. They just think, "Look, I'll just grab a puffer, so it's under $10. I'll just grab one of those," and whereas the Symbicort or one of the Seretides is up in the $40 mark for a general patient, …. it sort of makes them stop and think, and also they have to go in, and they have to have a script, and they have to go back to the doctor, and I think they find it all rather laborious, and they think, "Well, if I can just take a couple of squirts of my Ventolin, I don't have my breathlessness anymore, and I'm fine." (NSW2857RF)*

To help mitigate recruitment challenges, pharmacists recognised the importance of staff support and operational efficiency when conducting the service. Most indicated they had at least one other support pharmacist to manage the day-to-day pharmacy duties whilst they conducted the face-to-face components of the service. One pharmacist utilised after-hours appointments with participants to ensure face-to-face sessions were more suitable for the participant's schedule and lessened the likelihood for interruptions or 'no-shows'. Pharmacists also favoured the follow-up phone calls (at six months) with shorter service questionnaires, indicating these were less laborious and time consuming for the participant and themselves.

SERVICE FACILITATORS

Most pharmacists indicated that completion of the pre-training component and/or ensuring an organised service operation were important factors. Pharmacists perceived that well-trained, confident, and/or motivated pharmacy support staff, including themselves, appeared to be favourable facilitators. Additionally, some pharmacists perceived that having a dedicated consultation area and a structured appointment fostered an opportunity by offering a quiet environment for in-depth conversation with the participant. One pharmacist also mentioned that during the service, if they used an electronic device to complete questionnaires, the computer notably distracted their participants. Thus, switching to paper appeared a favourable facilitator for this pharmacist. Pharmacists also indicated that having an existing, strong rapport with participants, and a pharmacy business that was focused on promoting professional pharmacy services, were facilitators in conducting the asthma management service.

Service Barriers

The greatest barrier appeared to be time constraints. Most pharmacists perceived that conducting the asthma management service, including screening, and recruiting, took dedicated time from their otherwise busy day-to-day schedule. Pharmacists also sensed that participants tended to be time poor. Some mentioned that their participants wanted sessions completed faster than was expected. Additionally, pharmacists noted that participants would sometimes display poor attitudes regarding their asthma, which proved challenging for pharmacists when proposing how the service could be of benefit. Half of the pharmacists indicated that they found either the questionnaires were arduous, specifically questions pertaining to Quality of Life, and/or indicated that the frequency and intervals of follow-up sessions were too long. Some pharmacists also indicated that the strict eligibility criteria were a barrier to uptake, perceiving that this excluded many patients whom they deemed would benefit from the service. Those whom they thought would benefit included patients with asthma who did not frequent the pharmacy, who were under 18 years old (e.g. children), as well as people with a diagnosis of COPD and/or other complex comorbidities. Several pharmacists also mentioned that they entered the asthma trial later than expected, resulting in insufficient time to recruit participants. Technological issues also formed a barrier for around half of the pharmacists. This included issues with an unstable internet connection or loading problems with the service software and/or computer devices. Although rectified where possible during the trial, these appeared to cause delays for some of the pharmacists conducting the service.

Service Continuation and Future Improvements

All pharmacists agreed that they would continue with the service, with the majority expecting the service would likely offer a positive health benefit for their local demographic.

Suggestions for improving the service for the participant formed part of the discussion with most of the pharmacists. Notably, pharmacists suggested ways to save time for the participant and themselves by reducing the length of questionnaires to simplify sessions and reducing the frequency or extending the interval for initial and follow-up sessions. Most pharmacists recognised that the initial and one-month follow-up were important sessions to maintain, indicating that positive health outcomes are likely to result during this period of pharmacist and/or GP involvement. However, some perceived that questions were repetitive and were not of benefit or relevance for their participants. Others re-iterated the need to expand the participant eligibility criteria to increase uptake, as previously mentioned. Streamlining the service software programs into one instead of two, preferably *GuildCare*, offering the asthma management service in conjunction and/or alongside other professional pharmacy services, and ensuring adequate remuneration to match existing Government-funded service provision, were also included as suggestions for improvement.

Two pharmacists made interesting additional suggestions. One pharmacist suggested a change in process whereby the pharmacist conducting the service checks for the Asthma Action Plan at recruitment, and then follows up with the participant at the one-month, depending on asthma control and management recommendations. Another pharmacist suggested a Government-led asthma awareness campaign, perceiving that this may improve service uptake in the pharmacy.

> *"I think … if the Government did some sort of awareness throughout the community about it being a service available in pharmacies, and like we have a checklist that says, "Is your asthma waking you up at night? Are you having to use your puffer this many times per week?" If you just did a couple of the criteria and made some sort of add on that other – the people in the community would be aware of, stop that normalisation of asthma and actually get people understanding what it's about. I think that that would lead to it occurring more in the pharmacy." (NSW2857RF)*

Training Evaluation

Almost all pharmacists expressed satisfaction with the training offered, with most perceiving that information was well covered. Just under half of the pharmacists expressed the opinion that they benefited in some way from the inhaler technique assessments, with some indicating this particularly helped to prepare them by reinforcing information and skills. Some pharmacists appreciated that the asthma course was available online, enabling them to complete learning/refresher activities at their own pace and in their own time. One pharmacist also suggested that a series of upbeat and fun scenario vignettes, and incorporation of some key coaching techniques for approaching and recruiting participants, could be an improvement to the service training videos.

Participant Perception and Outcomes

All pharmacists indicated that the asthma management service was well received by most participants. Most pharmacists perceived that the service helped them to improve their participants' overall asthma management. Pharmacists saw themselves as an educator, and this appeared to be an important aspect of improving participant medication adherence and compliance. This also included being a reputable resource for participants, often reminding or providing new information to participants regarding asthma triggers. Pharmacists also mentioned that structured service protocol and appointments appeared to aid their interaction with some participants who thrived on dedicated and organised time with their pharmacist. One-third of pharmacists perceived that the service helped them improve and/or increase collaborative links and discussions with multidisciplinary healthcare teams.

> *"They love it. They love it, because you do develop such a great relationship with them, and you become part of their management team in their chronic care management, and I guess if I can say one thing, you see them change from their chronic illness controlling them to them being in control of their chronic illness, so my asthma was controlling me, now I'm in control of my asthma." (NSW2999SB)*

More than half of the pharmacists found the least useful part of the service for participants was the lengthy and repetitive questionnaires, notably the quality-of-life questions, as highlighted previously (These research instruments would not be included in any future implementation of this service). In these cases, participants appeared to be less responsive, less enthusiastic, and appeared pushed for

time when asked these questions; one pharmacist thought this may be because the questions were not directly related to their asthma condition.

Relationship with Local General Practitioners

More than half of the pharmacists either did not know or said that the asthma management service did not have any impact on their professional relationship with local GPs. Most of these pharmacists did not refer participants to GPs, and GPs were unlikely to refer participants to these pharmacists. However, some of pharmacists perceived that their clinical recommendations and referral to local GPs led to improved professional relationships by increasing collaboration. One of the pharmacists also noted GP referrals to the pharmacy during service provision. In this case, there appeared to be a pre-existing relationship with GPs who were aware that the pharmacy was specialised in asthma management and employed a pharmacist asthma educator.

Integration with Community Pharmacist Role

All pharmacists indicated that the service appeared relevant and some noted as an "ideal fit" with the community pharmacist's role. Just under half of pharmacists perceived strengthening of their educative role. Over half of the pharmacists indicated that the service challenged and/or extended their scope of practice by offering them a better understanding of asthma management. The majority of pharmacists also felt their experience with the service favourably changed their relationships with participants. Particularly, pharmacists perceived that they built a stronger rapport with their participants, whether they were involved in the service or not. These pharmacists also proposed that this led to opportunities where they could be more readily involved as part of the participant's trusted multidisciplinary team.

Service and Business Integration

Almost all pharmacists perceived that the service model would integrate well with their business practices, with most indicating that this was because the service appeared to align with, complement and/or be easily implemented alongside existing professional pharmacy services. Two pharmacists provided alternative views, with one mentioning that they were not familiar enough with their pharmacy's business model; offering no further thoughts to this when prompted. The other pharmacist expressed the opinion that this was the first time their pharmacy had been involved in a research trial, and they lacked experience with integrating professional pharmacy services. The pharmacist felt that this combination of factors contributed to their feeling that the service did not integrate as well as it could have. Despite this, more than half of the pharmacists also indicated their preference that that the service could integrate and align well if the structure, protocol, session time allocations and/or remuneration aspects of the service were similar to existing Australian Government-funded professional pharmacy services, e.g., MedsCheck and Diabetes MedsCheck services.

More than half of pharmacists mentioned that they and/or the pharmacy business experienced 'spinoffs', or unexpected occurrences because of offering the service. Notably, this included pharmacists perceiving that their participation in the service generated additional business, although

many pharmacists did not offer in-depth explanations. Several pharmacists mentioned their appreciation for the service and involvement in the trial. Pharmacists indicated that this provided them with a unique opportunity to increase their clinical knowledge, strengthen their participants' confidence in them, and/or raise community awareness regarding asthma.

INTERPRETATION OF CLINICAL RESULTS

This Pharmacy Asthma Service demonstrated that a significant improvement in asthma control for people with poorly controlled asthma was possible over a 12-month period, with a significant increase in the proportion of intervention participants experiencing good asthma control (ACQ score <1.5) at the trial's end. At the same time, there was a significant improvement in asthma control in the comparator arm, who were recipients of a lower-intensity service involving both the pharmacist and GP. The improvement in asthma control in both arms of the trial indicates that we were unable to demonstrate a difference between the intervention participants and the comparator participants. In other words, the null hypothesis – that the intervention participants would demonstrate *similar* clinical improvement to the comparator participants – could not be rejected.

The reasons for this improvement in both arms warranted further investigation. The service offered in the intervention arm followed a structured protocol, with interventions focussed on adherence, inhaler technique and optimal treatment of allergic rhinitis. The pharmacist assessed need in each of these three areas, and then undertook the structured intervention and documented actions for each participant. In the comparator arm, once baseline measures were collected, the pharmacists were asked to refer the participant to their GP. In this way, the comparator arm of the trial did not comprise a true control arm, more so, a 'low-intensity' multidisciplinary intervention. The investigative team undertook a supplementary mixed-methods analysis in order to determine the processes that had been undertaken by pharmacists within this comparator arm. This included post-intervention qualitative interviews, that were conducted with 20 actively involved pharmacists from comparator pharmacies that had completed a full 12-month comparator pathway for at least two participants. Additionally, a subgroup quantitative analysis was performed to compare participant outcomes between pharmacies found to adhere to the research protocol and those where additional interventions not described in the research protocol may have been conducted. Pharmacies were classified as either adherent or non-adherent, or inconclusive if unable to be classified. This process determined that 8 pharmacies were adherent and 14 were non-adherent to the research protocol.

Our quantitative analysis revealed that when comparator pharmacies were stratified in accordance to their adherence to the research protocol, participants reviewed in non-adherent pharmacies had a greater improvement in ACQ (mean difference 0.35) over time and a greater improvement in quality of life (mean difference 0.42). Although our sample size was small there appears to be a non-significant, but positive trend in the main outcome measure (ACQ) when we compare outcomes from adherent versus non-adherent pharmacies. Although this is an association rather than causation, this apparent difference in therapeutic outcomes is supportive of our hypothesis that the comparator arm was not a true control group within this trial but were active in their efforts to improve outcomes for their participants.

In parallel with the improvement in asthma control, there was a significant improvement in quality of life for both arms. This also reinforces the notion that our comparator arm participants were receiving interventions, which positively improved their quality of life. However, the negative impact of asthma on day-to-day life for comparator participants was significantly greater than for the intervention participants at month 12.

Using both the PBS data, pharmacy dispensing data and our operational definition of adherence (80% of days covered, based on the PDC value), there was no significant improvement in participant adherence in intervention or comparator arms during the trial irrespective of the method of data collection. As there was agreement between the PBS data and pharmacy dispensing data, this suggests that either may be a useful measure for measuring participant adherence.

Using PBS data, at month 12 in both the intervention and comparator arms, adherence was approximately 50%, which suggests only half the participants were having their asthma medications dispensed at appropriate intervals, according to our calculations. The pharmacy dispensing data showed a lower rate of adherence of 36% at month 12 for both the intervention and comparator arms compared to adherence assessment using PBS data. This difference in rates between the PBS data and Pharmacy Dispensing data may be due to the collection of prescription by participants from other pharmacies, which would be included in the PBS data and not the pharmacy data.

Despite the known benefits of regular preventer use on symptomatic control of asthma and reducing long term risks, asthma patients are known to not take their preventer therapy; they use it intermittently or self-titrate based on symptoms or seasonal expectations(23, 83-86). It may be unreasonable to expect participants to have 80 – 100% adherence as this does not represent reality. Rather, many people with asthma rely on reliever medications that provide immediate symptomatic relief, and can be purchased without a prescription in Australian pharmacies. A previous cross-sectional study which surveyed adults with asthma (*n* = 2686) in an Australian context found that 57% of the population that reported uncontrolled asthma symptoms were non-adherent or were not using a preventer (2). This is similar to the results in our trial. Indeed, 18% of our participants had not purchased a preventer in the previous 12 months to the trial. The high prevalence of poor adherence to preventer therapy or a lack of preventer therapy is consistent with international studies, despite variations in thresholds and measurements used to classify adherence.

In contrast to the insignificant changes in adherence using PBS Data or pharmacy dispensing data, results from participant reported adherence showed significant improvements in the use of their asthma medications, including an increase in preventer use and a decrease in reliever use over the 12 months of the study. This is not surprising, as participants are likely to report to the pharmacist that they are using their medications. In addition, the pharmacists only asked participants about the previous seven days, whereas the PBS and pharmacy dispensing data analysed a 12-month period where use may be intermittent.

For the interpretation of adherence, it may be that a different definition of 'non-adherence' (80% PDC) would yield different results. The value of 80% is widely used in the literature (72), but might not be relevant to all populations or healthcare systems. The lack of a change in adherence when using a systematic measure despite asthma control improving may seem surprising. Using patient reported

adherence, however, our results are consistent with previous results we have observed, i.e., patients report improved adherence after an intervention (47). Thus, it may be that patient reported measures are more of a reality to the patient, but not to the health system.

A proportion of participants were receiving add-on biologic therapy, and this had not been taken into account when considering preventive therapy. It may be that the proportion of participants on this anti-inflammatory therapy increased during the trial and the patients perceived need for a preventer decreased. It would be useful to look at this in the future.

Despite this apparent lack of change in preventer medication use, participant-reported reliever use reduced significantly in both intervention and comparator arms. At baseline, 75% of intervention participants were using at least three puffs of their reliever medication daily; this decreased to 26% at the end of the study. In the comparator arm, the decline was from 63% to 43%. Thus, the proportion of people with asthma who were using an inappropriate level of reliever medication was significantly reduced over the duration of the study. Inappropriate reliever use has been associated with increased risk of poorer health outcomes in asthma and therefore this reduction in inappropriate use is likely to be extremely important.

Regarding participant inhaler technique, the proportion of participants with device mastery at baseline is consistent with the published literature and what we would expect in a community sample of people with asthma (87). The almost doubling in proportion of participants who maintained device mastery at month 1 is consistent with inhaler device intervention studies (88-90) and previous pharmacy asthma services research (47, 50). The fact that this increase in device mastery was sustained beyond the first month is an important finding. It indicates that the pharmacist intervention as it relates to inhaler technique is sustained over time for at least half the individuals who were not able to use their inhaler correctly at the start of the study. Similar impact was shown when examining proportion of patients within the intervention arm that were competent in all their prescribed device types, which increased significantly during the trial from 28% at baseline to 52% at month 12. Future research and initiatives which lead to identifying the characteristics of patients at risk of not maintaining inhaler technique over time, needs to build on preliminary research in this area (90). In so doing, pharmacists will have the potential to eliminate one of the most common barriers to poor asthma control in the community. As expected, the number of participants using a SMI was low, therefore conclusions relating to the SMI should be interpreted with caution. It would be expected that this device was less commonly used in this population of participants because the current medications available for use in the SMI are primarily reserved for the treatment of COPD or severe asthma (which only affect 5% of the asthma population) (91, 92).

For allergic rhinitis, symptom control improved in both arms. In the intervention arm, pharmacists were required to undertake a detailed and structured assessment of symptoms and medication taking, using an evidence-based algorithm. However, allergic rhinitis symptom control improved in the comparator arm as well, where no structured intervention took place. Allergic rhinitis medication recommendations are part of routine clinical practice in pharmacy. Most rhinitis medicines are available over-the-counter, and sales are not reflected in PBS data. Thus, we cannot be certain that comparator pharmacists did not act outside of the boundaries of the trial protocol in the interest of

their participants and provide medication advice once it was determined the participant's rhinitis control was sub-optimal.

In previous studies, we had routinely included an active component of recommendation for referral to a GP for every asthma participant who did not have a current asthma action plan (50). In the current study, this was not a recommendation until the final visit in both arms. This was deliberate, because recommending an action plan is an intervention that improves asthma control (93), and we considered we needed to control this as a confounder. In terms of success, pharmacists in previous trials were able to double the number of people with an action plan compared to the general population, from 20% to 40 % (50). When asked at the final visit, 39% of our intervention participants and 50% of the comparator arm had an action plan. Given that the comparator arm received referral to the GP, it is likely that the GP initiated an asthma action plan where needed. Certainly, 50% is much higher than the proportion of the population with asthma in the community who possess an action plan, which is approximately 28% (94).

Previous trials have shown that if a true control arm (no intervention) is the comparator, we would expect no improvement in asthma severity/control in that comparator arm (50). Upon comparison of current trial participants to previous study participants, our participants were found to be comparable at baseline in terms of mean age, the higher proportion of females, smoking status and baseline inhaler technique. Therefore, if a true control arm could have been used in the current study, we may not have observed an improvement in the comparator arm.

One of the possible confounders for the improvement in asthma control is the season or time of recruitment and completion. Asthma is known to vary depending on the seasons; winter often increases the number of exacerbations or worsening asthma, and during springtime, allergic rhinitis and allergies are worse, and therefore asthma can be less well controlled (95). If perhaps all of our participants with asthma had been recruited during the winter/spring season and then completed the trial in summer, seasonal variability would account for a higher proportion of participants with controlled asthma. Both intervention and comparator arms were recruited over an extended period, and thus any possible seasonal effect applied to both arms. One other confounder that was unexpected was the disastrous bushfire season that occurred towards the end of the trial. The air quality in many regions became extremely poor and people with asthma were advised to stay indoors (26-28). Although a confounder, our participants were matched in terms of regions, thus we expect that this disaster would have similar effects on both arms of the study. This is unable to be determined retrospectively.

At the end of each visit, the pharmacists were required to estimate how long the consultation took. Based on self-estimates, the mean overall time for the intervention service was 96 (±30) mins, with a range of 32 to 225 mins. Based on the service requirements, the baseline visit was the longest and the telephone follow-up at six months the shortest; this was in line with our expectations when designing the protocol and had been indicated in the pharmacists' protocol training. A significant proportion of this time was reportedly consumed by the participant completing study-related questionnaires. As mentioned above, this component would not be required in any practice-based service. For the comparator arm, who were required to collect data and refer to the GP and perform two telephone

follow-ups, the overall time was 55 (±17) mins, with a range of 18-115 mins. The wide range is suggestive of additional advice provided as a duty of care to participants in the low-intervention arm.

Participants in both the intervention and comparator arms were remarkably similar in terms of their characteristics. There were more participants in the comparator arm older than 56 years, and more participants in the intervention arm between 36–45 years of age. Thus overall, the comparator arm was slightly older. This is unlikely to impact the integrity of our key findings and the differences in age were not significant. All other demographics, including asthma onset, smoking status and prevalence of allergic rhinitis, as well as mean asthma control score, quality of life and allergic rhinitis control score, were not significantly different, and thus we had similar samples to test the intervention.

Similar types of pharmacies were recruited for both the intervention and comparator arms. Participating pharmacists in active pharmacies represented a mix of proprietors and salaried pharmacists. The mean age of pharmacists in the intervention arm was 38.7 ± 10.6, and the comparator arm, 36.9 ±10.7 years (average national age 39.5 years) (96). Approximately half of both arms – 48% of intervention and 45% of comparator pharmacies – dispensed fewer than 200 prescriptions per day. This compares to a national average of 1,149 prescriptions per week across Australia (9,81). The average number of pharmacists working at any time was two in both arms; this is also similar to the national average (8). Interestingly, more than half of the pharmacists in both arms had been involved in previous research studies, and 92% of pharmacies (98% of intervention pharmacies and 82% of comparator pharmacies) reported providing other professional services. This factor or confounder could be part of the explanation for the improvement in people with asthma in the comparator arm if pharmacists knew what to do without additional training and support. The withdrawal of pharmacies at each stage of recruitment and training was greater than anticipated when designing the protocol (informed by our previous research (50)), and reasons are unclear. Withdrawals occurred to a similar extent in both arms of the study. In our study published in 2007, the withdrawal rate was minimal. In 2013, 74% of selected pharmacies recruited participants (50). In the current study, 145 pharmacies consented to participate; however, after completing training, only 95 (66%) pharmacies recruited participants. Of this group, many pharmacies recruited only one or two participants and did not achieve the recruitment target of seven participants. Pharmacists were asked about their experience with the service to explore reasons for low recruitment as well as motivations for being involved initially. Most pharmacists decided to participate because they had many people with asthma and anticipated demand for a clinical service. They also wanted to contribute to national asthma research.

Similarly, there was significant loss to follow-up of participants throughout the trial. Seventy-eight intervention and 49 comparator arm participants did not complete the full 12-month service out of the original total of 381 participants for both arms. Retention of asthma participants overall was 67%. Asthma control data were collected from 42% of participants who did not complete the service and results indicated most of these participants were poorly controlled. When participants were asked the reasons for not continuing, the primary reasons given were that they were too busy, did not wish to continue, had moved out of the area or were unwell. A large proportion of participants were also uncontactable, and so their pharmacists were unable to follow up.

In general, pharmacists' experience with the service was positive; however, they acknowledged that technical issues with the new software and protocol components may have hindered recruitment. They felt, as had been reported previously in other studies, that the time taken was too long and that the clinical questionnaires were repetitive (97). These questionnaires would not be administered beyond the research setting. The strict eligibility criteria became a barrier for pharmacists, as adults with poorly controlled asthma, in the absence of COPD and other co-morbidities, and who were a regular customer, were reportedly difficult to find. Since the overlap between COPD and asthma is widely reported in the literature, future research might consider including these patients for service benefit (98). Another modification would be to screen participants using a modified practice-based tool we have shown to have good sensitivity for identifying participants with sub-optimal asthma control and which has been incorporated in the National Asthma Guidelines (6, 54). It was not suitable for the current study, as we needed reliable longitudinal assessment, but it would be appropriate if pharmacists were screening for participants at higher risk from their poorly controlled asthma (54).

In terms of sustainability, pharmacists reported that the educational role they had in the service was a good fit for pharmacy. They believed that involvement in the trial improved their relationship with all their asthma patients, whether or not the patient was involved in the service. They also perceived that their overall business had improved. Pharmacists also reported that trial participants thought the service had helped them with their asthma, and this was reinforced when participants were asked directly about the service.

At the end of the service, participants who completed the full intervention were asked about their satisfaction. This was very positive, with 96% being "very" or "somewhat" satisfied, and the majority thought that they would participate in such a service in future. They expressed a high level of satisfaction with all aspects of the service, and a high proportion reported positive impacts. The aspects of the service they liked the most were the pharmacist's attention, and the opportunity to focus on their asthma. Feedback was collected from 71% of participants who completed the service, which may not be representative of all completing participants. In addition, it does not represent feedback from participants who decided to discontinue or who had an incomplete service. This group may well have held more negative views.

Over time, pharmacy trials of asthma services in Australia and internationally have transitioned from complex protocols including spirometry and goal setting to more targeted, simplified protocols to include effective interventions that are efficient in busy pharmacy settings. This service focused on three elements linked with improving asthma control, i.e. improved preventer adherence (and lower reliever use), improved inhaler technique and improved allergic rhinitis control. These three elements are within a pharmacist's skill set and can be implemented with a short educational refresher course. We can report reliever use decreased and both inhaler technique and allergic rhinitis control improved. We do not know if adherence, inhaler technique and allergic rhinitis control are all required to observe the increase in asthma control we observed. Together, however, they were very effective. Whether the service could be simplified would be of interest in future and may be informed by determining behaviours within the comparator arm.

In this trial, we set out to test a pharmacy service for asthma. The service had positive effects on the participants' asthma in terms of symptom control, quality of life and allergic rhinitis control. At the

same time, the comparator arm also demonstrated improvements in these key indicators. This warrants further investigation but does not detract from the positive results overall.

Clinical Validity

Distribution

To ensure that rural and urban pharmacies were represented in NSW, Tasmania and WA, pharmacies were classified by remoteness using the PhARIA and stratified according to the distribution of the Australian population. Then pharmacies were randomised to either the intervention or control arms. Due to pharmacy withdrawal, after stratification, the final distribution of participating pharmacies altered, based on state distribution. Relative to target numbers for each state there was a slight under-representation of pharmacies in Tasmania, in particularly in the comparator arm, and an over representation of NSW pharmacies in both intervention and comparator arms. Despite this, all categories of remoteness were represented according to target numbers, with a slight over representation of highly accessible pharmacies.

Baseline Comparability – Pharmacy/Pharmacist/Participant

Data for both intervention and comparator pharmacies and pharmacists actively participating in the trial were collected to ensure baseline comparability. Intervention pharmacies were comparable for state, location, remoteness, size, staffing levels and script quantities. Intervention pharmacies were more likely to offer other professional services at time of commencement. Prior to the trial those that reported such services used resources and processes which included a system to manage appointments, patient files, had dedicated periods of service delivery and they undertook pharmacy-based training for all staff to implement services. Pharmacists delivering the intervention and comparator protocol were comparable in age, experience, further accreditation, employment status, employment position and prior involvement in research. There were significantly more comparator pharmacists involved in delivering the protocol from each pharmacy (this could be due to the fact that training requirements were minimal and so more pharmacists could be trained from each participating pharmacy) and there was an overrepresentation of pharmacists from NSW and from highly accessible pharmacies in the comparator arm. Both intervention and comparator arm participants (people with asthma) are comparable in all investigated variables. Sensitivity analyses including age, lung function tests and other baseline covariates were conducted. They showed similar results to the primary, unadjusted, analysis.

Comparator Arm

Once it had been identified that the participant had poorly controlled asthma, the pharmacist duty of care required that there be some action. In the comparator arm the only action required was a referral to the GP. In order to ascertain if comparator pharmacists acted outside of the boundaries of the trial protocol, in the interest of their participants who were sub optimally managed, the investigative team conducted a mixed methods evaluation of the comparator arm. We thus have evidence that a proportion of pharmacists were doing much more than just referring. We do not know what occurred in GP care apart from participant reported medication changes (Appendix W). Pharmacists are a key source of expertise in asthma medications and device handling, additionally allergic rhinitis medication are available over the counter and recommendations are part of normal practice in pharmacy.

Seasons and Asthma

Recruitment ran over 7 months (Australian Winter-Australian Summer) therefore we cannot discount the effects of seasonality on asthma control, rhinitis control and medication use. Both intervention and comparator arms had an extended period of recruitment and thus any possible effects of seasons were the same for both arms. External climatic factors including dust storms and major bush fires which occurred during the trial are likely to have impacted negatively on participant control of their asthma. Although a confounder, since participants were matched in terms of regions, we expect that this disaster would have equal effects on both arms of the study. Of course, we cannot measure this.

Outcome Measures Used

Numerous interventions relied on participant self-report and may be subject to bias. Where possible validated scales and questionnaires have been used to help minimise this.

Preventer medications in Australia are scheduled as prescription only and so we have clear data trail for each of these purchases. Medication usage data presented is representative of what has been recorded for each recipient at the recruiting community pharmacy. We cannot be certain that the participants had not collected other medications elsewhere. To help mitigate this risk, an inclusion criterion for the trial was that the participant was a regular patient at the pharmacy, and this was part of the protocol training. To overcome any issues with measuring adherence and medication use, we also used government-based PBS data supplied by Services Australia (formerly the Department of Human Services).

Additionally, we can only report on what participants have chosen to get dispensed, there may be other medications prescribed but not presented to the pharmacy.

Participant Withdrawal

Participant withdrawal was relatively high. To mitigate the effects of loss to follow up two separate analyses were conducted. Firstly, the primary analysis used all available data with no imputation. In addition, because the ACQ score at month 12 (the primary endpoint) was missing for more than 10% of enrolled participants, missing data was imputed using a fully conditional specification. Additionally, the investigative team attempted to call withdrawn participants at the 12-month time point to administer the ACQ and assess asthma control to compare to the final cohort, a larger proportion of participants who withdrew from the trial remained poorly controlled at study end.

Clinical Utility

Given the high prevalence of asthma nationally, it is envisaged that this asthma intervention will be of benefit to the broader population of Australian adults with poorly controlled asthma. The Pharmacy Asthma Service was assessed in an adult population only, we cannot comment on clinical utility in children. Taking into account the population with asthma in Australia is 2.7 million (3) the number of people with poorly controlled asthma (50% = 1.35 million) (2) and those who are adults (~80%= 1.08 million) (94) and excluding those who might also have COPD (20%) (99), it is estimated that 864,000 people could benefit from this type of service. At an estimated 50% rate of uptake, we estimate

432,000 people with asthma would benefit immediately. In the intervention arm of the trial, 62% of participants were deemed to have controlled asthma at the 12-month point. If 432,000 Australians were to participate, we estimate that over a quarter of a million Australians (n=267,840) would demonstrate asthma control improvement and thus minimise their future exacerbation risk and associated costs of poor health.

SECTION C: TRANSLATION ISSUES

SERVICE BARRIERS AND ENABLERS

There were several enablers and barriers that affected the delivery of the Pharmacy Asthma Service. These critical enablers, barriers and ways of overcoming barriers are described below to assist in translation.

BARRIERS

The withdrawal rate of pharmacists once they had expressed an interest in delivering this service presented a major barrier. We explored reasons for this and published the work (Appendix A). The main barriers were the software, engaging participants, knowledge of requirements for research versus service and adequate remuneration for the time taken.

The issues with the software could be overcome by refining it (it was developed specifically for this project) so that it was streamlined and did not require multiple steps and aligned with pharmacy software. The issues regarding engaging participants are slightly more complex in that people with asthma are well known for being difficult to engage in discussion, given that they have had the disease for a long time and feel that they know all about it. Some of our pharmacists felt that their participants were in denial about the severity of their asthma. It would be important in the future to include some training for pharmacists regarding overcoming patient barriers and joining in a partnership around their health. The issue of service versus research would not be a barrier in translation as the research questionnaires would not be part of any proposed service. The issue of adequate remuneration for time taken could be addressed by having realistic time frames proposed for the service. Our pharmacists were paid a flat fee for completing each patient in two instalments over the 12 months regardless of time taken. However, the time taken to deliver the service ranged from 32 to 225 minutes. Some of the baseline visits were very long and perhaps unrealistic in a busy pharmacy. Removing the research data collection would also help with the time involved.

ENABLERS

Enablers for translation included the positive response from participants as well as the positive responses from pharmacists who completed the online training and skills assessment and delivered the service.

Participants who received the service expressed a high degree of satisfaction, the service improved their confidence in managing their asthma and they would recommend it to others as well as participate in the service if it were offered in the future. Thus, the uptake of the service is likely to be high.

Pharmacists thought the service would assist them and compliment their professional services, they also described how it would benefit their patients. Pharmacists liked that the service protocol was clear and streamlined and integrated well into day-to-day pharmacy work. They said that having more than one pharmacist available so that they did not get interrupted when delivering the service was an

advantage. The availability of a private consulting area, a requirement for this project, had enabled their delivery of the service.

The training was well received and because both theory and skills-based training were available online, it could be completed when the pharmacist had time. Pharmacists appreciated that this was available, and it made sure that pharmacies in remote locations were just as well trained and supported as those in urban regions. This enabled their education and thus their confidence in delivering the service.

Interprofessional barriers did not arise in this study. This could be because it was very clear that pharmacists were dealing with medication issues primarily. Pharmacists who were referring participants to the GP reported that this had improved their relationship. It would be important to stress this in future.

SECTION D: ECONOMIC EVALUATION

BACKGROUND

In Australia, the prevalence of asthma was estimated to be 11.2% across all ages and 11.6% in those 15+ years in 2018, and is reported to have one of the highest asthma death rates in the world (100-102). In 2015 the costs associated with the burden of asthma was estimated to be $24.7 billion in Australia (103). Costs of asthma are likely to continue to rise with prevalence expected to increase in the future. A new community-based Pharmacy Asthma Service has been proposed to check and manage poorly controlled asthma. To ascertain the effectiveness of this program, the Pharmacy Trial Program – Asthma and Rhinitis Control (PTP-ARC), a clustered randomised controlled design trial (RCT), was conducted. The program was compared with usual care. As there was no difference in effect between the intervention and the comparator arms of the study the economic analysis aimed to measure costs of both arms of the Pharmacy intervention study. The null hypothesis was that there would be no difference in the costs between intervention and comparator arm.

METHOD

Intervention costs were estimated from training materials development, payments to pharmacists, costs associated with items such as software licenses, tool development and hardware. These data were accessed from financial statements of the study.

Medical services and pharmaceutical costs were estimated in both the intervention and comparator arms over 12 months using linked MBS and PBS. Trial data were individually linked to MBS and PBS data patients' consent. Costs were derived from medical services including outpatient visits, specialized care and ambulatory services (e.g. imaging and laboratory services). Pharmaceutical usage, which included prescriptions of preventer or reliever medications, were also tracked over one year. Health services usage were costed based on identified MBS item numbers while pharmaceuticals were costed using PBS Item Code and benefit information.

Total costs included the sum of the intervention costs, the MBS and the PBS annual cost. These were calculated separately for 12 months of the trial in intervention and comparator arms.

All costs were presented in 2020 Australian dollars to adjust for inflation (using the health consumer price index (CPI) from the Australian Bureau of Statistics) (104).

STATISTICAL ANALYSIS (105)

We provided descriptive statistics of background variables and outcomes. Means and standard deviations are reported for continuous variables while percentages are reported for categorical variables on individuals with complete data. The correlations between categorical data and the two arms (intervention and comparator) were calculated using Pearson chi square ($\chi 2$), for continuous variables with normal distribution using ANOVA, and for continuous variables with skewed distribution using Wilcoxon rank-sum test. The Shapiro-Wilk test was used to test for normal distribution of the cost data. Due to the strong non-normal (right-skewed) distribution and outliers in the cost data,

comparison between the two arms were analysed with the non-parametric two-sample Wilcoxon rank-sum test and Spearman's correlation coefficient, where necessary. Costs were reported both as their mean with standard deviations (SD) as well as the median with interquartile range (IQR) with the exact p-values (106). The two-sample Wilcoxon rank-sum test tests the null hypothesis that the intervention – the Pharmacy Asthma Service – had no effect on the costs, and the null hypothesis was rejected at a significance level of 0.05. We further estimated the prevalence-based budget impact of full coverage to all individuals aged 15 years and above in Australia. We additionally identified the five costliest and most frequently used MBS and PBS items in both arms. A two-tailed P-value <0.05 was considered as statistically significant. All analyses were performed using STATA v.16 (Stata Corp., Lakeway Drive, College Station, TX, USA).

A secondary analysis examined costs incurred by participants in the 12 months prior to the intervention in both intervention and comparator arms. Wilcoxon matched-pairs signed-rank test was used to test the difference in annual costs before and during the RCT of the same sample. Additionally, the five costliest and most frequently used items over the 12 months period preceding the trial were identified.

FINDINGS

COMPARATIVE DESCRIPTIVE STATISTICS AT BASELINE

Data on a total of 381 participants were collected. Two-hundred and twenty-one participants were randomised into the intervention arm while the remainder formed the comparator arm. Of these, 378 consented to data linkage, and 345 had complete MBS and PBS data and we included this in the analysis. A flow diagram of participant retention and data collection in the trial is presented in Appendix Z. Thus, the final analytical sample included 205 (59%) participants from the intervention and 140 (41%) from the comparator arms (Table 27). The mean (standard deviation, SD) age of this cohort of participants was 56.4 ± 17.6 years, 70% identified as females, and 95% reported having high school or higher education. Of the total, 71% were diagnosed with asthma before age 35 years. At baseline, approximately 16% of participants had at least one hospital admission, and 24% had at least one Emergency Department presentation. At baseline, the mean asthma score was 2.50 ± 0.90, while the mean rhinitis control assessment score was 15.30 ± 9.91, and mean IAQLQ score was 3.36 ± 2.00. There were no statistically significant differences in key variables between the two arms at baseline.

Table 29: Baseline demographic and asthma characteristics of study participants

Characteristic	All n=345	Intervention n=205	Comparator n=140	*p-value
Age, years (mean, SD)	56.4 (17.6)	55.9 (17.0)	57.1 (18.6)	0.251
Gender n(%)				
Male	104 (30.1)	61 (29.8)	43 (30.7)	0.849
Female	241 (69.9)	144 (70.2)	97 (69.3)	
Education n(%)				
< High school (%)	16 (4.6)	9 (4.4)	7(5.0)	0.757

Characteristic	All n=345	Intervention n=205	Comparator n=140	*p-value
High school (%)	163 (47.3)	94 (45.9)	69 (49.3)	
> High school (%)	166 (48.1)	120 (49.8)	64 (45.7)	
Employment status n(%)				
Full-time	83 (24.1)	53 (25.9)	30 (21.4)	0.167
Part-time or casually employed	76 (22.0)	50 (24.4)	26 (18.6)	
Unemployed	186 (53.9)	102 (49.8)	84 (60.0)	
Location n(%)				
NSW	253 (73.3)	147 (71.7)	106 (73.3)	0.667
TAS	33 (9.6)	20 (9.8)	13 (9.3)	
WA	59 (17.1)	38 (18.5)	21 (15.0)	
Current smoker n(%)				
No	296 (85.8)	179 (87.3)	117 (83.6)	0.328
Yes	49 (14.2)	26 (12.7)	23 (16.4)	
Age of asthma onset n(%)				
< 35 years	245 (71.0)	147 (71.7)	98 (70.0)	0.731
³ 35 years	100 (29.0)	58 (28.3)	42 (30.0)	
Hospital admissions (mean, SD)	0.33 (1.18)	0.28 (0.97)	0.39 (1.43)	0.580
Emergency presentations (mean, SD)	0.528 (1.95)	0.51 (2.25)	0.56 (1.43)	0.052
ACQ Score (³ 1.5, mean, SD)	2.50 (0.90)	2.51 (0.90)	2.47 (0.90)	0.695
Baseline RCAT Score (mean, SD)[1]	15.30 (9.91)	15.46 (10.24)	15.05 (9.40)	0.282
Baseline IAQLQ score (mean, SD)	3.36 (2.00)	3.48 (1.95)	3.19 (2.06)	0.471
Hay fever n(%)				
No	91(26.4)	53 (25.9)	38 (27.1)	0.790
Yes	254 (73.6)	152 (74.2)	99 (72.9)	

Notes:

*p-value < 0.05 was determined as statistically significant

[1] Baseline RCAT score missing: n=7, all in comparator arm

INTERVENTION EFFECT ON COSTS

Annualised intervention cost was $349 per participant in the intervention arm. The intervention costs were estimated from training materials development, pharmacist payments and costs associated with items such as software licenses, tool development and hardware (Table 28-29). All participants in the comparator arm were assumed to have accessed the standard level of care. Even though there were differences in the mean costs between the two arms during the trial, these differences were not

statistically significant (Table 30). Thus, the mean costs of MBS (intervention, $2436 and comparator, $2496), PBS (intervention, $1599 and comparator, $1448) and the total costs (intervention, $4035 and comparator, $3943) were not statistically different between arms (Figure 27). Including the intervention costs, the overall annual total costs in the intervention arm were $4384 per participant.

Table 30: Budget summary for the Pharmacy Trial Program

Item Description		Costs	F/Y 17/18	F/Y 18/19	F/Y19/20	F/Y20/21
Training materials development and associated expenses	*Training material development including website hosting for 2 years (NAC and PSA)*	150000	150000	0	0	0
	Pharmacy resources (NAC and PSA)	30000	30000	0	0	0
Intervention	*Payment to pharmacies (Pharmacy Guild) $80/hr* – $120 per participant Intervention 280x120*	16040	0	0	16040	0
Other non-personnel Costs (software licenses, tool development, hardware etc.)	*Tablets for data collection intervention pharmacies $300 each x40*	20000	10167.14	3859.91	0	0
	Placebo Devices $100 each	4000	0	4000	0	0
Sub-total			190167.10	7859.91	16040	0
Actual total costs						214067.10
Inflated total costs						231418.80

Table 31: Intervention cost estimated for the intervention arm

	Total	Intervention
*Number of participants	381	221
Cost per year over 3 years of trial		71355.68
Cost (estimated) per participant per year of trial		322.88
Inflated cost per participant per arm over 3 years of trial		77139.61
Inflated cost (estimated) per participant per year of trial		349.05

Notes: *Number of participants were used from the baseline data.

The actual costs were over 3 years and not 4 years (F/Y20/21=0). Thus, average annual cost was estimated over 3 years.

Table 32: Cost summary of study participants during the trial

	Unindexed				Indexed			
Characteristic	**All**	**Intervention**	**Comparator**	***p*-value**	**All**	**Intervention**	**Comparator**	***p*-value**
Number of participants, n (%)	345[(1)] (100.0)	205 (59.4)	140 (40.6)		345 (100.0)	205 (59.4)	140 (40.6)	
MBS								
Mean (SD)	2409 (2911)	2385 (3056)	2443 (2694)	0.163	2460 (2975)	2436 (3126)	2496 (2750)	0.162
Median (IQR)	1556 (619, 2823)	1420 (597, 2823)	1813 (913, 2782)		1583 (635, 2872)	1445 (609, 2872)	1850 (930, 2831)	
PBS								
Mean (SD)	1501 (2695)	1561 (3060)	1414 (2058)	0.346	1537 (2770)	1599 (3149)	1448 (2103)	0.339
Median (IQR)	591 (88, 1725)	442 (64, 1665)	798 (122, 1751)		451 (65, 1762)	603 (93, 1699)	814 (124, 1792)	
MBS+PBS								
Mean (SD)	3910 (4662)	3946 (5107)	3857 (3939)	0.159	3997 (4776)	4035 (5238)	3943 (4024)	0.862
Median (IQR)	2285 (1021, 4699)	1885 (949, 4589)	2648 (1350, 4954)		2349 (1044, 4803)	1922 (977, 4715)	2706 (1373, 5079)	
Intervention costs		323	0			349	0	
Total cost (MBS+PBS+Intervention costs)	4102 (4667)	4269 (5107)	3857 (3939)		4205 (4781)	4384 (5238)	3943 (4024)	

Notes:

*p-value < 0.05 was determined as statistically significant.

†Annualised cost per person (AU$)

[†]All costs were actualised to account for year 2020 Australian dollars. Wilcoxon rank-sum test for median used as cost data was right-skewed of cost, and exact p-values reported.

[(1)] Full number=346. Missing, n=1 (0.3%).

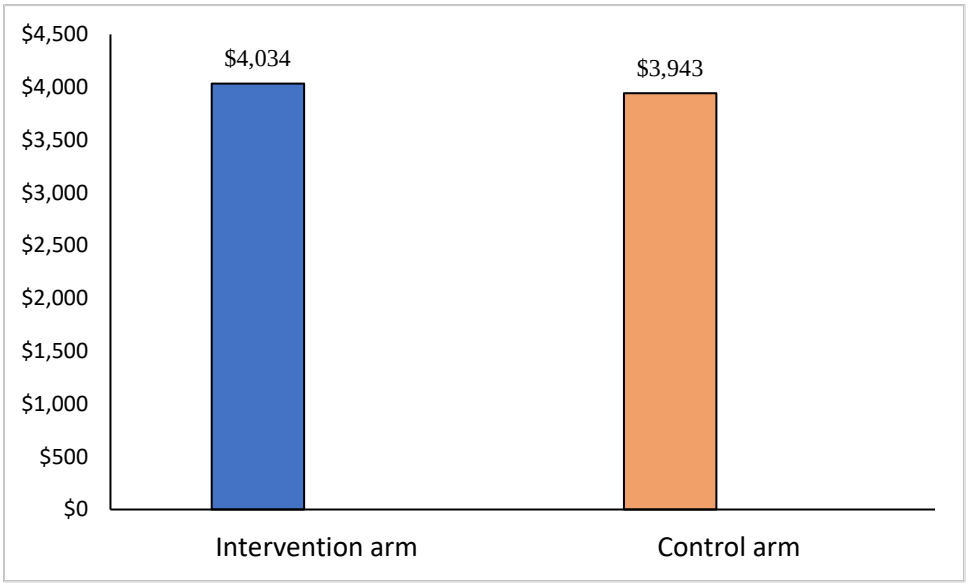
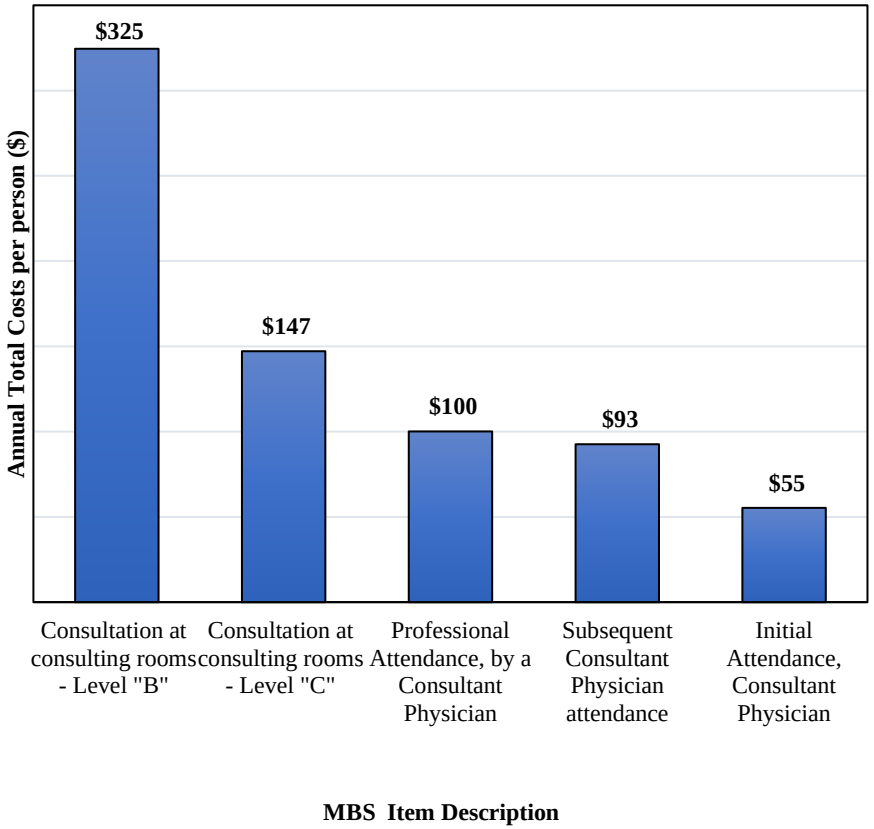


Figure 28: Average annual total cost per participant in trial arms

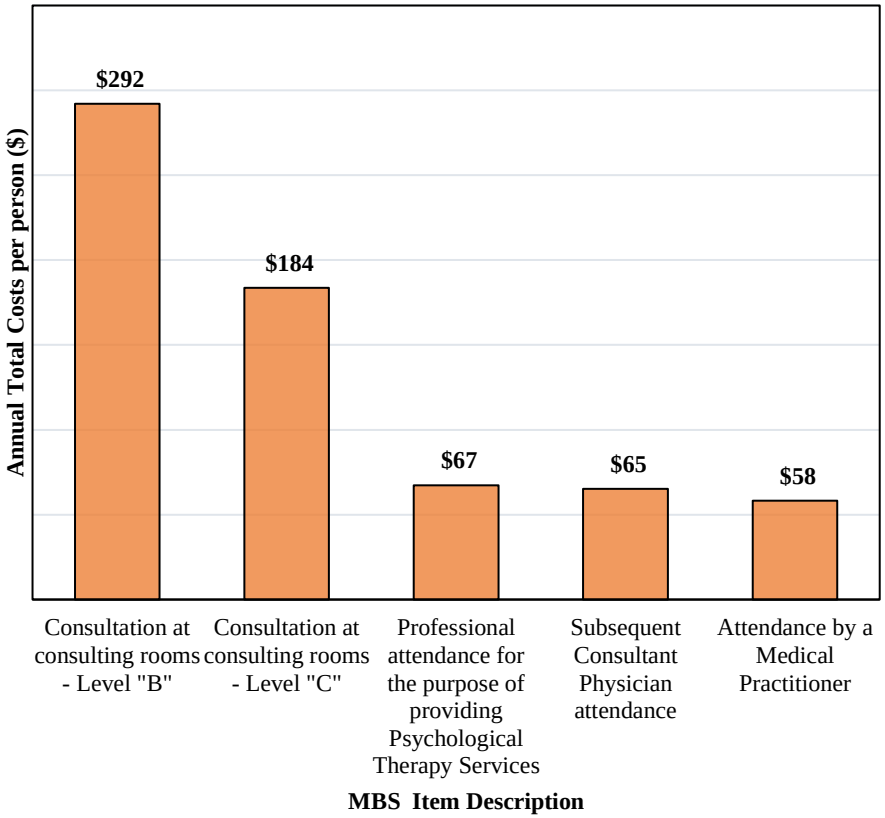
COSTLIEST AND MOST-USED MBS AND PBS ITEMS

Medical services and medication costs incurred over the one-year period are presented in Figure 28-30. These focused on the top five costliest and most used MBS and PBS items. The two costliest MBS items, consultation at consulting rooms (Level B and Level C[1)] were the same in both intervention and comparator arms. Together, these two items accounted for 28% and 26% of the total annual MBS cost of items incurred by intervention and comparator arms, respectively. While the annual MBS total cost per person at Level B was higher in the intervention arm ($325) compared with the comparator arm ($292), the costs at Level C were higher in the comparator arm (intervention, $147 and comparator, $184). Higher annual frequencies were observed in the intervention arm (Level B: n=1722; Level C: n=403) compared with the comparator arm (Level B: n=1057; and Level C: n=344). Even though the most frequently used PBS items were similar in both arms, with a higher frequency among the intervention arm, the costliest PBS items differed, and costs were higher among the comparators compared with the intervention arm. Thus, while adalimumab 40mg/0.8mL injection was ranked as the top costliest PBS item in the intervention arm, secukinumab 150mg/mL, injection was at the top for the comparator arm. Both arms had salbutamol 100mcg inhaler and fluticasone 250mcg.

[1]Consultation at a consulting room Level B (MBS item 23) denotes a professional (General Practitioners) attendances at a consulting room with a consultation lasting less than 20 minutes and a Level C (MBS item 36) is used for a consultation lasting at least 20 minutes and at most 40 minutes 107. Practitioners. RACoG. Medicare Benefits Schedule fee summary 2020 [Available from: https://www.racgp.org.au/running-a-practice/practice-resources/medicare/medicare-benefits-schedule-fee-summary.

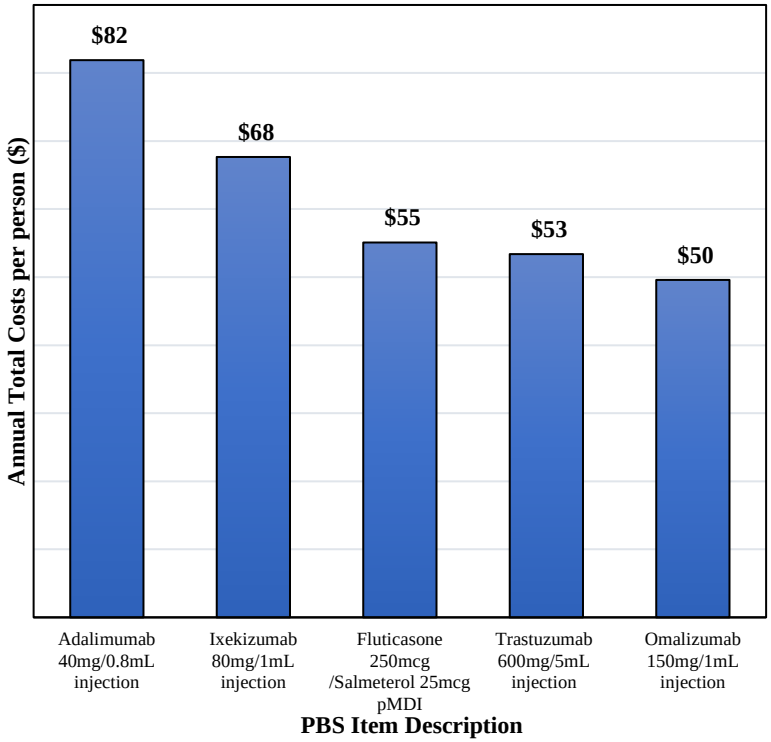


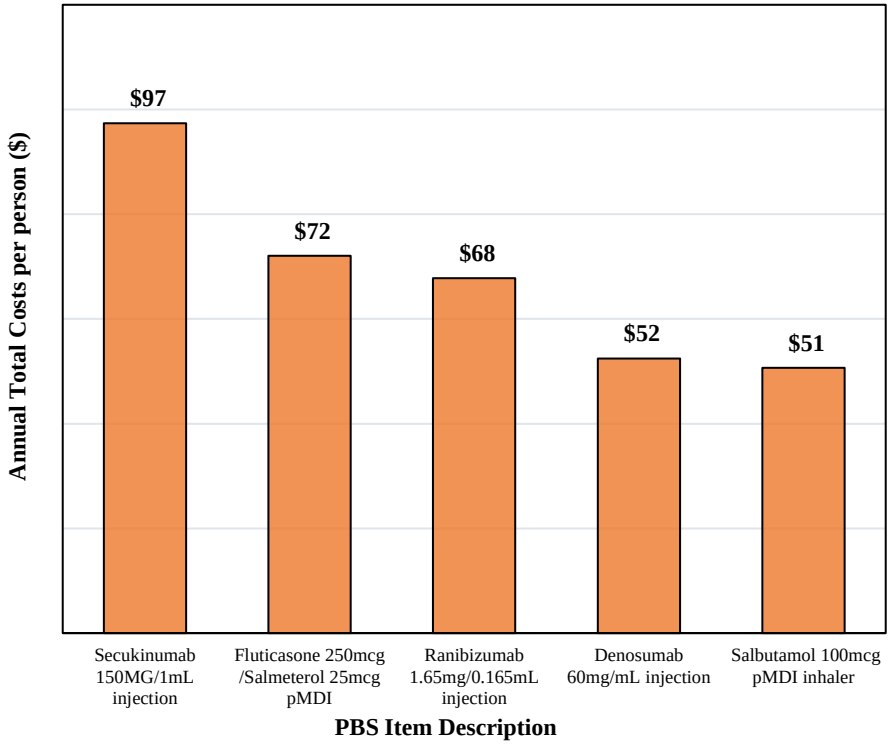
a) Intervention arm (n=205 participants)



b) Comparator arm (n=140 participants)

Figure 29: Top five costliest MBS items (services) used among the Intervention (n=205) and Comparator arm (n=140) participants. ***Estimated as the average annual costs per person per service. All costs were actualised to account for year 2020 Australian dollars. Consultation at a consulting room Level B (MBS item 23) denotes a professional (general practitioner) attendances at a consulting room with a consultation lasting less than 20 minutes and a Level C (MBS item 36) is used for a consultation lasting at least 20 minutes and at most 40 minutes(107).***

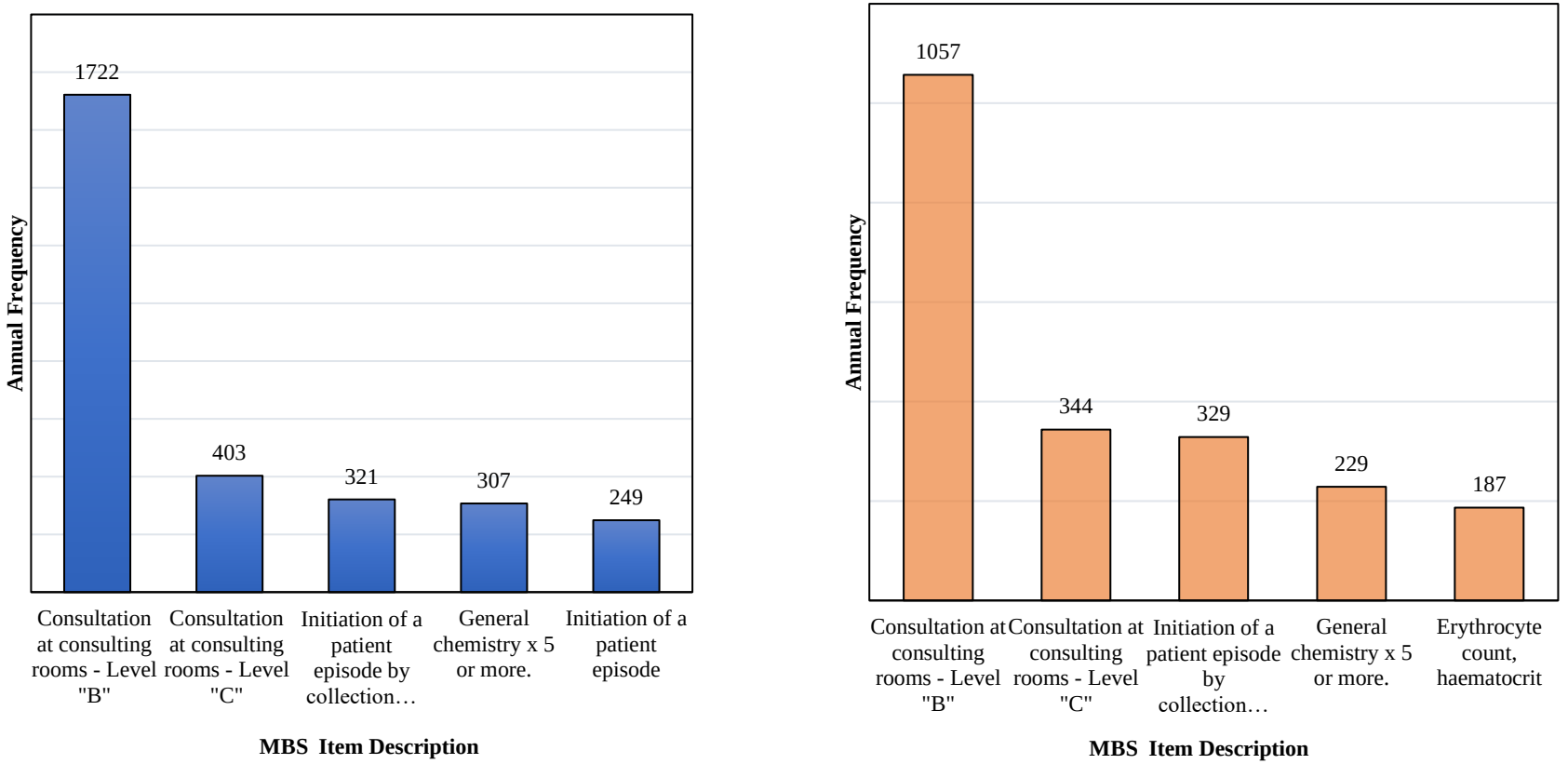




a) **Intervention arm (n=205 participants).** Listed as prescribed in descending order: adalimumab 40mg/0.8mL injection, ixekizumab 80mg/1mL injection, fluticasone 250mcg / salmeterol 25mcg combination pMDI inhaler, trastuzumab 600mg/5mL injection and omalizumab 150mg/1mL injection.

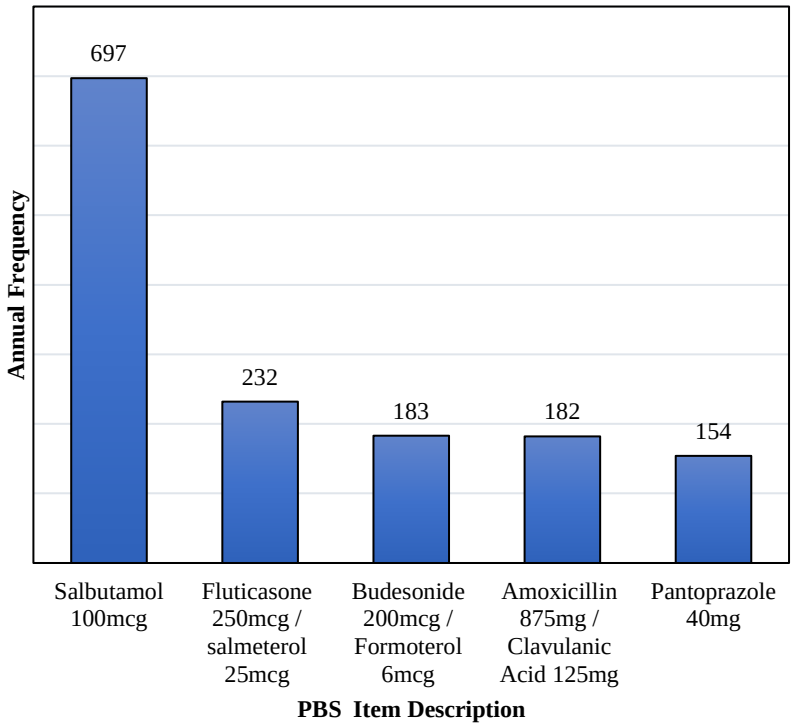
b) **Comparator Arm (n=140 participants).** Listed as prescribed in descending order: secukinumab 150MG/1mL injection, fluticasone 250mcg / salmeterol 25mcg combination pMDI inhaler, ranibizumab 1.65mg/0.165mL injection, denosumab 60mg/mL injection and salbutamol 100mcg pMDI inhaler.

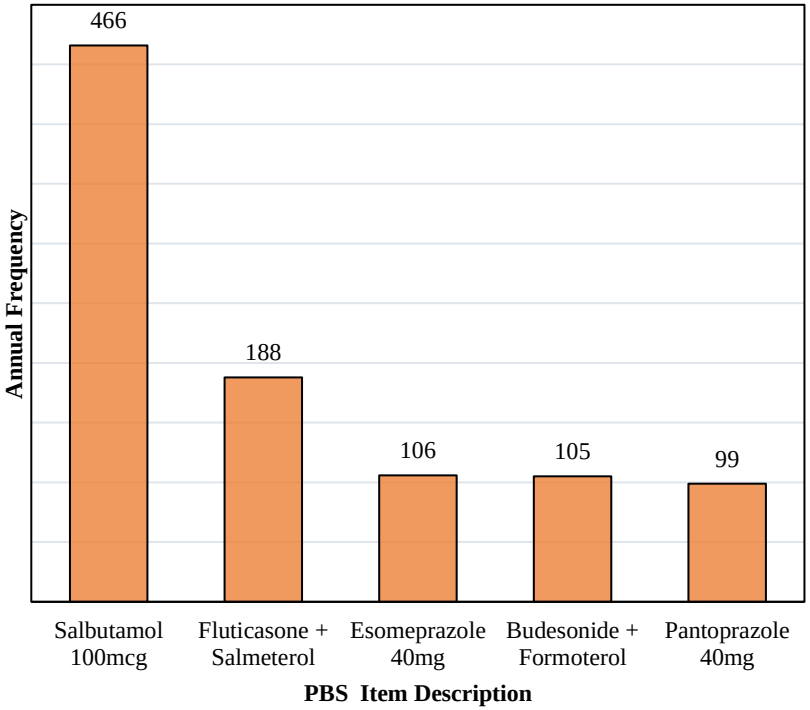
Figure 30: Top five costliest PBS items used among the Intervention (n=205) and Comparator arm (n=140) participants. ***Estimated as the average annual costs per person. All costs were actualised to account for year 2020 Australian dollars.***



a) Intervention arm (n=205 participants) **b) Comparator arm (n=140 participants)**

Figure 31: Top five most used MBS items (services) used among the Intervention (n=205) and Comparator arm (n=140) participants. ***Consultation at a consulting room Level B (MBS item 23) denotes a professional (general practitioner) attendances at a consulting room with a consultation lasting less than 20 minutes and a Level C (MBS item 36) is used for a consultation lasting at least 20 minutes and at most 40 minutes (107)***





a) **Intervention Arm (n=205 participants).** Listed as prescribed in descending order: salbutamol 100mcg pMDI inhaler, fluticasone 250mcg / salmeterol 25mcg combination pMDI inhaler, budesonide 200mcg / formoterol 6mcg combination turbuhaler, amoxicillin 875mg / clavulanic acid 125mg tablet, and pantoprazole 40mg tablet).

b) **Comparator arm (n=140 participants).** Listed as prescribed in descending order: salbutamol 100mcg pMDI inhaler, fluticasone 250mcg / salmeterol 25mcg combination pMDI inhaler, esomeprazole 20mg tablet, budesonide 200mcg / formoterol 6mcg combination turbuhaler and pantoprazole 40mg tablet

Figure 32: Five most-used PBS items (Services) among the Intervention (n=205) and Comparator arm (n=140) participants. Health Care Costs Pre-randomisation

HEALTH CARE COSTS PRE-RANDOMISATION

As a secondary analysis we looked at the costs incurred by participants in the 12 months preceding the trial to examine whether resource use observed in the trial was reflective of 'real life' practice. The most notable finding was that there was a significant change in mean annual total costs before and during the trial in the intervention arm participants. Total costs of per intervention participant was $5067 before the trial, during the trial this significantly decreased to $4035 per participant (p-value=0.02). This fall in costs was $1032 per participant. Over the same time period there was no significant change in mean annual costs for comparator participants ($3690 before vs $3943 after (p= 0.93)).

This fall in costs in the intervention arm occurred because participants in that arm incurred substantially higher costs ($5067) compared to comparator arm participants ($3690) in the corresponding pre-trial period. This was largely due to higher PBS costs ($2340 before vs $1599 after (p=.001)) and in particular the cost of hepatitis treatment (elbasvir 50mg/ grazoprevir 100mg tablets) in the intervention arm pre-trial. During this period, it was dispensed 3 times at a total cost of $65249.54 (unadjusted for inflation) and not dispensed at all during the trial. A possible reason is that participants are unlikely to enrol in a trial while on such treatment. As indicated in the primary economic analysis above, there is a subsequent convergence in intervention and comparator arm in MBS and PBS costs during the trial such that there we no statistically significant cost-offsets. Table 33: Cost summary of study participants (12 months before the trial)

	Unindexed				Indexed			
Characteristic	**All**	**Intervention**	**Control**	***P*-value**	**All**	**Intervention**	**Control**	***P*-value**
Number of participants, n (%)	345[(1)] (100)	205 (59.4)	140 (40.6)		345 (100)	205 (59.4)	140 (40.6)	
MBS-Schedule								
Mean (SD)	2403 (3269)	2628 (3874)	2074 (2062)	0.771	2494 (3393)	2726 (4021)	2154 (2136)	0.774
Median (IQR)	1530 (665, 2845)	1515 (665, 3057)	1576 (667, 2705)		1593 (694, 2996)	1581 (694, 3184)	1635 (691, 2791)	
PBS-Benefits								
Mean (SD)	1938 (5313)	2254 (6583)	1475 (2430)	0.617	2013 (5489)	2340 (6796)	1536 (2525)	0.619
Median (IQR)	615 (87, 1868)	534 (81, 1885)	650 (124, 1851)		638 (89, 1939)	560 (83, 1971)	675 (130, 1921)	
MBS+PBS								
Mean (SD)	4341 (7575)	4882 (9343)	3549 (3580)	0.943	4508 (7831)	5067 (9656)	3690 (3716)	0.946

Characteristic	Unindexed				Indexed			
	All	Intervention	Control	*P*-value	All	Intervention	Control	*P*-value
Median (IQR)	2460 (1060, 4946)	2436 (1040, 5079)	2474 (1104, 4792)		2540 (1084, 5132)	2502 (1084, 5239)	2556 (1149, 4995)	

Notes:

*P-value <0.05 was determined as statistically significant.

†Annualised cost per person (AU$)

†All costs were actualised to account for year 2020 Australian dollars. Wilcoxon rank-sum test for median used as cost data was right-skewed of cost, and exact p-values reported.

(1) Full number=346. Missing, n=1 (0.3%).

Table 34: Cost comparison for before and after the 12 months trial (Only indexed/inflated costs)

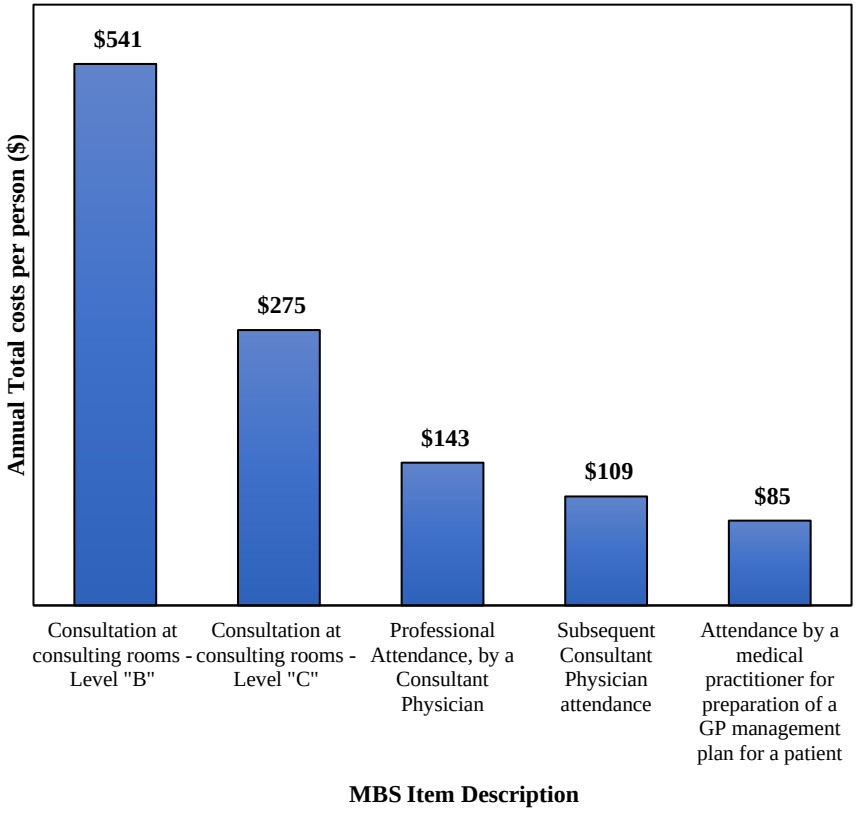
Characteristic	All			Intervention			Control		
	Mean (SD)			Mean (SD)			Mean (SD)		
	Before	After	*P*-value	Before	After	*P*-value	Before	After	*P*-value
MBS-Schedule	2494 (3393)	2460 (2975)	0.689	2726 (4021)	2436 (3126)	0.105	2154 (2136)	2496 (2750)	0.400
PBS-Benefits	2013 (5489)	1537 (2770)	<0.001*	2340 (6796)	1599 (3149)	0.001*	1536 (2525)	1448 (2103)	0.052
Total Costs (MBS+PBS)	4508 (7831)	3997 (4776)	0.140	5067 (9656)	4035 (5238)	0.020*	3690 (3716)	3943 (4024)	0.928

Notes:

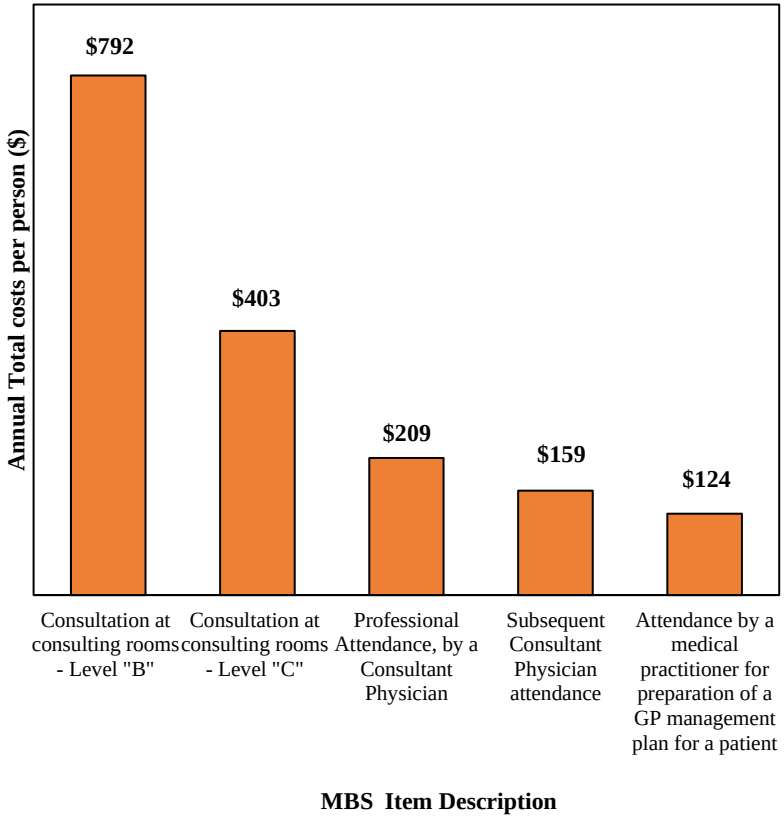
*P-value <0.05 was determined as statistically significant.

†All costs were actualised to account for year 2020 Australian dollars.

Wilcoxon matched-pairs signed-rank test used as cost data was right-skewed of cost, and exact p-values report.

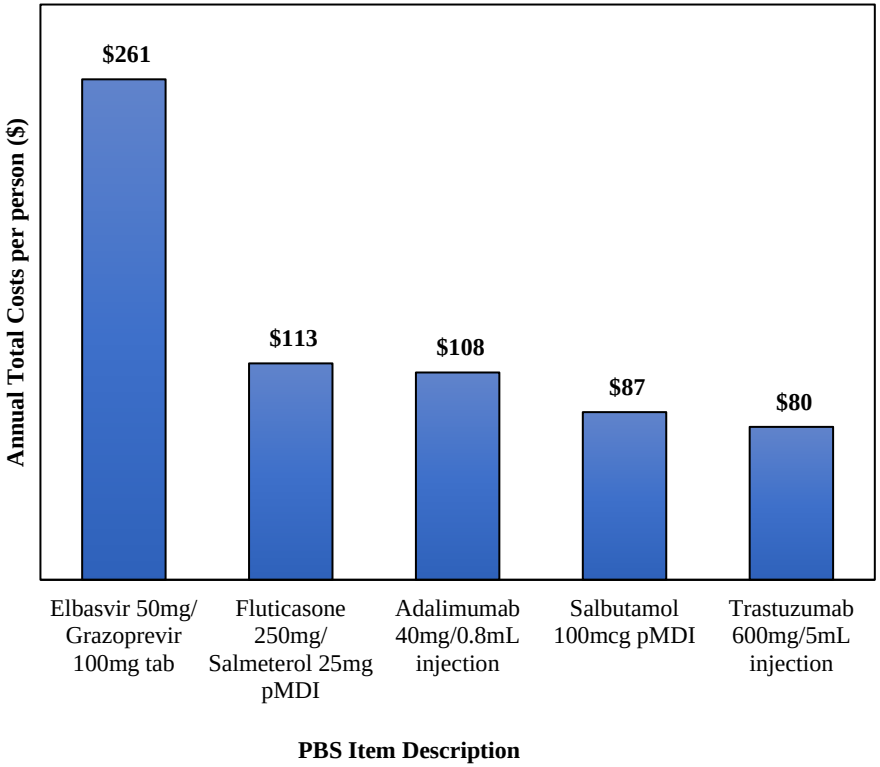


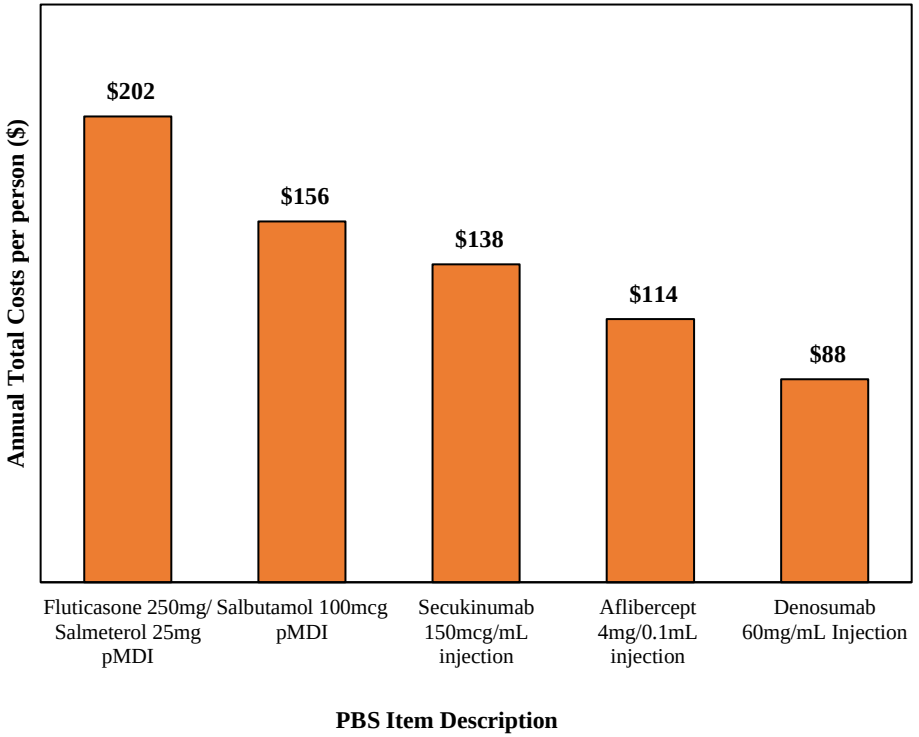
a) **Intervention arm (n=205 participants)**



b) **Comparator arm (n=140 participants)**

Figure 33: Top five costliest MBS items (services) used among the Intervention (n=205) and Comparator arm (n=140) participants before the trial. ***Estimated as the average annual costs per person per service. All costs were actualised to account for year 2020 Australian dollars. Consultation at a consulting room Level B (MBS item 23) denotes a professional (general practitioner) attendances at a consulting room with a consultation lasting less than 20 minutes and a Level C (MBS item 36) is used for a consultation lasting at least 20 minutes and at most 40 minutes (107).***

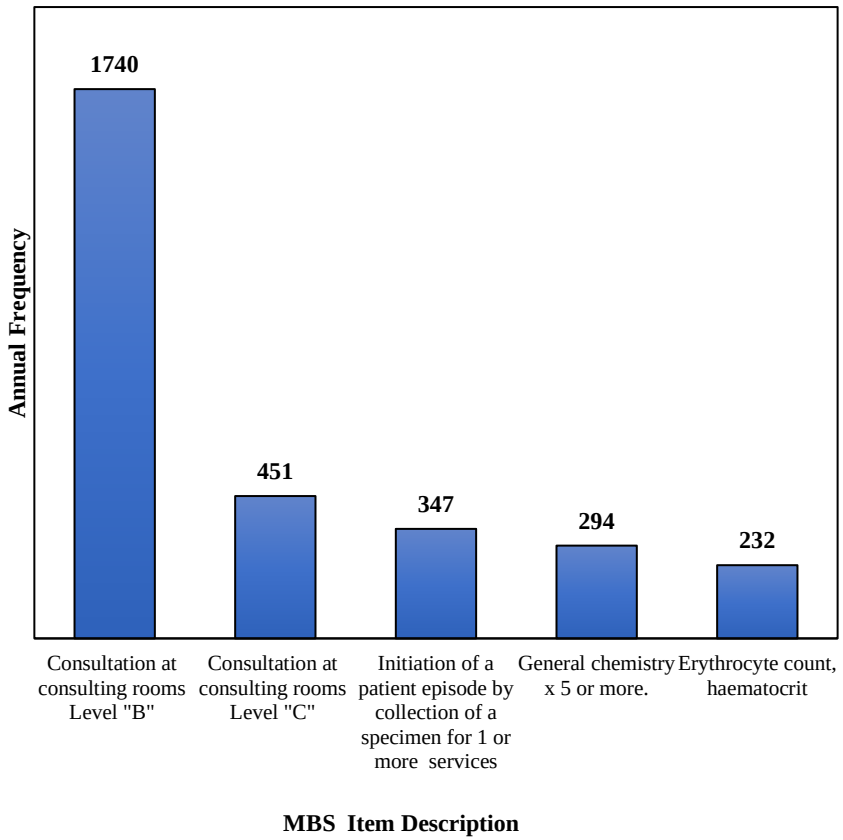




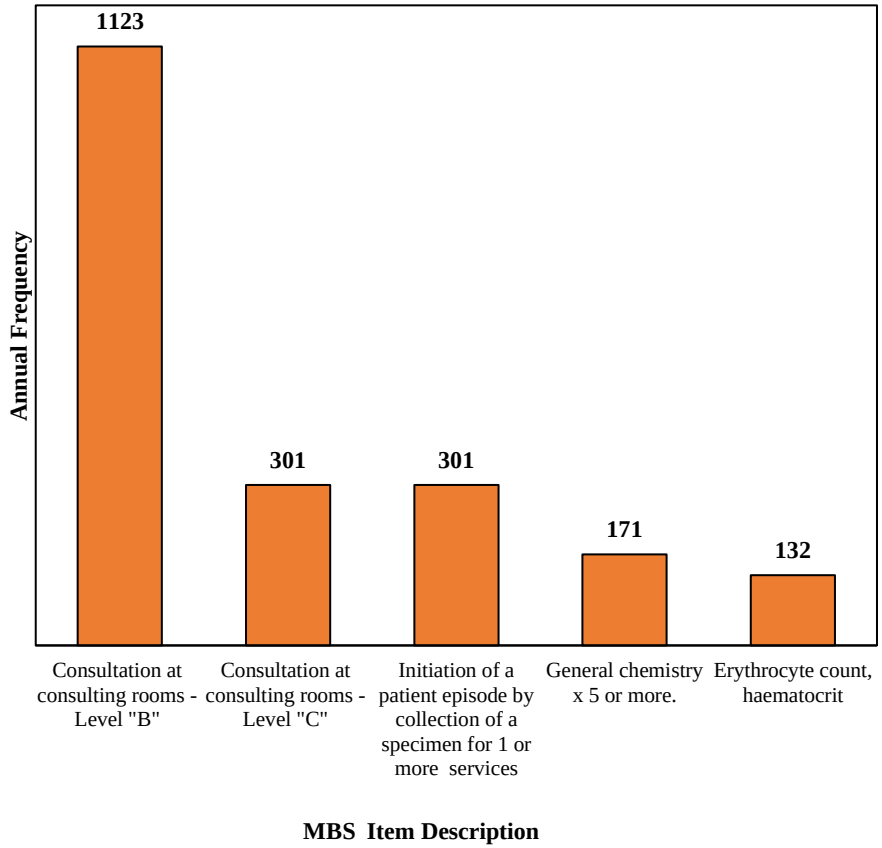
a) **Intervention arm (n=205 participants).** Listed as prescribed in descending order: elbasvir 50mg/ grazoprevir 100mg tablets, fluticasone 250mg/ salmeterol 25mg combination pMDI inhaler, adalimumab 40mg/0.8mL injection, salbutamol 100mcg pMDI and trastuzumab 600mg/5mL injection

b) **Comparator arm (n=140 participants).** Listed as prescribed in descending order: fluticasone 250mg/ salmeterol 25mg combination pMDI inhaler, salbutamol 100mcg pMDI inhaler, secukinumab 150mcg/mL injection, aflibercept 4mg/0.1mL injection and denosumab 60mg/mL injection.

Figure 34: Top five costliest PBS items used among the Intervention arm (n=205) and Comparator arm (n=140) participants before the trial. ***estimated as the average annual costs per person. All costs were actualised to account for year 2020 Australian dollars.***

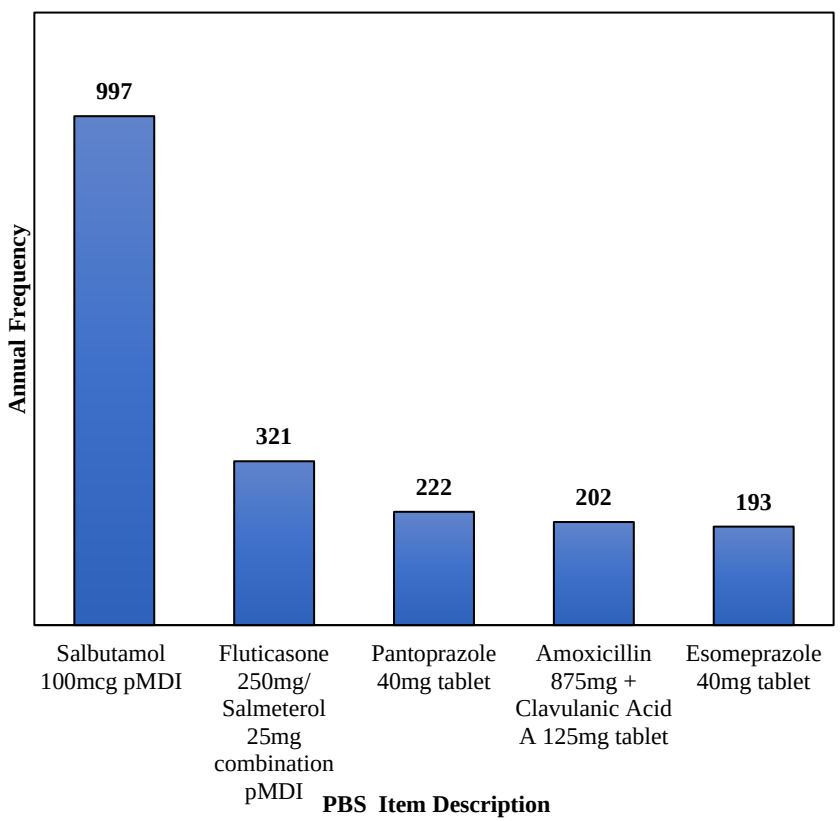


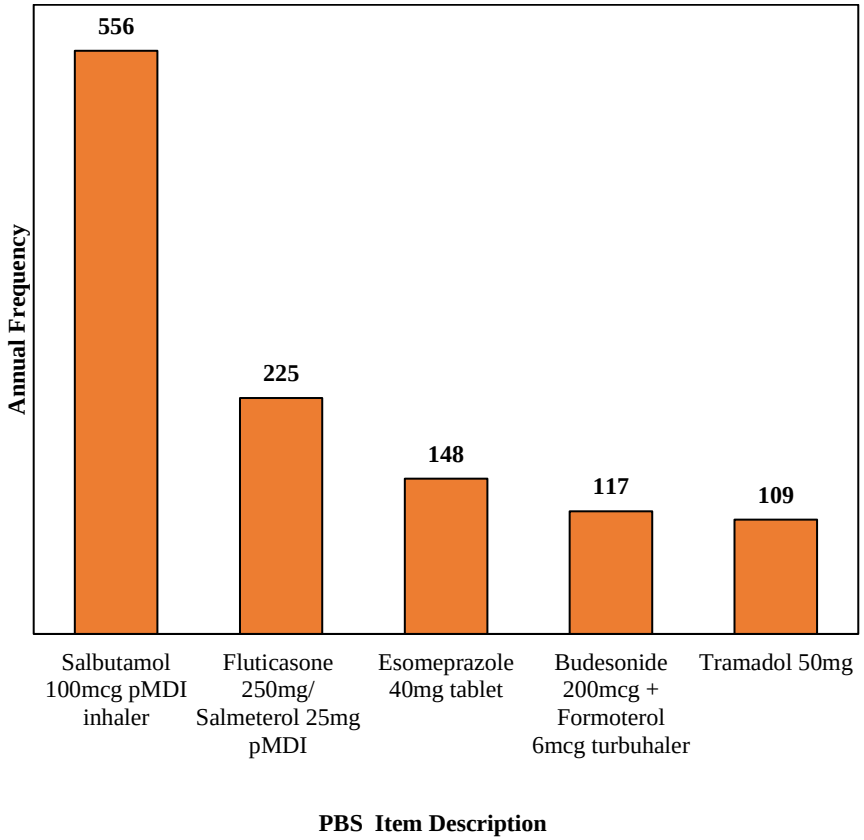
a) **Intervention arm (n=205 participants)**



b) **Comparator arm (n=140 participants)**

Figure 35: Top five most used MBS items (services) used among the Intervention (n=205) and Comparator arm (n=140) participants before the trial. ***Consultation at a consulting room Level B (MBS item 23) denotes a professional (general practitioner) attendances at a consulting room with a consultation lasting less than 20 minutes and a Level C (MBS item 36) is used for a consultation lasting at least 20 minutes and at most 40 minutes (107).***





a) **Intervention arm (n=205 participants)**: Listed as prescribed in descending order: salbutamol 100mcg pMDI inhaler, fluticasone 250mg/ salmeterol 25mg combination pMDI inhaler, pantoprazole 40mg tablet, amoxicillin 875mg + clavulanic Acid A 125mg tablet, and esomeprazole 40mg tablet.

b) **Comparator arm (n=140 participants)**: Listed as prescribed in descending order: salbutamol 100mcg pMDI inhaler, fluticasone 250mg/ salmeterol 25mg combination pMDI inhaler, esomeprazole 40mg tablet, budesonide 200mcg + formoterol 6mcg turbuhaler and tramadol 50mg capsule.

Figure 36: Top five most used PBS items (services) used among the Intervention (n=205) and Comparator arm (n=140) participants before the trial.

LIMITATIONS AND ASSUMPTIONS:

1. The analysis of health care costs incurred during the 12 months of the trial only includes those recorded in the MBS and PBS data and excludes hospital costs, and non-health sector costs (e.g. time off work, travel costs)
2. Costing relies on PBS capturing all medications costs. Cost estimations do not include drugs purchased without a prescription, alternative therapies or non-prescribed over the counter medications.
3. Likewise, costing does not capture health care use that was not claimed on the MBS (e.g some allied health services)
4. From 381 study participants, 345 had full MBS and PBS data and were included in this analysis. Of the 36 participants with missing values, 16 were in the intervention arm and 20 in the comparator arm. Given that less than 10% of the sample were missing, with similar numbers in intervention and comparator arms, no statistical adjustments were made regarding missing data.
5. It was assumed that payments to pharmacists to participate in the intervention represented compensation to pharmacists for the time spent on training and participation. To cost these items separately along with including the compensation payments would entail a double-counting of this item of resource use.

CONCLUSION

This study has shown that substantial direct healthcare costs and cost burden are associated with asthma in the Australian population, and this highlights the importance of asthma control and prevention. The cost analysis suggests that the intervention costs around $349 per participant. There was no significant difference in costs between the intervention and comparator arms during the trial and as such no estimated cost-offsets. A secondary analysis revealed that, there was a significant reduction in costs for the intervention arm during the trial compared to the 12 months prior to the trial. No such fall in costs were observed in the comparator arm. The fall in costs in the intervention arm was due to the substantially higher costs incurred by patients in that arm in the 12 months before the trial ($5067) compared to costs incurred by comparator arm participants in the corresponding pre-trial period. Evidence in this research suggests the need to continue the search for sustainable effective and cost-saving interventions for asthma control as this could reduce asthma-attributable costs in Australia.

SECTION E: FINANCIAL IMPLICATIONS

It is envisaged that the Pharmacy Asthma Service will be of similar benefit to all Australian adults with poorly controlled asthma. The current population with asthma in Australia is 2.7 million (1) and the number of patients with poorly controlled asthma (50% = 1.35 million) (2) and those who are adults (~80%= 1.08 million) (3) and excluding those who might also have COPD (20%), so 864,000 remain (4). With the assumption that only half of these would potentially use the service, we conservatively estimate that 432,000 people with asthma would benefit from the implementation of a Pharmacy Asthma Service.

The cost of the Pharmacy Asthma Service was calculated as $349 per participant. The cost to deliver the 12-month service to 432,000 participants would be $151M.

In 2015, using an estimated prevalence of 9.94%, the estimated all-costs comprising both direct and indirect costs of asthma in Australia was $28 billion including $1.2 billion healthcare costs (103). We do not have Australian data on the size of the burden of uncontrolled asthma and there are no prior Australian data available to assess the cost saving/impact of having asthma patients under control. Most measures used in the Australian context are based on quality of life. There are Canadian data available for comparison. In Canada, the medical cost saving (inpatient and outpatient care and medication) associated with getting asthma under control was $326 per patient (108). These savings are related to direct medical costs and do not include the significant savings related to work productivity as work days lost are reduced and the benefits associated with an improved patient quality of life when a patient's asthma is well controlled.

With an increasing prevalence, and potentially health resource utilisation, costs are more likely to be higher in spite of the many developed intervention modalities. Further investigation is required to identify patient characteristics that could be contributing to high annual total costs such as age, education, employment, prior hospital admissions or exacerbations to guide future more targeted and efficient use of any service to maximise return on MBS investments in patients.

APPENDIX

APPENDIX A: PHARMACISTS' EXPERIENCE OF AND PERSPECTIVES ABOUT RECRUITING PATIENTS IN PHARMACY ASTHMA SERVICE

The published paper is available via https://www.sciencedirect.com/science/article/pii/S1551741120301236.

APPENDIX B: INVESTIGATIVE TEAM PRIOR RESEARCH

Research conducted by the investigative team over the past decade in this field utilised three approaches: comprehensive disease state management (DSM), streamlined DSM and primary care collaboration. A selection of work has been highlighted in Table 1.

A. Comprehensive DSM: This approach involves identifying people with poor asthma control and providing comprehensive management and monitoring in the community pharmacy. In this approach, the patient's management provided by the pharmacist includes all aspects of asthma treatment and control. These can include asthma history taking, mapping patients' asthma control, checking lung function through spirometry, environment management advice to reduce trigger exposure, medication review to check adherence and inhaler skills, recommendations to GPs to provide written Asthma Action Plans, asthma education and coaching for appropriate asthma self- management behaviours. The results and recommendations that involve medical intervention are provided to a patient's GP for further action, so that the asthma primary care loop is maintained.

The initial Australian DSM model was developed by investigators Bandana Saini, Ines Krass and Carol Armour, at The University of Sydney (109). Tested in a small parallel group quasi-experimental trial the results indicated significant effect of pharmacist provided DSM services on asthma control, inhaler use, appropriateness of therapy, adherence and patient quality of life (109). This model was then further tested in a Department of Health-funded large-scale multi-site RCT (3rd Community Pharmacy Agreement) and an implementation trial (4th Community Pharmacy Agreement) in Australia, and was found to be both clinically and cost effective (47, 49, 50). As a result of this body of work, pharmacists' roles are particularly highlighted in the national asthma guidelines (16).

B. Streamlined DSM: The second approach has been to focus on specific problematic elements in asthma management. Using a systematic method of identifying those with poor asthma control as part of a pharmacy-based asthma intervention, the research team (Bandana Saini, Carol Armour, Ines Krass, Lynne Emmerton and Sinthia Bosnic-Anticevich) demonstrated that patients who smoked, had incorrect inhaler technique or low adherence with medications were more likely to have poor asthma control (18). Clearly inhaler skills and adherence are important elements of self-management education that pharmacists providing asthma services should focus on.

Sinthia Bosnic-Anticevich and her team at the Woolcock Institute of Medical Research have conducted a robust corpus of research on inhaler use, showcasing pharmacists' effectiveness in coaching patients to improve inhaler skills and thereby achieve better asthma control (65, 110). This research has provided evidence-based pathways to inhaler technique education (e.g. a teach-back method) and determined the need for repeated education provision. The evidence generated by this team has been incorporated into the National Asthma Guidelines.

Researcher Bandana Saini (111) and Sinthia Bosnic-Anticevich (36, 43, 44) have also explored pharmacy roles in comorbid conditions such as allergic rhinitis (111). In a previous 4CPA project, pharmacists were trained to identify people with AR, provide rhinitis-related education, and coach patients to adopt rhinitis symptom-control behaviours such as adherence to topical corticosteroids (111).

C. Primary care collaboration: Sinthia Bosnic-Anticevich and Carol Armour have undertaken significant research to develop and test inter-professional models of asthma care including GPs, pharmacists and practice nurses (112, 113). Bonnie Bereznicki from the University of Tasmania has used a data-mining approach to identify people with poorly managed asthma as evidenced by over-supply of asthma reliever medications (refill history) to address asthma management using a GP-pharmacist communication path with highly positive results (67). Luke Bereznicki and colleagues have also utilised this approach to improve medication adherence and disease outcomes in people with

hypertension (114). Bandana Saini and Carol Armour have also recently explored how non-dispensing pharmacists can facilitate improved asthma outcomes in the General Practice Pharmacist model (115, 116).

The investigator team have also conducted research in special needs populations such as children (117-121), those in regional/rural settings (122), and those living with disability (123), with a view to understanding needs and improving asthma care. In patient preference modelling and satisfaction surveys, patients have expressed a strong preference for pharmacists' services (124, 125). The investigative team have also explored the asthma experience of culturally and linguistically diverse populations in Australia (20, 21).

Appendix Table B-1: Evidence supporting the service

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
DISEASE STATE MANAGEMENT				
Multisite cluster RCT. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S, Krass I, Emmerton L, Saini B	Pharmacy Asthma Care Program (PACP) improves outcomes for patients in the community	A pharmacist-delivered DSM service (n=186) compared to usual practice (n=165), using asthma control as the primary outcome. The intervention resulted in improved asthma control: patients receiving the intervention were 2.7 times more likely to improve from "severe" to "not severe" than control patients (OR 2.68, 95% CI 1.64 to 4.37); p<0.001).	https://www.ncbi.nlm.nih.gov/pubmed/17251316	2006

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
Cost effectiveness analyses study. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S, Krass I, Emmerton L and Saini B	Cost-effectiveness analysis of a pharmacy asthma care program in Australia	A Markov model applied to data in the study above estimated the cost effectiveness of pharmacist delivered asthma DSM over five years from the Australian healthcare system. Five years following baseline review, the model generated 0.131 additional quality-adjusted life-years (QALYs), at an additional net cost of $A623, resulting in costs per QALY gained of $A4753.	http://link.springer.com/article/10.2165/00115677-200715060-00006	2007
Cluster RCT Implementation trial. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S, Emmerton L, Krass I and Saini B	Feasibility and effectiveness of an evidence-based asthma service in Australian community pharmacies: a pragmatic cluster randomized trial.	Implementation trial of the model tested above. Ninety-six pharmacists enrolled 570 patients, with 398 (70%) completing. Asthma control significantly improved with service, (good/fair control 29% and 21% at baseline, 61% and 59% at end, p = .791). Significant improvements were also evident in the inhaler technique and adherence.	https://www.ncbi.nlm.nih.gov/pubmed/23270495	2013

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
IDENTIFYING FACTORS FOR POOR CONTROL IN PHARMACY PATIENTS WITH ASTHMA				
As above. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S, Emmerton L, Krass I and Saini B	Using the community pharmacy to identify patients at risk of poor asthma control and factors which contribute to this poor control.	Data extracted from the above trial for a logistic regression exploring predictors of poor asthma control in patients. Data indicated that 437 (77%) recruited patients had poor asthma control. Of the 570 patients, 19% had an action plan, and only 17-28% used their inhaler device correctly. 90% had their ICS or ICS/LABA dispensed <6 times in the previous six months. Those who smoked, had incorrect inhaler technique or low adherence were more likely to have poor asthma control.	https://www.ncbi.nlm.nih.gov/pubmed/21942306	2011
ADDRESSING ASTHMA MANAGEMENT GAPS IN RURAL REGIONAL SETTING				
A parallel group controlled repeated measures study. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S, Krass I and Saini B	An evaluation of a community pharmacy-based rural asthma management service.	In central west NSW, 51 and 39 patients were recruited by intervention (asthma DSM) and control pharmacists respectively. The intervention patient had a significant reduction in the asthma severity scores (7.9 +/- 2.6 versus 10.4 +/- 2.6, p <0.001) and in the risk of non-adherence to medication scores (1.6 +/- 0.7 versus 2.3 +/- 1.1, p <0.001) at six-month close-out.	www.ncbi.nlm.nih.gov/pubmed/18318852	2008

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
PATIENT PREFERENCE FOR PHARMACIST ASTHMA SERVICE ELEMENTS: HEALTH ECONOMIC MODELLING				
Discrete Choice Experiment. Authors who are investigators in this trial application: Armour C, and Saini B	Patient preferences for community pharmacy asthma services: a discrete choice experiment.	Asthma service levels provided by pharmacies were tested for patient preference in a discrete choice experiment. Patients considered all attributes of the service to be important when making a choice and especially valued provision of lung function testing and frequent service visits.	https://www.ncbi.nlm.nih.gov/pubmed/22823521	2012
FOCUSING ON DISCRETE ELEMENTS OF ASTHMA DSM				
Cluster RCT. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S	Evaluation of a novel educational strategy, including inhaler-based reminder labels, to improve asthma inhaler technique.	Tested usual pharmacy care vs focussed inhaler education. At baseline, patients (active: 53, control: 44) demonstrated poor inhaler technique (mean+/-S.D. score out of 9, 5.7+/-1.6). At six months, improvement in inhaler technique score was significantly greater in active cf. control patients (2.8+/-1.6 cf. 0.9+/-1.4, p<0.001), and asthma severity was significantly improved (p=0.015).	www.sciencedirect.com/science/article/pii/S0738399108000141	2007

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
Cluster RCT. Authors who are investigators in this trial application: Armour C, Bosnic-Anticevich S	Improved asthma outcomes with a simple inhaler technique intervention by community pharmacists.	Tested pharmacist provided inhaler education versus control. In 97/116 completers, there was a significant difference in the proportion of Turbuhaler and Diskus users in the intervention group who demonstrated correct technique after six months compared with the control group (Turbuhaler: 10/20 [50%] vs 2/14 [14%], p= 0.032; Diskus: 23/29 [79%] vs 3/21 [14%], p <0.001, $\chi 2$ test).	https://www.ncbi.nlm.nih.gov/pubmed/17433831	2008
DATA MINING AND GP COLLABORATION APPROACHES				
RCT. Author who is an investigator in this trial application: Bereznicki B	Data-mining of medication records to improve asthma management.	Data mining of dispensing records for asthma patients followed by education and referral to GPs in the intervention group, versus usual care in the control group. 35 pharmacies completed the study (702 intervention and 849 control patients). The intervention resulted in a threefold increase in the preventer-to-reliever ratio.	http://www.ncbi.nlm.nih.gov/pubmed/18601636	2008

Type of study design*	Title of journal article or research project	Short description of research (max 50 words)**	Website link to journal article or research (if available)	Date of publication ***
RCT. Author who is an investigator in this trial application: Bereznicki B	Pharmacist-initiated general practitioner referral of patients with poor asthma management.	Same study as listed directly above, describing patient-reported outcomes. Intervention patients' asthma control and asthma-related quality of life scores at 6 six months were significantly higher compared to the control patients (p <0.01 and p <0.05, respectively).	http://www.ncbi.nlm.nih.gov/pubmed/18679820	2008
RCT. Author who is an investigator in this trial application: Bereznicki B	Uptake and effectiveness of a community pharmacy intervention programme to improve asthma management	Data mining of dispensing records to identify patients with poor asthma management. 71 pharmacies were randomised to perform either a mailed or face-to-face intervention (education plus GP referral), matching patients received usual care. 1483 patients were included. Fewer face-to-face interventions were offered than mailed interventions (66.6% vs. 89.4%, respectively, P <0.0001). There were significant improvements in the preventer-to-reliever ratio after the intervention (P <0.0001).	http://www.ncbi.nlm.nih.gov/pubmed/23437933	2013

APPENDIX C: IMPLEMENTATION TEAM AND ROLES

Appendix Table C-1: Members and roles of the implementation team

Organisation Legal name	ABN	Role in consortium
Woolcock Institute of Medical Research	88 002 198 905	**Lead agency and contract signatory. Management of the project overall project.** ***Professor Carol Armour and Associate Professor Sinthia Bosnic-Anticevich located here.***
University of Sydney	15211513464	**Pharmacy academics experienced with asthma projects – contribute to project design and running of protocol and data analysis.** ***Professor Ines Krass and Professor Bandana Saini located here.***
Curtin University	99143842569	**Pharmacy academic experienced with asthma projects – contribute to project design and running of protocol and data gathering. Management of project in WA.** ***Professor Lynne Emmerton located here.***
University of Tasmania	30764374782	**Pharmacy academics experienced with asthma projects contribute to project design and running of protocol and data gathering. Management of project in Tasmania.** ***Professor Luke Bereznicki and Dr Bonnie Bereznicki located here.***
National Asthma Council (NAC)	61058044634	**Provide input into the training and implementation strategy. Provision of resources.** ***Siobhan Brophy located here.***
Pharmacy Guild of Australia (Guild)	84 519 669 143	**Recruit pharmacists, pay pharmacists for completion. Provide help and support for development of the pharmacy software. Provide input into the training and implementation strategy.** ***Rebecca Segrott located here.***
Pharmaceutical Society of Australia (PSA)	**49008532072**	**Provide input into the training and implementation strategy.** ***Naomi Weir located here.***

APPENDIX D: ORIGINALLY APPROVED PICO

Appendix Table D-1: Original approved grant PICO

Component	Description
Patients	The target population for the study comprises of individuals ≥18 years of age with poorly controlled asthma. Eligibility criteria: • ACQ score ≥1.5 (indicative of poorly controlled asthma) (ACQ=Asthma Control Questionnaire) • Able to communicate with the pharmacist in English • A regular client of the pharmacy (receiving asthma medications from that pharmacy for the previous 12 months) • Managing their own medications (as judged by the pharmacist) The following exclusion criteria will apply, as determined by the pharmacist: • High dependence on medical care (5 or more morbidities with specialist care) • Unable to manage own medication • A confirmed diagnosis of COPD (as reported by the patient) • Terminal illness The feasibility of patient recruitment using these criteria has already been demonstrated by investigators CA, BS, SBA, LE and IK in several previous trials (Armour et al, 2007, Armour et al., 2011).
Intervention	**Overview of intervention:** The intervention (The Pharmacy Asthma Service) is a simpler version of a comprehensive evidence-based pharmacist-delivered intervention for patients with poorly controlled asthma (Armour et al., 2007). The Pharmacy Asthma Service targets three key factors associated with poorly controlled asthma: • Suboptimal adherence characterised by underuse of preventer medication and/or over use of reliever medication (as defined in the National Asthma Handbook), • Suboptimal inhaler technique and/ or • Uncontrolled allergic rhinitis. To deliver the intervention the pharmacist will undertake three private consultations with the individual over a period of 12 months: at baseline, one month and twelve months with one telephone follow-up at six months to monitor progress and identify potential risks. These patients will comprise the intervention arm.

Component	Description
	Note: For all other possible causes of poorly controlled asthma, the patient will be referred to their GP and will not receive the intervention. **Detailed description of intervention:** The Pharmacy Asthma Service intervention involves an initial assessment of service eligibility using the ACQ tool (Asthma Control Questionnaire). • If ACQ score ≥1.5 the individual will be invited to participate in the service and if they agree they will be given a Patient Information Sheet about the project (PIS) and asked to sign two consent forms (study consent and a separate Medicare consent form). • To deliver the intervention the pharmacist will undertake 3 private consultations with the individual over a period of 12 months; baseline, 1-month and 12-month follow-up. The pharmacist will also contact the patient by telephone at 6 months. **In the initial/ baseline visit the pharmacist will:** • Assess Asthma related Quality of Life (QOL). • Review short-acting β2 agonist use. • Assess asthma medication adherence with the Brief Medicine Questionnaire (BMQ), and using the dispensed medication history from the previous 12 months, then address any issues identified. • Assess and correct inhaler technique. • Assess allergic rhinitis control Rhinitis Control Assessment Test (RCAT) and recommend appropriate therapy/refer to the General Practitioner (GP) as appropriate. • Use the Short Form 12 (SF12) QOL for economic evaluation • Ask about Action Plan ownership and prompt to obtain an asthma action plan from their GP (if the individual does not already have one) • Undertake collaborative goal setting to help the patient set 2–3 SMART goals to improve asthma control. • Download preventer medication dispensing over the previous 12 months. **At the 1-month follow-up the pharmacist will:** • Reassess asthma control (ACQ). • Remeasure Asthma related QOL • Reassess Inhaler technique • Review SABA use • Assess allergic rhinitis control if appropriate • Check on Asthma Action Plan ownership (if still not then refer with a draft to GP) • Review goals from the baseline visit and help the individual to commit to further goals to improve asthma control.

Component	Description
	At 6 months the pharmacist will contact the patient by phone and will: • Reassess asthma control (ACQ) • Review goals set at last visit • Ask if there are any issues to address **At the 12-month follow-up the pharmacist will:** • Reassess asthma control (ACQ) • Reassess asthma medication adherence (BMQ + dispensing history; see below) • Assess asthma-related QOL • Reassess Inhaler technique • Record action plan ownership • Assess allergic rhinitis control if appropriate • Use the SF12 for economic evaluation • Review short-acting β2 agonists use • Download preventer dispensing over the previous 12 months. **Generation of goals and appointment card.** Software, which will guide the pharmacist in the provision of the intervention and data collection, via the Guildlink platform will be provided to pharmacists. Currently this software is used by over 90% of pharmacies nationally, and can be made available for the trial to non-Guild members. The Guildlink software will enable the production of a report to be provided to the individual recording, the agreed goals and next appointment and any other recommendations. A separate GP report/referral will also be generated and given to the individual.
Comparator	There will be two comparator groups: **1. Group B – Asthma minimal intervention Pharmacy Group.** A group of patients with asthma will have their asthma control assessed (ACQ) by the pharmacist and those identified as having poorly controlled asthma (ACQ score ≥1.5 (Juniper et al., 2005)) will be invited to participate in the service. If the patient agrees, they will be given a Patient Information Sheet (PIS) and then asked to sign two consent forms (study consent and a separate Medicare consent form). The pharmacist will: • Assess Asthma related QOL • Review short-acting β2 agonist use • Ask about Action Plan ownership • Assess allergic rhinitis control (RCAT) • Use the Short Form 12 for QOL for economic evaluation • Download preventer dispensing over the previous 12 months.

Component	Description
	The patient will then be given a referral to their GP. They will be contacted by the research team at 1 month and 12 months to reassess asthma control (ACQ), Asthma related QoL, Asthma Action Plan ownership, allergic rhinitis control (RACT score), SF12. The pharmacist will also download the preventer medication dispensed since the beginning of the study. **2. Group C – Standard care General Practice Group** A sample of patients with asthma, matched on age, gender, ACQ scores will be identified using a system to access general practice medical records through Primary Health Care Limited which has a nationwide network of 1100 General Practices and records of over 8,000,000 patients. De-identified data will be retrospectively extracted from the GP database using their software to enable comparison of asthma control over the period of the trial, i.e., baseline and post-intervention. Full details are provided in the protocol.
Outcomes (Full details provided in relevant Table in Criteria 2)	**Primary** The change in proportion of patients in each arm who have controlled asthma from baseline to post intervention at 12 months. **Secondary** • Mean change in asthma control (ACQ score) between baseline and 12 months post-intervention. • Mean change in asthma related quality of life (AQoL score) between baseline and 12 months post-intervention. • Mean change in adherence (BMQ adherence scores) between baseline and six months, and baseline and 12 months post-intervention. • Mean change in inhaler technique (inhaler technique scores) between baseline and 12 months post-intervention. • Mean change in the proportion of patients with an Asthma Action Plan between baseline and 12 months post-intervention. • Patient, pharmacist and GP satisfaction with the intervention and comparator processes. **Effectiveness** – Same as primary outcome.

APPENDIX E: SUMMARY OF EVALUATION COMPONENTS AND STATISTICAL ANALYSIS PLAN (SAP)

Appendix Table E-1: Summary of evaluation components and Statistical Analysis Plan (SAP)

Type of evaluation	Description/measure	Data source
Formative	To identify overall experience, with service implementation, any difficulties with compliance, and options for overcoming these; and (b) perceptions of sustainability of the risk assessment model, and requirements for sustainability	Qualitative interviews with a 10% sample of participating pharmacists
Process	Median number of services/pharmacy/week	Pharmacy records
	Total number of services per pharmacy	Pharmacy records
	Patient satisfaction with the Pharmacy Asthma Service	Follow up patient survey of a 10% sample of all patients
Outcome	Change in ACQ Change in Asthma-related quality of life Change in preventer dispensing Change in inhaler technique score Change in RCAT Change in quality adjusted life years	Pharmacy records
Economic Appraisal	Trial-based economic evaluation Modelled economic evaluation to extend the time horizon beyond the trial period Financial evaluation	Costs and outcomes collected during the trial period including Medicare (MBS and PBS) and hospitalisation costs

Data analysis will be carried out in accordance to the statistical analysis plan created by the research team. The statistical analysis plan has been published online and located at https://osf.io/mjzrn.

APPENDIX F: PHARMACIST SCOPE OF PRACTICE

The Pharmacy Asthma Service falls within the scope of professional practice for pharmacists, as covered by the Australian Health Practitioner Registration Authority (AHPRA). Specifically, as per guidelines on practice-specific issues of the AHPRA (126), the Pharmacy Asthma Service follows established practice and quality-assurance standards, including relevant guidelines issued by professional associates or registered authorities.

Furthermore, as per the Code of Conduct for Pharmacists (127), the Pharmacy Asthma Service aligns with the articulated code for the delivery of good care, shared responsibility and decision-making, access to care, effective communication, confidentiality and privacy, informed consent, working with other practitioners (including delegation, referral and handover) and principles of teamwork. The process for the Pharmacy Asthma Service is also consistent with the Code of Conduct for Pharmacists (127), as it relates to undertaking research.

APPENDIX G: ONLINE EDUCATION MODULE DESCRIPTIONS AND OBJECTIVES.

Appendix Table G-1: Online education module descriptions and objectives

Module	Module Description	Module Objectives
1. Introducing the Trial	The opening module provides an overview of the pathophysiology of asthma and how it is managed as well as providing all the introductory information that the pharmacists need to know to participate in the trial. The module will introduce the resources available to help pharmacists meet their responsibilities to their patients and to the trial.	After completing this module, pharmacists should be able to: • Discuss the aims and objectives of the Pharmacy Trial Program – Asthma and Rhinitis Control trial (PTP-ARC) • Identify the responsibilities of pharmacists participating in the PTP-ARC • Describe the responsibilities of the pharmacist to the patient when delivering the service • Discuss the pathophysiology and management of asthma.
2. Medication and Adherence	This module explores asthma treatment and management, the importance of adherence in asthma management and strategies to both identify barriers to adherence and assist patients in optimizing adherence.	After completing this module, pharmacists should be able to: • Describe the principles of asthma management and treatments commonly used • Discuss the importance of adherence when managing asthma • Identify common reasons why patients have suboptimal adherence to asthma medicines • Identify evidence-based strategies to improve adherence in asthma • Describe the role pharmacists can play in optimising adherence.
3. Inhaler Devices and Technique	Module three provides an extensive overview of asthma devices in Australia and the importance of correct inhaler technique. We explore all device types, how to best care for each device, optimal inhaler technique including videos to support learning and advice and strategies on how best to educate and improve their patients' inhaler technique.	After completing this module, pharmacists should be able to: • Identify asthma inhalers currently available • Discuss the evidence for the importance of inhaler technique on asthma outcomes • Identify the correct steps in using different inhaler devices and discuss the principles of delivering effective inhaler technique education • Discuss the relationship between inhaler technique and adherence

Module	Module Description	Module Objectives
		• Identify clinical situations that require a review of device suitability.
4. Allergic Rhinitis and Co-Morbid Conditions	This module explores the impact other medical conditions can have on asthma control. In particular, we will cover the relationship between allergic rhinitis and asthma and the importance of adequately treating allergic rhinitis. Other co-morbidities explored include GORD, sleep problems including obstructive sleep apnoea, obesity, depression and/or anxiety and eczema.	After completing this module, pharmacists should be able to: • Discuss the relationship between asthma and allergic rhinitis and other co-morbidities • Describe the prevalence of allergic rhinitis in the Australian community • Identify tools to assess the presence and severity of allergic rhinitis • Discuss the clinical pathway for determining appropriate management of allergic rhinitis in asthma • Identify appropriate treatment options for allergic rhinitis.
5. Putting it into Practice	This module focuses on the practical application of the trial. It provides a brief overview of tools pharmacists will have to help them complete the consultations and a video case study has been provided to demonstrate the four patient consultations in practice.	After completing this module, pharmacists should be able to: • Describe the requirements for each consultation and information that will need to be collected • Identify resources available to support pharmacists to complete patient consultations • Discuss how resources available can be used in the patient consultation • Describe a process to follow when conducting each patient consultation.

APPENDIX H: VISUAL ANALOGUE SCALES (VAS) UTILISED IN PTP-ARC TRIAL.

Appendix Table H-1: Visual analogue scales (VAS) utilised in PTP-ARC Trial.

Measure	Question	Scale	Cut off points	Data Source
Adherence	All things considered, how much of the time do you use ALL of your asthma preventer/controller medications EXACTLY as directed?	1 (none of the time)-10 (all of the time)	<10 non-adherent, 10 = adherent	Baseline, 12-month
Medication efficacy	How well are your asthma medications working?	1 (does not work at all) -5 (works very well)	1-2 – explore, >2 – proceed	Baseline, 1-month
Nasal symptom severity (allergic rhinitis)	How bothersome are your current NASAL symptoms?	1 (not at all bothersome)-10 (extremely bothersome)	n/a	Baseline, 1-month
Ocular symptom severity (allergic rhinitis)	How bothersome are your current EYE symptoms?	1 (not at all bothersome)-10 (extremely bothersome)	n/a	Baseline, 1-month

APPENDIX I: INTERVENTION ARM QUALITATIVE INTERVIEW GUIDE

Appendix Table I-1: Post intervention qualitative interview guide for pharmacists

Type	PHARMACIST'S EXPERIENCE	Prompts
Process	1. Why did you decide to participate in the asthma management service?	• *To promote my business* • *To help my patients* • *To improve my clinical skills*
Process	2. Please tell me about your general experience in conducting the asthma service at your pharmacy.	• *Recruitment: Problems/successful strategies* • *Patient response* • *Visits: Time taken, number of visits, visit schedule* • *Project software: GuildCare/GuildPath* • *Staff involvement*
Process	3. What factors facilitated the service in your pharmacy?	
Process	4. What barriers impeded the service in your pharmacy?	
Process	5. Recognising that in future implementation, the service would not include lengthy quality of life questionnaires, rather it would screen for asthma control and then identify areas of need – adherence, inhaler technique and allergic rhinitis control. a) Would you continue with the service? Why? b) How do you think the service could be improved for patients in the future?	
Process	6. How well did the training equip you to deliver the service? Both online and in person (if applicable)?	• *What worked particularly well/helped to prepare you?* • *Were there any gaps in the training?*
Type	**PHARMACIST'S PERSPECTIVE OF PATIENT'S EXPERIENCE**	
Outcome	7. How do you think the service has been received by your patients? How do you think they have benefitted?	• *What have been the most useful parts of the service for your patients?* • *What have been the least useful parts of the service for your patients?* • *How much demand do you think there is for a service like this in community pharmacy?*
Type	**GP/SPECIALIST INTERACTION WITH THE SERVICE**	
Outcome	8. What, if any, impact has this service had on your professional relationship with local GPs?	• *Did you refer patients to the GP?* • *Did GPs refer patients to you?* • *What happened after the referral, if anything?*

Type	CLINICAL PRACTICE AND FUTURE IMPLEMENTATION	Prompts
Outcome	9. How does this service fit with your role as a community pharmacist?	• *In what ways does it extend or challenge your scope of practice (before and after training)?* • *Has this experience changed your relationship with patients?*
Outcome	10. How well did the service model integrate with your business practices?	• *How does the service fit with the business model of your pharmacy?* • *Are you operating a business model that incorporates services within your pharmacy? To what extent do services contribute to the business model?*
Outcome	11. What other spinoffs did you experience as a result of offering the service?	• *Generation of business* • *Demands for other services* • *How do you think this will influence your future practice of pharmacy?*

APPENDIX J: ACQ QUESTIONS BY VISIT

Appendix Table J-1: Participant responses to Asthma Control Questionnaire (ACQ) by visit

	Intervention	Comparator	Overall
ACQ – BASELINE			
On average in the last week how often were you WOKEN BY YOUR ASTHMA during the night?	n=221	n=160	n=381
Not at all	48 (21.7%)	35 (21.9%)	83 (21.8%)
Hardly ever	33 (14.9%)	29 (18.1%)	62 (16.3%)
A few times	72 (32.6%)	58 (36.3%)	130 (34.1%)
Several times	41 (18.6%)	21 (13.1%)	62 (16.3%)
Many times	17 (7.7%)	12 (7.5%)	29 (7.6%)
A great many times	7 (3.2%)	3 (1.9%)	10 (2.6%)
Unable to sleep because of asthma	3 (1.4%)	2 (1.3%)	5 (1.3%)
On average in the last week how WERE YOUR ASTHMA SYMPTOMS WHEN YOU WOKE UP in the morning?	n=221	n=160	n=381
No symptoms	8 (3.6%)	6 (3.8%)	14 (3.7%)
Very mild symptoms	32 (14.5%)	20 (12.5%)	52 (13.6%)
Mild symptoms	76 (34.4%)	64 (40.0%)	140 (36.7%)
Moderate symptoms	67 (30.3%)	50 (31.3%)	117 (30.7%)
Quite severe symptoms	26 (11.8%)	9 (5.6%)	35 (9.2%)
Severe symptoms	10 (4.5%)	8 (5.0%)	18 (4.7%)
Very severe symptoms	2 (0.9%)	3 (1.9%)	5 (1.3%)
In general, in the last week how LIMITED WERE YOU IN YOUR DAY-TO-DAY ACTIVITIES because of your asthma?	n=221	n=160	n=381
Not at all limited	18 (8.1%)	21 (13.1%)	39 (10.2%)
Very slightly limited	34 (15.4%)	20 (12.5%)	54 (14.2%)
Slightly limited	63 (28.5%)	51 (31.9%)	114 (29.9%)
Moderately limited	74 (33.5%)	42 (26.3%)	116 (30.4%)
Very limited	22 (10.0%)	17 (10.6%)	39 (10.2%)
Extremely limited	8 (3.6%)	5 (3.1%)	13 (3.4%)
Totally limited	2 (0.9%)	4 (2.5%)	6 (1.6%)
In general, in the last week how much SHORTNESS OF BREATH did you experience because of your asthma?	n=221	n=160	n=381
None	1 (0.5%)	3 (1.9%)	4 (1.0%)
Very little	8 (3.6%)	6 (3.8%)	14 (3.7%)
A little	56 (25.3%)	44 (27.5%)	100 (26.2%)
A moderate amount	81 (36.7%)	57 (35.6%)	138 (36.2%)

	Intervention	Comparator	Overall
Quite a lot	53 (24.0%)	30 (18.8%)	83 (21.8%)
A great deal	18 (8.1%)	15 (9.4%)	33 (8.7%)
An extreme amount	4 (1.8%)	5 (3.1%)	9 (2.4%)
In general, in the last week how often did you WHEEZE?	n=221	n=160	n=381
None of the time	14 (6.3%)	7 (4.4%)	21 (5.5%)
Hardly any of the time	20 (9.0%)	13 (8.1%)	33 (8.7%)
A little of the time	68 (30.8%)	52 (32.5%)	120 (31.5%)
A moderate amount of the time	57 (25.8%)	41 (25.6%)	98 (25.7%)
A lot of the time	41 (18.6%)	19 (11.9%)	60 (15.7%)
Most of the time	10 (4.5%)	17 (10.6%)	27 (7.1%)
All the time	11 (5.0%)	11 (6.9%)	22 (5.8%)
On average in the last week how many PUFFS OF RELIEF MEDICATION (short-acting bronchodilator such as Ventolin Bricanyl etc) have you used each day?	n=221	n=160	n=381
None	9 (4.1%)	12 (7.5%)	21 (5.5%)
1-2 puffs/inhalations most days	46 (20.8%)	47 (29.4%)	93 (24.4%)
3-4 puffs/inhalations most days	65 (29.4%)	40 (25.0%)	105 (27.6%)
5-8 puffs/inhalations most days	59 (26.7%)	40 (25.0%)	99 (26.0%)
9-12 puffs/inhalations most days	26 (11.8%)	13 (8.1%)	39 (10.2%)
13-16 puffs/inhalations most days	9 (4.1%)	3 (1.9%)	12 (3.1%)
More than 16 puffs/inhalations most days	7 (3.2%)	5 (3.1%)	12 (3.1%)
ACQ – 1 MONTH FOLLOW-UP VISIT			
On average in the last week how often were you WOKEN BY YOUR ASTHMA during the night?	n=190	n=131	n=321
Not at all	82 (43.2%)	63 (48.1%)	145 (45.2%)
Hardly ever	35 (18.4%)	32 (24.4%)	67 (20.9%)
A few times	55 (28.9%)	25 (19.1%)	80 (24.9%)
Several times	10 (5.3%)	5 (3.8%)	15 (4.7%)
Many times	5 (2.6%)	3 (2.3%)	8 (2.5%)
A great many times	2 (1.1%)	1 (0.8%)	3 (0.9%)
Unable to sleep because of asthma	1 (0.5%)	2 (1.5%)	3 (0.9%)
On average in the last week how WERE YOUR ASTHMA SYMPTOMS WHEN YOU WOKE UP in the morning?	n=190	n=131	n=321
No symptoms	38 (20.0%)	28 (21.4%)	66 (20.6%)
Very mild symptoms	50 (26.3%)	39 (29.8%)	89 (27.7%)

	Intervention	Comparator	Overall
Mild symptoms	64 (33.7%)	39 (29.8%)	103 (32.1%)
Moderate symptoms	30 (15.8%)	17 (13.0%)	47 (14.6%)
Quite severe symptoms	5 (2.6%)	4 (3.1%)	9 (2.8%)
Severe symptoms	2 (1.1%)	3 (2.3%)	5 (1.6%)
Very severe symptoms	1 (0.5%)	1 (0.8%)	2 (0.6%)
In general, in the last week how LIMITED WERE YOU IN YOUR DAY-TO-DAY ACTIVITIES because of your asthma?	n=190	n=131	n=321
Not at all limited	59 (31.1%)	44 (33.6%)	103 (32.1%)
Very slightly limited	32 (16.8%)	36 (27.5%)	68 (21.2%)
Slightly limited	53 (27.9%)	20 (15.3%)	73 (22.7%)
Moderately limited	36 (18.9%)	24 (18.3%)	60 (18.7%)
Very limited	8 (4.2%)	3 (2.3%)	11 (3.4%)
Extremely limited	2 (1.1%)	3 (2.3%)	5 (1.6%)
Totally limited	0 (0.0%)	1 (0.8%)	1 (0.3%)
In general, in the last week how much SHORTNESS OF BREATH did you experience because of your asthma?	n=190	n=131	n=321
None	15 (7.9%)	17 (13.0%)	32 (10.0%)
Very little	46 (24.2%)	40 (30.5%)	86 (26.8%)
A little	58 (30.5%)	36 (27.5%)	94 (29.3%)
A moderate amount	51 (26.8%)	15 (11.5%)	66 (20.6%)
Quite a lot	13 (6.8%)	16 (12.2%)	29 (9.0%)
A great deal	6 (3.2%)	6 (4.6%)	12 (3.7%)
An extreme amount	1 (0.5%)	1 (0.8%)	2 (0.6%)
In general, in the last week how often did you WHEEZE?	n=190	n=131	n=321
None of the time	40 (21.1%)	30 (22.9%)	70 (21.8%)
Hardly any of the time	50 (26.3%)	29 (22.1%)	79 (24.6%)
A little of the time	60 (31.6%)	32 (24.4%)	92 (28.7%)
A moderate amount of the time	26 (13.7%)	21 (16.0%)	47 (14.6%)
A lot of the time	8 (4.2%)	10 (7.6%)	18 (5.6%)
Most of the time	6 (3.2%)	5 (3.8%)	11 (3.4%)
All the time	0 (0.0%)	4 (3.1%)	4 (1.2%)
On average in the last week how many PUFFS OF RELIEF MEDICATION (short-acting bronchodilator such as Ventolin Bricanyl etc) have you used each day?	n=190	n=131	n=321
None	28 (14.7%)	23 (17.6%)	51 (15.9%)
1-2 puffs/inhalations most days	69 (36.3%)	51 (38.9%)	120 (37.4%)

	Intervention	Comparator	Overall
3-4 puffs/inhalations most days	51 (26.8%)	25 (19.1%)	76 (23.7%)
5-8 puffs/inhalations most days	30 (15.8%)	16 (12.2%)	46 (14.3%)
9-12 puffs/inhalations most days	10 (5.3%)	10 (7.6%)	20 (6.2%)
13-16 puffs/inhalations most days	0 (0.0%)	4 (3.1%)	4 (1.2%)
More than 16 puffs/inhalations most days	2 (1.1%)	2 (1.5%)	4 (1.2%)
ACQ – 6 MONTHS FOLLOW-UP VISIT			
On average in the last week how often were you WOKEN BY YOUR ASTHMA during the night?	n=182		n=182
Not at all	101 (55.5%)		101 (55.5%)
Hardly ever	33 (18.1%)		33 (18.1%)
A few times	23 (12.6%)		23 (12.6%)
Several times	10 (5.5%)		10 (5.5%)
Many times	11 (6.0%)		11 (6.0%)
A great many times	3 (1.6%)		3 (1.6%)
Unable to sleep because of asthma	1 (0.5%)		1 (0.5%)
On average in the last week how WERE YOUR ASTHMA SYMPTOMS WHEN YOU WOKE UP in the morning?	n=182		n=182
No symptoms	54 (29.7%)		54 (29.7%)
Very mild symptoms	46 (25.3%)		46 (25.3%)
Mild symptoms	52 (28.6%)		52 (28.6%)
Moderate symptoms	19 (10.4%)		19 (10.4%)
Quite severe symptoms	5 (2.7%)		5 (2.7%)
Severe symptoms	5 (2.7%)		5 (2.7%)
Very severe symptoms	1 (0.5%)		1 (0.5%)
In general, in the last week how LIMITED WERE YOU IN YOUR DAY-TO-DAY ACTIVITIES because of your asthma?	n=182		n=182
Not at all limited	74 (40.7%)		74 (40.7%)
Very slightly limited	36 (19.8%)		36 (19.8%)
Slightly limited	36 (19.8%)		36 (19.8%)
Moderately limited	24 (13.2%)		24 (13.2%)
Very limited	6 (3.3%)		6 (3.3%)
Extremely limited	5 (2.7%)		5 (2.7%)
Totally limited	1 (0.5%)		1 (0.5%)
In general, in the last week how much SHORTNESS OF BREATH did you experience because of your asthma?	n=182		n=182

	Intervention	Comparator	Overall
None	33 (18.1%)		33 (18.1%)
Very little	43 (23.6%)		43 (23.6%)
A little	51 (28.0%)		51 (28.0%)
A moderate amount	33 (18.1%)		33 (18.1%)
Quite a lot	19 (10.4%)		19 (10.4%)
A great deal	2 (1.1%)		2 (1.1%)
An extreme amount	1 (0.5%)		1 (0.5%)
In general, in the last week how often did you WHEEZE?	n=182		n=182
None of the time	55 (30.2%)		55 (30.2%)
Hardly any of the time	40 (22.0%)		40 (22.0%)
A little of the time	51 (28.0%)		51 (28.0%)
A moderate amount of the time	20 (11.0%)		20 (11.0%)
A lot of the time	8 (4.4%)		8 (4.4%)
Most of the time	7 (3.8%)		7 (3.8%)
All the time	1 (0.5%)		1 (0.5%)
On average in the last week how many PUFFS OF RELIEF MEDICATION (short-acting bronchodilator such as Ventolin Bricanyl etc) have you used each day?	n=182		n=182
None	43 (23.6%)		43 (23.6%)
1-2 puffs/inhalations most days	63 (34.6%)		63 (34.6%)
3-4 puffs/inhalations most days	40 (22.0%)		40 (22.0%)
5-8 puffs/inhalations most days	21 (11.5%)		21 (11.5%)
9-12 puffs/inhalations most days	8 (4.4%)		8 (4.4%)
13-16 puffs/inhalations most days	4 (2.2%)		4 (2.2%)
More than 16 puffs/inhalations most days	3 (1.6%)		3 (1.6%)
ACQ – 12 MONTHS FOLLOW-UP VISIT			
On average in the last week how often were you WOKEN BY YOUR ASTHMA during the night?	n=143	n=111	n=254
Not at all	85 (59.4%)	57 (51.4%)	142 (55.9%)
Hardly ever	25 (17.5%)	18 (16.2%)	43 (16.9%)
A few times	22 (15.4%)	23 (20.7%)	45 (17.7%)
Several times	6 (4.2%)	7 (6.3%)	13 (5.1%)
Many times	1 (0.7%)	2 (1.8%)	3 (1.2%)
A great many times	4 (2.8%)	4 (3.6%)	8 (3.1%)

	Intervention	Comparator	Overall
On average in the last week how WERE YOUR ASTHMA SYMPTOMS WHEN YOU WOKE UP in the morning?	n=143	n=111	n=254
No symptoms	49 (34.3%)	29 (26.1%)	78 (30.7%)
Very mild symptoms	40 (28.0%)	28 (25.2%)	68 (26.8%)
Mild symptoms	30 (21.0%)	36 (32.4%)	66 (26.0%)
Moderate symptoms	17 (11.9%)	17 (15.3%)	34 (13.4%)
Quite severe symptoms	5 (3.5%)	1 (0.9%)	6 (2.4%)
Severe symptoms	2 (1.4%)	0 (0.0%)	2 (0.8%)
In general, in the last week how LIMITED WERE YOU IN YOUR DAY-TO-DAY ACTIVITIES because of your asthma?	n=143	n=111	n=254
Not at all limited	60 (42.0%)	42 (37.8%)	102 (40.2%)
Very slightly limited	26 (18.2%)	24 (21.6%)	50 (19.7%)
Slightly limited	23 (16.1%)	21 (18.9%)	44 (17.3%)
Moderately limited	21 (14.7%)	20 (18.0%)	41 (16.1%)
Very limited	7 (4.9%)	3 (2.7%)	10 (3.9%)
Extremely limited	6 (4.2%)	1 (0.9%)	7 (2.8%)
In general, in the last week how much SHORTNESS OF BREATH did you experience because of your asthma?	n=143	n=111	n=254
None	33 (23.1%)	22 (19.8%)	55 (21.7%)
Very little	36 (25.2%)	25 (22.5%)	61 (24.0%)
A little	33 (23.1%)	30 (27.0%)	63 (24.8%)
A moderate amount	29 (20.3%)	19 (17.1%)	48 (18.9%)
Quite a lot	9 (6.3%)	10 (9.0%)	19 (7.5%)
A great deal	3 (2.1%)	5 (4.5%)	8 (3.1%)
In general, in the last week how often did you WHEEZE?	n=143	n=111	n=254
None of the time	53 (37.1%)	25 (22.5%)	78 (30.7%)
Hardly any of the time	29 (20.3%)	26 (23.4%)	55 (21.7%)
A little of the time	26 (18.2%)	35 (31.5%)	61 (24.0%)
A moderate amount of the time	23 (16.1%)	14 (12.6%)	37 (14.6%)
A lot of the time	8 (5.6%)	7 (6.3%)	15 (5.9%)
Most of the time	3 (2.1%)	2 (1.8%)	5 (2.0%)
All the time	1 (0.7%)	2 (1.8%)	3 (1.2%)
On average in the last week how many PUFFS OF RELIEF MEDICATION (short-acting bronchodilator such as Ventolin Bricanyl etc) have you used each day?	n=143	n=111	n=254
None	40 (28.0%)	21 (18.9%)	61 (24.0%)

	Intervention	Comparator	Overall
1-2 puffs/inhalations most days	51 (35.7%)	42 (37.8%)	93 (36.6%)
3-4 puffs/inhalations most days	31 (21.7%)	25 (22.5%)	56 (22.0%)
5-8 puffs/inhalations most days	10 (7.0%)	14 (12.6%)	24 (9.4%)
9-12 puffs/inhalations most days	3 (2.1%)	5 (4.5%)	8 (3.1%)
13-16 puffs/inhalations most days	4 (2.8%)	2 (1.8%)	6 (2.4%)
More than 16 puffs/inhalations most days	4 (2.8%)	2 (1.8%)	6 (2.4%)

APPENDIX K: FACTORS ASSOCIATED WITH POOR ASTHMA CONTROL

Appendix Table K-1: Multivariate linear regression for poor asthma control (ACQ score) at baseline

		Univariate model		Multivariate model (n=381)	
Risk factors	**Values**	**Mean (95%CI)**	**P-value**	**Mean (95%CI)**	**P-value**
Pharmacy state	NSW	2.48 (2.34, 2.61)	0.5720	2.97 (2.67, 3.26)	0.5154
	WA	2.37 (2.11, 2.63)		2.81 (2.44, 3.18)	
	TAS	2.32 (1.99, 2.65)		2.83 (2.40, 3.27)	
Pharmacy remoteness	Highly Accessible	2.42 (2.28, 2.56)	0.6656	2.84 (2.54, 3.15)	0.4781
	Accessible	2.53 (2.29, 2.78)		3.00 (2.63, 3.37)	
	Moderately Accessible, Remote, Very remote	2.37 (2.01, 2.73)		2.77 (2.33, 3.21)	
Age	18 to 25	2.37 (2.01, 2.72)	0.5933	2.99 (2.51, 3.47)	0.1583
	26 to 35	2.45 (2.16, 2.74)		2.87 (2.47, 3.28)	
	36 to 45	2.40 (2.16, 2.63)		2.78 (2.42, 3.15)	
	46 to 55	2.61 (2.38, 2.84)		2.90 (2.55, 3.25)	
	Above 56	2.41 (2.27, 2.55)		2.81 (2.48, 3.14)	
Sex	Male	2.46 (2.29, 2.63)	0.7496	2.87 (2.54, 3.20)	0.7529
	Female	2.43 (2.30, 2.56)		2.87 (2.55, 3.18)	
Work situation	Full-time employed	2.26 (2.07, 2.45)	0.0328	2.61 (2.27, 2.96)	0.6816
	Home duties			2.98 (2.57, 3.39)	
	Home duties/full-time carer	2.59 (2.31, 2.87)			
	Part time or casually employed	2.36 (2.17, 2.56)		2.73 (2.38, 3.09)	
	Retired/Pensioner	2.46 (2.29, 2.63)		2.88 (2.52, 3.24)	
	Unemployed or seeking work	2.82 (2.46, 3.17)		3.02 (2.57, 3.46)	
	Full-time carer			2.99 (2.53, 3.45)	
	Other	2.70 (2.31, 3.08)			
Level of education	No formal education	3.27 (2.63, 3.91)	0.1988	3.47 (2.76, 4.18)	0.0104*
	Primary school	2.23 (1.72, 2.75)		2.51 (1.94, 3.08)	

Risk factors	Values	Univariate model Mean (95%CI)	P-value	Multivariate model (n=381) Mean (95%CI)	P-value
	High school	2.42 (2.27, 2.57)		2.71 (2.42, 2.99)	
	Tertiary non-university (e.g. TAFE)	2.42 (2.23, 2.60)		2.77 (2.46, 3.08)	
	University	2.45 (2.24, 2.66)		2.91 (2.57, 3.26)	
	Post-graduate	2.39 (1.95, 2.84)		2.85 (2.33, 3.37)	
Did the participant have at least one accident or ER visits in the past 12 months	No	2.38 (2.26, 2.51)	0.0380	2.81 (2.47, 3.15)	0.0301*
	Yes	2.60 (2.41, 2.79)		2.93 (2.60, 3.26)	
Did the participant have at least one hospital visits in the past 12 months	No	2.40 (2.28, 2.52)	0.0597	2.78 (2.48, 3.09)	0.7233
	Yes	2.63 (2.40, 2.86)		2.96 (2.58, 3.34)	
Age began to experience asthma	0-5 years of age	2.30 (2.11, 2.49)	0.2455	2.81 (2.47, 3.16)	0.9699
	6-15 years of age	2.49 (2.29, 2.69)		2.96 (2.61, 3.31)	
	16-34 years of age	2.56 (2.37, 2.74)		2.99 (2.65, 3.34)	
	35-55 years of age	2.47 (2.26, 2.69)		2.81 (2.45, 3.18)	
	above 55 years	2.33 (2.07, 2.58)		2.77 (2.37, 3.16)	
Ever had a lung function test	No	2.37 (2.20, 2.55)	0.3472	2.81 (2.48, 3.15)	0.2514
	Yes	2.47 (2.34, 2.59)		2.93 (2.62, 3.24)	
Active smoker	No	2.37 (2.25, 2.48)	<.0001	2.61 (2.31, 2.91)	0.0076*
	Yes	2.89 (2.64, 3.13)		3.13 (2.77, 3.50)	
History of hay fever	No	2.54 (2.36, 2.73)	0.1544	2.95 (2.61, 3.30)	0.2134
	Yes	2.40 (2.28, 2.52)		2.79 (2.49, 3.09)	
Use of intranasal corticosteroid in last 12 months	No	2.44 (2.32, 2.55)	0.9038	2.84 (2.55, 3.14)	0.3936

Risk factors	Values	Univariate model		Multivariate model (n=381)	
		Mean (95%CI)	P-value	Mean (95%CI)	P-value
	Yes	2.46 (2.15, 2.76)		2.89 (2.50, 3.29)	0.5154

APPENDIX L: IAQLQ QUESTION BY VISIT

Appendix Table L-1: Participant responses to Asthma Quality of Life Questionnaire (IAQLQ) by visit

	Intervention	Comparator	Overall
IAQLQ – BASELINE			
I have been troubled by episodes of shortness of breath	n=221	n=160	n=381
Not at all	12 (5.4%)	9 (5.6%)	21 (5.5%)
Mildly	62 (28.1%)	64 (40.0%)	126 (33.1%)
Moderately	96 (43.4%)	57 (35.6%)	153 (40.2%)
Severely	40 (18.1%)	22 (13.8%)	62 (16.3%)
Very severely	11 (5.0%)	8 (5.0%)	19 (5.0%)
I have been troubled by wheezing attacks	n=221	n=160	n=381
Not at all	44 (19.9%)	35 (21.9%)	79 (20.7%)
Mildly	69 (31.2%)	52 (32.5%)	121 (31.8%)
Moderately	67 (30.3%)	45 (28.1%)	112 (29.4%)
Severely	31 (14.0%)	19 (11.9%)	50 (13.1%)
Very severely	10 (4.5%)	9 (5.6%)	19 (5.0%)
I have been troubled by tightness in the chest	n=221	n=160	n=381
Not at all	48 (21.7%)	43 (26.9%)	91 (23.9%)
Mildly	76 (34.4%)	44 (27.5%)	120 (31.5%)
Moderately	56 (25.3%)	49 (30.6%)	105 (27.6%)
Severely	35 (15.8%)	18 (11.3%)	53 (13.9%)
Very severely	6 (2.7%)	6 (3.8%)	12 (3.1%)
I have been restricted in walking down the street on level ground or doing light housework because of asthma or shortness of breath	n=221	n=160	n=381
Not at all	73 (33.0%)	63 (39.4%)	136 (35.7%)
Mildly	68 (30.8%)	44 (27.5%)	112 (29.4%)
Moderately	50 (22.6%)	25 (15.6%)	75 (19.7%)
Severely	20 (9.0%)	25 (15.6%)	45 (11.8%)
Very severely	10 (4.5%)	3 (1.9%)	13 (3.4%)
I have been restricted in walking up hills or doing heavy housework because of asthma or shortness of breath	n=221	n=160	n=381
Not at all	36 (16.3%)	23 (14.4%)	59 (15.5%)
Mildly	60 (27.1%)	43 (26.9%)	103 (27.0%)
Moderately	63 (28.5%)	47 (29.4%)	110 (28.9%)
Severely	39 (17.6%)	28 (17.5%)	67 (17.6%)

	Intervention	Comparator	Overall
Very severely	23 (10.4%)	19 (11.9%)	42 (11.0%)
I have felt tired or a general lack of energy	n=221	n=160	n=381
Not at all	12 (5.4%)	11 (6.9%)	23 (6.0%)
Mildly	62 (28.1%)	48 (30.0%)	110 (28.9%)
Moderately	80 (36.2%)	56 (35.0%)	136 (35.7%)
Severely	53 (24.0%)	32 (20.0%)	85 (22.3%)
Very severely	14 (6.3%)	13 (8.1%)	27 (7.1%)
I have been unable to sleep at night	n=221	n=160	n=381
Not at all	39 (17.6%)	39 (24.4%)	78 (20.5%)
Mildly	58 (26.2%)	45 (28.1%)	103 (27.0%)
Moderately	60 (27.1%)	44 (27.5%)	104 (27.3%)
Severely	53 (24.0%)	20 (12.5%)	73 (19.2%)
Very severely	11 (5.0%)	12 (7.5%)	23 (6.0%)
I have felt sad or depressed	n=221	n=160	n=381
Not at all	86 (38.9%)	79 (49.4%)	165 (43.3%)
Mildly	71 (32.1%)	34 (21.3%)	105 (27.6%)
Moderately	42 (19.0%)	27 (16.9%)	69 (18.1%)
Severely	18 (8.1%)	12 (7.5%)	30 (7.9%)
Very severely	4 (1.8%)	8 (5.0%)	12 (3.1%)
I have felt frustrated with myself	n=221	n=160	n=381
Not at all	59 (26.7%)	50 (31.3%)	109 (28.6%)
Mildly	63 (28.5%)	45 (28.1%)	108 (28.3%)
Moderately	60 (27.1%)	38 (23.8%)	98 (25.7%)
Severely	34 (15.4%)	18 (11.3%)	52 (13.6%)
Very severely	5 (2.3%)	9 (5.6%)	14 (3.7%)
I have felt anxious under tension or stressed	n=221	n=160	n=381
Not at all	54 (24.4%)	61 (38.1%)	115 (30.2%)
Mildly	72 (32.6%)	37 (23.1%)	109 (28.6%)
Moderately	59 (26.7%)	36 (22.5%)	95 (24.9%)
Severely	26 (11.8%)	16 (10.0%)	42 (11.0%)
Very severely	10 (4.5%)	10 (6.3%)	20 (5.2%)
I have felt that asthma or shortness of breath is preventing me from achieving what I want from life	n=221	n=160	n=381
Not at all	55 (24.9%)	55 (34.4%)	110 (28.9%)
Mildly	66 (29.9%)	53 (33.1%)	119 (31.2%)

	Intervention	Comparator	Overall
Moderately	52 (23.5%)	28 (17.5%)	80 (21.0%)
Severely	39 (17.6%)	16 (10.0%)	55 (14.4%)
Very severely	9 (4.1%)	8 (5.0%)	17 (4.5%)
Asthma or shortness of breath has interfered with my social life	n=221	n=160	n=381
Not at all	87 (39.4%)	80 (50.0%)	167 (43.8%)
Mildly	60 (27.1%)	42 (26.3%)	102 (26.8%)
Moderately	47 (21.3%)	25 (15.6%)	72 (18.9%)
Severely	18 (8.1%)	5 (3.1%)	23 (6.0%)
Very severely	9 (4.1%)	8 (5.0%)	17 (4.5%)
I have been limited in going to certain places because they are bad for my asthma	n=221	n=160	n=381
Not at all	83 (37.6%)	70 (43.8%)	153 (40.2%)
Mildly	49 (22.2%)	41 (25.6%)	90 (23.6%)
Moderately	57 (25.8%)	36 (22.5%)	93 (24.4%)
Severely	27 (12.2%)	7 (4.4%)	34 (8.9%)
Very severely	5 (2.3%)	6 (3.8%)	11 (2.9%)
I have been limited in going to certain places because I have been afraid of getting an asthma attack and not being able to get help	n=221	n=160	n=381
Not at all	125 (56.6%)	95 (59.4%)	220 (57.7%)
Mildly	45 (20.4%)	35 (21.9%)	80 (21.0%)
Moderately	30 (13.6%)	17 (10.6%)	47 (12.3%)
Severely	15 (6.8%)	11 (6.9%)	26 (6.8%)
Very severely	6 (2.7%)	2 (1.3%)	8 (2.1%)
I have been restricted in the sports hobbies or other recreations I can engage in because of my asthma or shortness of breath	n=221	n=160	n=381
Not at all	60 (27.1%)	47 (29.4%)	107 (28.1%)
Mildly	50 (22.6%)	52 (32.5%)	102 (26.8%)
Moderately	64 (29.0%)	36 (22.5%)	100 (26.2%)
Severely	30 (13.6%)	15 (9.4%)	45 (11.8%)
Very severely	17 (7.7%)	10 (6.3%)	27 (7.1%)
I have felt generally restricted	n=221	n=160	n=381
Not at all	65 (29.4%)	59 (36.9%)	124 (32.5%)
Mildly	65 (29.4%)	45 (28.1%)	110 (28.9%)

	Intervention	Comparator	Overall
Moderately	60 (27.1%)	35 (21.9%)	95 (24.9%)
Severely	21 (9.5%)	14 (8.8%)	35 (9.2%)
Very severely	10 (4.5%)	7 (4.4%)	17 (4.5%)
I have felt that asthma is controlling my life	n=221	n=160	n=381
Not at all	96 (43.4%)	73 (45.6%)	169 (44.4%)
Mildly	45 (20.4%)	48 (30.0%)	93 (24.4%)
Moderately	44 (19.9%)	20 (12.5%)	64 (16.8%)
Severely	27 (12.2%)	14 (8.8%)	41 (10.8%)
Very severely	9 (4.1%)	5 (3.1%)	14 (3.7%)
I have been worried about my present or future health because of asthma	n=221	n=160	n=381
Not at all	73 (33.0%)	59 (36.9%)	132 (34.6%)
Mildly	60 (27.1%)	43 (26.9%)	103 (27.0%)
Moderately	54 (24.4%)	37 (23.1%)	91 (23.9%)
Severely	27 (12.2%)	12 (7.5%)	39 (10.2%)
Very severely	7 (3.2%)	9 (5.6%)	16 (4.2%)
I have been worried about asthma shortening my life	n=221	n=160	n=381
Not at all	110 (49.8%)	82 (51.3%)	192 (50.4%)
Mildly	48 (21.7%)	33 (20.6%)	81 (21.3%)
Moderately	31 (14.0%)	20 (12.5%)	51 (13.4%)
Severely	25 (11.3%)	14 (8.8%)	39 (10.2%)
Very severely	7 (3.2%)	11 (6.9%)	18 (4.7%)
I have felt dependent on my asthma inhalers	n=221	n=160	n=381
Not at all	32 (14.5%)	29 (18.1%)	61 (16.0%)
Mildly	61 (27.6%)	38 (23.8%)	99 (26.0%)
Moderately	50 (22.6%)	40 (25.0%)	90 (23.6%)
Severely	46 (20.8%)	34 (21.3%)	80 (21.0%)
Very severely	32 (14.5%)	19 (11.9%)	51 (13.4%)
IAQLQ – 1 MONTH FOLLOW-UP VISIT			
I have been troubled by episodes of shortness of breath	n=190	n=131	n=321
Not at all	32 (16.8%)	27 (20.6%)	59 (18.4%)
Mildly	85 (44.7%)	59 (45.0%)	144 (44.9%)
Moderately	56 (29.5%)	32 (24.4%)	88 (27.4%)
Severely	14 (7.4%)	12 (9.2%)	26 (8.1%)
Very severely	3 (1.6%)	1 (0.8%)	4 (1.2%)

	Intervention	Comparator	Overall
I have been troubled by wheezing attacks	n=190	n=131	n=321
Not at all	83 (43.7%)	53 (40.5%)	136 (42.4%)
Mildly	64 (33.7%)	43 (32.8%)	107 (33.3%)
Moderately	35 (18.4%)	21 (16.0%)	56 (17.4%)
Severely	6 (3.2%)	13 (9.9%)	19 (5.9%)
Very severely	2 (1.1%)	1 (0.8%)	3 (0.9%)
I have been troubled by tightness in the chest	n=190	n=131	n=321
Not at all	72 (37.9%)	52 (39.7%)	124 (38.6%)
Mildly	75 (39.5%)	45 (34.4%)	120 (37.4%)
Moderately	35 (18.4%)	22 (16.8%)	57 (17.8%)
Severely	5 (2.6%)	9 (6.9%)	14 (4.4%)
Very severely	3 (1.6%)	3 (2.3%)	6 (1.9%)
I have been restricted in walking down the street on level ground or doing light housework because of asthma or shortness of breath	n=190	n=131	n=321
Not at all	93 (48.9%)	64 (48.9%)	157 (48.9%)
Mildly	58 (30.5%)	29 (22.1%)	87 (27.1%)
Moderately	25 (13.2%)	24 (18.3%)	49 (15.3%)
Severely	10 (5.3%)	11 (8.4%)	21 (6.5%)
Very severely	4 (2.1%)	3 (2.3%)	7 (2.2%)
I have been restricted in walking up hills or doing heavy housework because of asthma or shortness of breath	n=190	n=131	n=321
Not at all	53 (27.9%)	37 (28.2%)	90 (28.0%)
Mildly	54 (28.4%)	44 (33.6%)	98 (30.5%)
Moderately	50 (26.3%)	29 (22.1%)	79 (24.6%)
Severely	26 (13.7%)	15 (11.5%)	41 (12.8%)
Very severely	7 (3.7%)	6 (4.6%)	13 (4.0%)
I have felt tired or a general lack of energy	n=190	n=131	n=321
Not at all	35 (18.4%)	24 (18.3%)	59 (18.4%)
Mildly	59 (31.1%)	48 (36.6%)	107 (33.3%)
Moderately	63 (33.2%)	44 (33.6%)	107 (33.3%)
Severely	24 (12.6%)	13 (9.9%)	37 (11.5%)
Very severely	9 (4.7%)	2 (1.5%)	11 (3.4%)
I have been unable to sleep at night	n=190	n=131	n=321
Not at all	73 (38.4%)	59 (45.0%)	132 (41.1%)

	Intervention	Comparator	Overall
Mildly	58 (30.5%)	38 (29.0%)	96 (29.9%)
Moderately	43 (22.6%)	18 (13.7%)	61 (19.0%)
Severely	13 (6.8%)	9 (6.9%)	22 (6.9%)
Very severely	3 (1.6%)	7 (5.3%)	10 (3.1%)
I have felt sad or depressed	n=190	n=131	n=321
Not at all	108 (56.8%)	81 (61.8%)	189 (58.9%)
Mildly	45 (23.7%)	29 (22.1%)	74 (23.1%)
Moderately	25 (13.2%)	14 (10.7%)	39 (12.1%)
Severely	8 (4.2%)	2 (1.5%)	10 (3.1%)
Very severely	4 (2.1%)	5 (3.8%)	9 (2.8%)
I have felt frustrated with myself	n=190	n=131	n=321
Not at all	74 (38.9%)	65 (49.6%)	139 (43.3%)
Mildly	65 (34.2%)	40 (30.5%)	105 (32.7%)
Moderately	26 (13.7%)	16 (12.2%)	42 (13.1%)
Severely	16 (8.4%)	7 (5.3%)	23 (7.2%)
Very severely	9 (4.7%)	3 (2.3%)	12 (3.7%)
I have felt anxious under tension or stressed	n=190	n=131	n=321
Not at all	72 (37.9%)	68 (51.9%)	140 (43.6%)
Mildly	66 (34.7%)	32 (24.4%)	98 (30.5%)
Moderately	33 (17.4%)	23 (17.6%)	56 (17.4%)
Severely	13 (6.8%)	5 (3.8%)	18 (5.6%)
Very severely	6 (3.2%)	3 (2.3%)	9 (2.8%)
I have felt that asthma or shortness of breath is preventing me from achieving what I want from life	n=190	n=131	n=321
Not at all	88 (46.3%)	66 (50.4%)	154 (48.0%)
Mildly	48 (25.3%)	35 (26.7%)	83 (25.9%)
Moderately	42 (22.1%)	16 (12.2%)	58 (18.1%)
Severely	8 (4.2%)	12 (9.2%)	20 (6.2%)
Very severely	4 (2.1%)	2 (1.5%)	6 (1.9%)
Asthma or shortness of breath has interfered with my social life	n=190	n=131	n=321
Not at all	115 (60.5%)	78 (59.5%)	193 (60.1%)
Mildly	37 (19.5%)	26 (19.8%)	63 (19.6%)
Moderately	25 (13.2%)	20 (15.3%)	45 (14.0%)
Severely	10 (5.3%)	5 (3.8%)	15 (4.7%)

	Intervention	Comparator	Overall
Very severely	3 (1.6%)	2 (1.5%)	5 (1.6%)
I have been limited in going to certain places because they are bad for my asthma	n=190	n=131	n=321
Not at all	100 (52.6%)	72 (55.0%)	172 (53.6%)
Mildly	51 (26.8%)	31 (23.7%)	82 (25.5%)
Moderately	27 (14.2%)	20 (15.3%)	47 (14.6%)
Severely	10 (5.3%)	5 (3.8%)	15 (4.7%)
Very severely	2 (1.1%)	3 (2.3%)	5 (1.6%)
I have been limited in going to certain places because I have been afraid of getting an asthma attack and not being able to get help	n=190	n=131	n=321
Not at all	123 (64.7%)	84 (64.1%)	207 (64.5%)
Mildly	46 (24.2%)	24 (18.3%)	70 (21.8%)
Moderately	12 (6.3%)	15 (11.5%)	27 (8.4%)
Severely	7 (3.7%)	5 (3.8%)	12 (3.7%)
Very severely	2 (1.1%)	3 (2.3%)	5 (1.6%)
I have been restricted in the sports hobbies or other recreations I can engage in because of my asthma or shortness of breath	n=190	n=131	n=321
Not at all	89 (46.8%)	57 (43.5%)	146 (45.5%)
Mildly	50 (26.3%)	38 (29.0%)	88 (27.4%)
Moderately	34 (17.9%)	18 (13.7%)	52 (16.2%)
Severely	12 (6.3%)	11 (8.4%)	23 (7.2%)
Very severely	5 (2.6%)	7 (5.3%)	12 (3.7%)
I have felt generally restricted	n=190	n=131	n=321
Not at all	80 (42.1%)	69 (52.7%)	149 (46.4%)
Mildly	60 (31.6%)	30 (22.9%)	90 (28.0%)
Moderately	39 (20.5%)	18 (13.7%)	57 (17.8%)
Severely	9 (4.7%)	11 (8.4%)	20 (6.2%)
Very severely	2 (1.1%)	3 (2.3%)	5 (1.6%)
I have felt that asthma is controlling my life	n=190	n=131	n=321
Not at all	102 (53.7%)	70 (53.4%)	172 (53.6%)
Mildly	49 (25.8%)	34 (26.0%)	83 (25.9%)
Moderately	29 (15.3%)	15 (11.5%)	44 (13.7%)
Severely	9 (4.7%)	10 (7.6%)	19 (5.9%)
Very severely	1 (0.5%)	2 (1.5%)	3 (0.9%)

	Intervention	Comparator	Overall
I have been worried about my present or future health because of asthma	n=190	n=131	n=321
Not at all	83 (43.7%)	60 (45.8%)	143 (44.5%)
Mildly	60 (31.6%)	39 (29.8%)	99 (30.8%)
Moderately	38 (20.0%)	24 (18.3%)	62 (19.3%)
Severely	7 (3.7%)	6 (4.6%)	13 (4.0%)
Very severely	2 (1.1%)	2 (1.5%)	4 (1.2%)
I have been worried about asthma shortening my life	n=190	n=131	n=321
Not at all	110 (57.9%)	78 (59.5%)	188 (58.6%)
Mildly	54 (28.4%)	29 (22.1%)	83 (25.9%)
Moderately	16 (8.4%)	14 (10.7%)	30 (9.3%)
Severely	7 (3.7%)	7 (5.3%)	14 (4.4%)
Very severely	3 (1.6%)	3 (2.3%)	6 (1.9%)
IAQLQ – 12 MONTHS FOLLOW-UP VISIT			
I have been troubled by episodes of shortness of breath	n=143	n=111	n=254
Not at all	37 (25.9%)	27 (24.3%)	64 (25.2%)
Mildly	60 (42.0%)	47 (42.3%)	107 (42.1%)
Moderately	40 (28.0%)	23 (20.7%)	63 (24.8%)
Severely	4 (2.8%)	12 (10.8%)	16 (6.3%)
Very severely	2 (1.4%)	2 (1.8%)	4 (1.6%)
I have been troubled by wheezing attacks	n=143	n=111	n=254
Not at all	73 (51.0%)	42 (37.8%)	115 (45.3%)
Mildly	39 (27.3%)	46 (41.4%)	85 (33.5%)
Moderately	29 (20.3%)	17 (15.3%)	46 (18.1%)
Severely	1 (0.7%)	5 (4.5%)	6 (2.4%)
Very severely	1 (0.7%)	1 (0.9%)	2 (0.8%)
I have been troubled by tightness in the chest	n=143	n=111	n=254
Not at all	72 (50.3%)	51 (45.9%)	123 (48.4%)
Mildly	36 (25.2%)	29 (26.1%)	65 (25.6%)
Moderately	27 (18.9%)	23 (20.7%)	50 (19.7%)
Severely	5 (3.5%)	8 (7.2%)	13 (5.1%)
Very severely	3 (2.1%)	0 (0.0%)	3 (1.2%)
I have been restricted in walking down the street on level ground or doing light housework because of asthma or shortness of breath	n=143	n=111	n=254

	Intervention	Comparator	Overall
Not at all	79 (55.2%)	62 (55.9%)	141 (55.5%)
Mildly	34 (23.8%)	18 (16.2%)	52 (20.5%)
Moderately	22 (15.4%)	20 (18.0%)	42 (16.5%)
Severely	6 (4.2%)	9 (8.1%)	15 (5.9%)
Very severely	2 (1.4%)	2 (1.8%)	4 (1.6%)
I have been restricted in walking up hills or doing heavy housework because of asthma or shortness of breath	n=143	n=111	n=254
Not at all	59 (41.3%)	39 (35.1%)	98 (38.6%)
Mildly	32 (22.4%)	29 (26.1%)	61 (24.0%)
Moderately	31 (21.7%)	19 (17.1%)	50 (19.7%)
Severely	15 (10.5%)	19 (17.1%)	34 (13.4%)
Very severely	6 (4.2%)	5 (4.5%)	11 (4.3%)
I have felt tired or a general lack of energy	n=143	n=111	n=254
Not at all	31 (21.7%)	31 (27.9%)	62 (24.4%)
Mildly	59 (41.3%)	30 (27.0%)	89 (35.0%)
Moderately	33 (23.1%)	34 (30.6%)	67 (26.4%)
Severely	17 (11.9%)	15 (13.5%)	32 (12.6%)
Very severely	3 (2.1%)	1 (0.9%)	4 (1.6%)
I have been unable to sleep at night	n=143	n=111	n=254
Not at all	58 (40.6%)	50 (45.0%)	108 (42.5%)
Mildly	39 (27.3%)	31 (27.9%)	70 (27.6%)
Moderately	26 (18.2%)	18 (16.2%)	44 (17.3%)
Severely	16 (11.2%)	10 (9.0%)	26 (10.2%)
Very severely	4 (2.8%)	2 (1.8%)	6 (2.4%)
I have felt sad or depressed	n=143	n=111	n=254
Not at all	76 (53.1%)	66 (59.5%)	142 (55.9%)
Mildly	38 (26.6%)	13 (11.7%)	51 (20.1%)
Moderately	22 (15.4%)	23 (20.7%)	45 (17.7%)
Severely	6 (4.2%)	7 (6.3%)	13 (5.1%)
Very severely	1 (0.7%)	2 (1.8%)	3 (1.2%)
I have felt frustrated with myself	n=143	n=111	n=254
Not at all	72 (50.3%)	56 (50.5%)	128 (50.4%)
Mildly	29 (20.3%)	24 (21.6%)	53 (20.9%)
Moderately	24 (16.8%)	18 (16.2%)	42 (16.5%)
Severely	17 (11.9%)	9 (8.1%)	26 (10.2%)

	Intervention	Comparator	Overall
Very severely	1 (0.7%)	4 (3.6%)	5 (2.0%)
I have felt anxious under tension or stressed	n=143	n=111	n=254
Not at all	66 (46.2%)	52 (46.8%)	118 (46.5%)
Mildly	33 (23.1%)	24 (21.6%)	57 (22.4%)
Moderately	32 (22.4%)	20 (18.0%)	52 (20.5%)
Severely	10 (7.0%)	13 (11.7%)	23 (9.1%)
Very severely	2 (1.4%)	2 (1.8%)	4 (1.6%)
I have felt that asthma or shortness of breath is preventing me from achieving what I want from life	n=143	n=111	n=254
Not at all	83 (58.0%)	57 (51.4%)	140 (55.1%)
Mildly	35 (24.5%)	27 (24.3%)	62 (24.4%)
Moderately	14 (9.8%)	15 (13.5%)	29 (11.4%)
Severely	8 (5.6%)	10 (9.0%)	18 (7.1%)
Very severely	3 (2.1%)	2 (1.8%)	5 (2.0%)
Asthma or shortness of breath has interfered with my social life	n=143	n=111	n=254
Not at all	100 (69.9%)	71 (64.0%)	171 (67.3%)
Mildly	24 (16.8%)	19 (17.1%)	43 (16.9%)
Moderately	13 (9.1%)	12 (10.8%)	25 (9.8%)
Severely	3 (2.1%)	7 (6.3%)	10 (3.9%)
Very severely	3 (2.1%)	2 (1.8%)	5 (2.0%)
I have been limited in going to certain places because they are bad for my asthma	n=143	n=111	n=254
Not at all	81 (56.6%)	53 (47.7%)	134 (52.8%)
Mildly	27 (18.9%)	25 (22.5%)	52 (20.5%)
Moderately	21 (14.7%)	21 (18.9%)	42 (16.5%)
Severely	9 (6.3%)	9 (8.1%)	18 (7.1%)
Very severely	5 (3.5%)	3 (2.7%)	8 (3.1%)
I have been limited in going to certain places because I have been afraid of getting an asthma attack and not being able to get help	n=143	n=111	n=254
Not at all	112 (78.3%)	75 (67.6%)	187 (73.6%)
Mildly	20 (14.0%)	14 (12.6%)	34 (13.4%)
Moderately	7 (4.9%)	15 (13.5%)	22 (8.7%)
Severely	2 (1.4%)	6 (5.4%)	8 (3.1%)
Very severely	2 (1.4%)	1 (0.9%)	3 (1.2%)

	Intervention	Comparator	Overall
I have been restricted in the sports hobbies or other recreations I can engage in because of my asthma or shortness of breath	n=143	n=111	n=254
Not at all	86 (60.1%)	52 (46.8%)	138 (54.3%)
Mildly	23 (16.1%)	29 (26.1%)	52 (20.5%)
Moderately	23 (16.1%)	15 (13.5%)	38 (15.0%)
Severely	5 (3.5%)	8 (7.2%)	13 (5.1%)
Very severely	6 (4.2%)	7 (6.3%)	13 (5.1%)
I have felt generally restricted	n=143	n=111	n=254
Not at all	79 (55.2%)	55 (49.5%)	134 (52.8%)
Mildly	40 (28.0%)	29 (26.1%)	69 (27.2%)
Moderately	15 (10.5%)	14 (12.6%)	29 (11.4%)
Severely	8 (5.6%)	11 (9.9%)	19 (7.5%)
Very severely	1 (0.7%)	2 (1.8%)	3 (1.2%)
I have felt that asthma is controlling my life	n=143	n=111	n=254
Not at all	99 (69.2%)	70 (63.1%)	169 (66.5%)
Mildly	25 (17.5%)	17 (15.3%)	42 (16.5%)
Moderately	13 (9.1%)	17 (15.3%)	30 (11.8%)
Severely	5 (3.5%)	6 (5.4%)	11 (4.3%)
Very severely	1 (0.7%)	1 (0.9%)	2 (0.8%)
I have been worried about my present or future health because of asthma	n=143	n=111	n=254
Not at all	90 (62.9%)	63 (56.8%)	153 (60.2%)
Mildly	31 (21.7%)	23 (20.7%)	54 (21.3%)
Moderately	19 (13.3%)	13 (11.7%)	32 (12.6%)
Severely	2 (1.4%)	11 (9.9%)	13 (5.1%)
Very severely	1 (0.7%)	1 (0.9%)	2 (0.8%)
I have been worried about asthma shortening my life	n=143	n=111	n=254
Not at all	105 (73.4%)	72 (64.9%)	177 (69.7%)
Mildly	19 (13.3%)	13 (11.7%)	32 (12.6%)
Moderately	16 (11.2%)	14 (12.6%)	30 (11.8%)
Severely	2 (1.4%)	10 (9.0%)	12 (4.7%)
Very severely	1 (0.7%)	2 (1.8%)	3 (1.2%)
I have felt dependent on my asthma inhalers	n=143	n=111	n=254
Not at all	67 (46.9%)	37 (33.3%)	104 (40.9%)

	Intervention	Comparator	Overall
Mildly	27 (18.9%)	29 (26.1%)	56 (22.0%)
Moderately	31 (21.7%)	19 (17.1%)	50 (19.7%)
Severely	11 (7.7%)	18 (16.2%)	29 (11.4%)
Very severely	7 (4.9%)	8 (7.2%)	15 (5.9%)

APPENDIX M: SF-12 QUESTIONS BY VISIT

Appendix Table M-1: Participant responses to Short Form-12 quality of life questionnaire (SF-12) by visit

	Intervention (N=221)	Comparator (N=160)	Overall (N=381)
SF-12 – BASELINE			
In general, would you say your health is			
Excellent	5/221 (2.3%)	6/160 (3.8%)	11/381 (2.9%)
Very Good	41/221 (18.6%)	32/160 (20.0%)	73/381 (19.2%)
Good	102/221 (46.2%)	67/160 (41.9%)	169/381 (44.4%)
Fair	58/221 (26.2%)	42/160 (26.3%)	100/381 (26.2%)
Poor	15/221 (6.8%)	13/160 (8.1%)	28/381 (7.3%)
MODERATE ACTIVITIES such as moving a table or pushing a vacuum cleaner or bowling or playing golf			
Yes, limited a lot	47/221 (21.3%)	33/160 (20.6%)	80/381 (21.0%)
Yes, limited a little	104/221 (47.1%)	63/160 (39.4%)	167/381 (43.8%)
No, not limited at all	70/221 (31.7%)	64/160 (40.0%)	134/381 (35.2%)
Climbing SEVERAL flights of stairs?			
Yes, limited a lot	90/221 (40.7%)	54/160 (33.8%)	144/381 (37.8%)
Yes, limited a little	98/221 (44.3%)	66/160 (41.3%)	164/381 (43.0%)
No, not limited at all	33/221 (14.9%)	40/160 (25.0%)	73/381 (19.2%)
ACCOMPLISHED LESS than you would like?			
All of the time	19/221 (8.6%)	8/160 (5.0%)	27/381 (7.1%)
Most of the time	42/221 (19.0%)	36/160 (22.5%)	78/381 (20.5%)
Some of the time	79/221 (35.7%)	50/160 (31.3%)	129/381 (33.9%)
A little of the time	48/221 (21.7%)	39/160 (24.4%)	87/381 (22.8%)
None of the time	33/221 (14.9%)	27/160 (16.9%)	60/381 (15.7%)
Were limited in the KIND of work or other activities			
All of the time	19/221 (8.6%)	10/160 (6.3%)	29/381 (7.6%)
Most of the time	40/221 (18.1%)	34/160 (21.3%)	74/381 (19.4%)
Some of the time	79/221 (35.7%)	52/160 (32.5%)	131/381 (34.4%)
A little of the time	45/221 (20.4%)	36/160 (22.5%)	81/381 (21.3%)
None of the time	38/221 (17.2%)	28/160 (17.5%)	66/381 (17.3%)
ACCOMPLISHED LESS than you would like			
All of the time	7/221 (3.2%)	10/160 (6.3%)	17/381 (4.5%)
Most of the time	29/221 (13.1%)	26/160 (16.3%)	55/381 (14.4%)
Some of the time	60/221 (27.1%)	35/160 (21.9%)	95/381 (24.9%)

	Intervention (N=221)	Comparator (N=160)	Overall (N=381)
A little of the time	48/221 (21.7%)	32/160 (20.0%)	80/381 (21.0%)
None of the time	77/221 (34.8%)	57/160 (35.6%)	134/381 (35.2%)
Did work or other activities LESS CAREFULLY THAN USUAL			
All of the time	6/221 (2.7%)	5/160 (3.1%)	11/381 (2.9%)
Most of the time	23/221 (10.4%)	20/160 (12.5%)	43/381 (11.3%)
Some of the time	53/221 (24.0%)	31/160 (19.4%)	84/381 (22.0%)
A little of the time	44/221 (19.9%)	40/160 (25.0%)	84/381 (22.0%)
None of the time	95/221 (43.0%)	64/160 (40.0%)	159/381 (41.7%)
How much did PAIN interfere with your normal work (including both work outside the home and housework)?			
Not at all	56/221 (25.3%)	36/160 (22.5%)	92/381 (24.1%)
A little bit	69/221 (31.2%)	49/160 (30.6%)	118/381 (31.0%)
Moderately	39/221 (17.6%)	42/160 (26.3%)	81/381 (21.3%)
Quite a bit	43/221 (19.5%)	25/160 (15.6%)	68/381 (17.8%)
Extremely	14/221 (6.3%)	8/160 (5.0%)	22/381 (5.8%)
Have you felt calm and peaceful?			
All of the time	15/221 (6.8%)	18/160 (11.3%)	33/381 (8.7%)
Most of the time	80/221 (36.2%)	66/160 (41.3%)	146/381 (38.3%)
Some of the time	66/221 (29.9%)	40/160 (25.0%)	106/381 (27.8%)
A little of the time	48/221 (21.7%)	23/160 (14.4%)	71/381 (18.6%)
None of the time	12/221 (5.4%)	13/160 (8.1%)	25/381 (6.6%)
Did you have a lot of energy?			
All of the time	3/221 (1.4%)	8/160 (5.0%)	11/381 (2.9%)
Most of the time	37/221 (16.7%)	32/160 (20.0%)	69/381 (18.1%)
Some of the time	74/221 (33.5%)	53/160 (33.1%)	127/381 (33.3%)
A little of the time	72/221 (32.6%)	47/160 (29.4%)	119/381 (31.2%)
None of the time	35/221 (15.8%)	20/160 (12.5%)	55/381 (14.4%)
Have you felt downhearted and depressed?			
All of the time	6/221 (2.7%)	10/160 (6.3%)	16/381 (4.2%)
Most of the time	18/221 (8.1%)	14/160 (8.8%)	32/381 (8.4%)
Some of the time	45/221 (20.4%)	35/160 (21.9%)	80/381 (21.0%)
A little of the time	83/221 (37.6%)	44/160 (27.5%)	127/381 (33.3%)
None of the time	69/221 (31.2%)	57/160 (35.6%)	126/381 (33.1%)

	Intervention (N=221)	Comparator (N=160)	Overall (N=381)
How much of the time has your PHYSICAL HEALTH OR EMOTIONAL PROBLEMS interfered with your social activities (like visiting with friends, relatives etc.)?			
All of the time	11/221 (5.0%)	8/160 (5.0%)	19/381 (5.0%)
Most of the time	29/221 (13.1%)	18/160 (11.3%)	47/381 (12.3%)
Some of the time	61/221 (27.6%)	37/160 (23.1%)	98/381 (25.7%)
A little of the time	43/221 (19.5%)	34/160 (21.3%)	77/381 (20.2%)
None of the time	77/221 (34.8%)	63/160 (39.4%)	140/381 (36.7%)
SF-12 – 12 MONTH FOLLOW-UP VISIT			
In general, would you say your health is			
Excellent	11/143 (7.7%)	10/111 (9.0%)	21/254 (8.3%)
Very Good	44/143 (30.8%)	32/111 (28.8%)	76/254 (29.9%)
Good	52/143 (36.4%)	36/111 (32.4%)	88/254 (34.6%)
Fair	24/143 (16.8%)	22/111 (19.8%)	46/254 (18.1%)
Poor	12/143 (8.4%)	11/111 (9.9%)	23/254 (9.1%)
MODERATE ACTIVITIES such as moving a table or pushing a vacuum cleaner or bowling or playing golf			
Yes, limited a lot	26/143 (18.2%)	24/111 (21.6%)	50/254 (19.7%)
Yes, limited a little	41/143 (28.7%)	37/111 (33.3%)	78/254 (30.7%)
No, not limited at all	76/143 (53.1%)	50/111 (45.0%)	126/254 (49.6%)
Climbing SEVERAL flights of stairs?			
Yes, limited a lot	36/143 (25.2%)	32/111 (28.8%)	68/254 (26.8%)
Yes, limited a little	55/143 (38.5%)	46/111 (41.4%)	101/254 (39.8%)
No, not limited at all	52/143 (36.4%)	33/111 (29.7%)	85/254 (33.5%)
ACCOMPLISHED LESS than you would like?			
All of the time	7/143 (4.9%)	7/111 (6.3%)	14/254 (5.5%)
Most of the time	19/143 (13.3%)	15/111 (13.5%)	34/254 (13.4%)
Some of the time	30/143 (21.0%)	28/111 (25.2%)	58/254 (22.8%)
A little of the time	29/143 (20.3%)	23/111 (20.7%)	52/254 (20.5%)
None of the time	58/143 (40.6%)	38/111 (34.2%)	96/254 (37.8%)
Were limited in the KIND of work or other activities			
All of the time	7/143 (4.9%)	6/111 (5.4%)	13/254 (5.1%)
Most of the time	21/143 (14.7%)	14/111 (12.6%)	35/254 (13.8%)
Some of the time	28/143 (19.6%)	26/111 (23.4%)	54/254 (21.3%)

	Intervention (N=221)	Comparator (N=160)	Overall (N=381)
A little of the time	32/143 (22.4%)	27/111 (24.3%)	59/254 (23.2%)
None of the time	55/143 (38.5%)	38/111 (34.2%)	93/254 (36.6%)
ACCOMPLISHED LESS than you would like			
All of the time	4/143 (2.8%)	5/111 (4.5%)	9/254 (3.5%)
Most of the time	12/143 (8.4%)	10/111 (9.0%)	22/254 (8.7%)
Some of the time	23/143 (16.1%)	19/111 (17.1%)	42/254 (16.5%)
A little of the time	30/143 (21.0%)	19/111 (17.1%)	49/254 (19.3%)
None of the time	74/143 (51.7%)	58/111 (52.3%)	132/254 (52.0%)
Did work or other activities LESS CAREFULLY THAN USUAL			
All of the time	2/143 (1.4%)	2/111 (1.8%)	4/254 (1.6%)
Most of the time	8/143 (5.6%)	12/111 (10.8%)	20/254 (7.9%)
Some of the time	19/143 (13.3%)	14/111 (12.6%)	33/254 (13.0%)
A little of the time	26/143 (18.2%)	14/111 (12.6%)	40/254 (15.7%)
None of the time	88/143 (61.5%)	69/111 (62.2%)	157/254 (61.8%)
How much did PAIN interfere with your normal work (including both work outside the home and housework)?			
Not at all	58/143 (40.6%)	45/111 (40.5%)	103/254 (40.6%)
A little bit	32/143 (22.4%)	26/111 (23.4%)	58/254 (22.8%)
Moderately	23/143 (16.1%)	19/111 (17.1%)	42/254 (16.5%)
Quite a bit	24/143 (16.8%)	16/111 (14.4%)	40/254 (15.7%)
Extremely	6/143 (4.2%)	5/111 (4.5%)	11/254 (4.3%)
Have you felt calm and peaceful?			
All of the time	14/143 (9.8%)	16/111 (14.4%)	30/254 (11.8%)
Most of the time	65/143 (45.5%)	44/111 (39.6%)	109/254 (42.9%)
Some of the time	47/143 (32.9%)	31/111 (27.9%)	78/254 (30.7%)
A little of the time	11/143 (7.7%)	11/111 (9.9%)	22/254 (8.7%)
None of the time	6/143 (4.2%)	9/111 (8.1%)	15/254 (5.9%)
Did you have a lot of energy?			
All of the time	6/143 (4.2%)	7/111 (6.3%)	13/254 (5.1%)
Most of the time	46/143 (32.2%)	31/111 (27.9%)	77/254 (30.3%)
Some of the time	48/143 (33.6%)	36/111 (32.4%)	84/254 (33.1%)
A little of the time	30/143 (21.0%)	27/111 (24.3%)	57/254 (22.4%)
None of the time	13/143 (9.1%)	10/111 (9.0%)	23/254 (9.1%)
Have you felt downhearted and depressed?			

	Intervention (N=221)	Comparator (N=160)	Overall (N=381)
All of the time	1/143 (0.7%)	3/111 (2.7%)	4/254 (1.6%)
Most of the time	13/143 (9.1%)	13/111 (11.7%)	26/254 (10.2%)
Some of the time	30/143 (21.0%)	20/111 (18.0%)	50/254 (19.7%)
A little of the time	36/143 (25.2%)	19/111 (17.1%)	55/254 (21.7%)
None of the time	63/143 (44.1%)	56/111 (50.5%)	119/254 (46.9%)
How much of the time has your PHYSICAL HEALTH OR EMOTIONAL PROBLEMS interfered with your social activities (like visiting with friends, relatives etc.)?			
All of the time	2/143 (1.4%)	5/111 (4.5%)	7/254 (2.8%)
Most of the time	14/143 (9.8%)	8/111 (7.2%)	22/254 (8.7%)
Some of the time	23/143 (16.1%)	27/111 (24.3%)	50/254 (19.7%)
A little of the time	22/143 (15.4%)	14/111 (12.6%)	36/254 (14.2%)
None of the time	82/143 (57.3%)	57/111 (51.4%)	139/254 (54.7%)

APPENDIX N: ADHERENCE

Appendix Table N-1: Participant adherence and factors affecting adherence (Intervention arm only)

	Intervention	
	Baseline (n=221)	Month 12 (n=143)
Adherence status determined by pharmacist		
Adherent	105/178 (59.0%)	-
Non-adherent	73/178 (41.0%)	-
Concerns about their asthma		
No	30/73 (41.1%)	135/143 (94.4%)
Yes	43/73 (58.9%)	8/143 (5.6%)
Information need	7/73 (9.6%)	
Medication related concerns	14/73 (19.2%)	
Concern about effect of asthma on comorbidities	7/73 (9.6%)	
Concern about effect of asthma on work or lifestyle	22/73 (30.1%)	
Asthma outcome concerns	13/73 (17.8%)	
Concerns about trigger management	11/73 (15.1%)	
How well are your asthma medications working?[2]		
n	73	-
Mean (SD)	3.4 (1.27)	-
Median (Q1; Q3)	3.6 (2.5; 4.3)	-
min max	0 5	-
Does your asthma medication bother you in any way		
No	55/73 (75.3%)	-
Yes	18/73 (24.7%)	-
Any problems remembering to use medications		
No	37/73 (50.7%)	-
Yes	36/73 (49.3%)	-
Any problems getting repeats filled on time		
No	56/73 (76.7%)	-
Yes	17/73 (23.3%)	-

Note:

1. Adherence visual analogue scale (All things considered, how much of the time do you use ALL of your asthma preventer/controller medications EXACTLY as directed?) Responses ranged from 1(none of the time) to 10 (all of the time).
2. Medication efficacy visual analogue scale (How well are your asthma medications working?) Responses ranged from 1(does not work at all) to 5(works very well)

APPENDIX O: RCAT QUESTIONS BY VISIT

Appendix Table O-1: Participant responses to Rhinitis Control Assessment Test (RCAT) by visit

	Intervention	Comparator	Overall
RCAT – BASELINE			
During the past week how often did you have nasal congestion?	n=161	n=111	n=272
Extremely often	33 (20.5%)	4 (3.6%)	37 (13.6%)
Often	28 (17.4%)	39 (35.1%)	67 (24.6%)
Sometimes	39 (24.2%)	32 (28.8%)	71 (26.1%)
Rarely	26 (16.1%)	17 (15.3%)	43 (15.8%)
Never	35 (21.7%)	19 (17.1%)	54 (19.9%)
During the past week how often did you sneeze?	n=161	n=111	n=272
Extremely often	20 (12.4%)	15 (13.5%)	35 (12.9%)
Often	37 (23.0%)	28 (25.2%)	65 (23.9%)
Sometimes	56 (34.8%)	39 (35.1%)	95 (34.9%)
Rarely	32 (19.9%)	21 (18.9%)	53 (19.5%)
Never	16 (9.9%)	8 (7.2%)	24 (8.8%)
During the past week how often did you have watery eyes?	n=161	n=111	n=272
Extremely often	11 (6.8%)	16 (14.4%)	27 (9.9%)
Often	28 (17.4%)	19 (17.1%)	47 (17.3%)
Sometimes	46 (28.6%)	36 (32.4%)	82 (30.1%)
Rarely	33 (20.5%)	25 (22.5%)	58 (21.3%)
Never	43 (26.7%)	15 (13.5%)	58 (21.3%)
During the past week to what extent did your nasal or other allergy symptoms interfere with your sleep?	n=161	n=111	n=272
All the time	7 (4.3%)	7 (6.3%)	14 (5.1%)
A lot	15 (9.3%)	15 (13.5%)	30 (11.0%)
Somewhat	34 (21.1%)	19 (17.1%)	53 (19.5%)
A little	37 (23.0%)	31 (27.9%)	68 (25.0%)
Not at all	68 (42.2%)	39 (35.1%)	107 (39.3%)
During the past week how often did you avoid any activities (e.g. visiting a house with a dog or cat or gardening) because of your nasal or other allergy symptoms?	n=161	n=111	n=272
Extremely often	5 (3.1%)	5 (4.5%)	10 (3.7%)
Often	9 (5.6%)	9 (8.1%)	18 (6.6%)

	Intervention	Comparator	Overall
Sometimes	29 (18.0%)	23 (20.7%)	52 (19.1%)
Rarely	18 (11.2%)	17 (15.3%)	35 (12.9%)
Never	100 (62.1%)	57 (51.4%)	157 (57.7%)
During the past week how well were your nasal or other allergy symptoms controlled?	n=161	n=111	n=272
Not at all	15 (9.3%)	9 (8.1%)	24 (8.8%)
A little	26 (16.1%)	21 (18.9%)	47 (17.3%)
Somewhat	55 (34.2%)	30 (27.0%)	85 (31.3%)
Very	30 (18.6%)	33 (29.7%)	63 (23.2%)
Completely	35 (21.7%)	18 (16.2%)	53 (19.5%)
RCAT – 1 MONTH FOLLOW-UP VISIT			
During the past week how often did you have nasal congestion?	n=128	n=89	n=217
Extremely often	5 (3.9%)	10 (11.2%)	15 (6.9%)
Often	26 (20.3%)	12 (13.5%)	38 (17.5%)
Sometimes	35 (27.3%)	30 (33.7%)	65 (30.0%)
Rarely	30 (23.4%)	22 (24.7%)	52 (24.0%)
Never	32 (25.0%)	15 (16.9%)	47 (21.7%)
During the past week how often did you sneeze?	n=128	n=89	n=217
Extremely often	3 (2.3%)	7 (7.9%)	10 (4.6%)
Often	28 (21.9%)	19 (21.3%)	47 (21.7%)
Sometimes	39 (30.5%)	34 (38.2%)	73 (33.6%)
Rarely	36 (28.1%)	19 (21.3%)	55 (25.3%)
Never	22 (17.2%)	10 (11.2%)	32 (14.7%)
During the past week how often did you have watery eyes?	n=128	n=89	n=217
Extremely often	8 (6.3%)	6 (6.7%)	14 (6.5%)
Often	9 (7.0%)	16 (18.0%)	25 (11.5%)
Sometimes	33 (25.8%)	27 (30.3%)	60 (27.6%)
Rarely	30 (23.4%)	21 (23.6%)	51 (23.5%)
Never	48 (37.5%)	19 (21.3%)	67 (30.9%)
During the past week to what extent did your nasal or other allergy symptoms interfere with your sleep?	n=128	n=89	n=217
All the time	3 (2.3%)	3 (3.4%)	6 (2.8%)
A lot	9 (7.0%)	9 (10.1%)	18 (8.3%)
Somewhat	14 (10.9%)	9 (10.1%)	23 (10.6%)

	Intervention	Comparator	Overall
A little	26 (20.3%)	20 (22.5%)	46 (21.2%)
Not at all	76 (59.4%)	48 (53.9%)	124 (57.1%)
During the past week how often did you avoid any activities (e.g. visiting a house with a dog or cat or gardening) because of your nasal or other allergy symptoms?	n=128	n=89	n=217
Extremely often	0 (0.0%)	3 (3.4%)	3 (1.4%)
Often	3 (2.3%)	6 (6.7%)	9 (4.1%)
Sometimes	19 (14.8%)	11 (12.4%)	30 (13.8%)
Rarely	16 (12.5%)	13 (14.6%)	29 (13.4%)
Never	90 (70.3%)	56 (62.9%)	146 (67.3%)
During the past week how well were your nasal or other allergy symptoms controlled?	n=128	n=89	n=217
Not at all	4 (3.1%)	4 (4.5%)	8 (3.7%)
A little	12 (9.4%)	10 (11.2%)	22 (10.1%)
Somewhat	40 (31.3%)	28 (31.5%)	68 (31.3%)
Very	43 (33.6%)	33 (37.1%)	76 (35.0%)
Completely	29 (22.7%)	14 (15.7%)	43 (19.8%)
RCAT – 12 MONTHS FOLLOW-UP VISIT			
During the past week how often did you have nasal congestion?	n=102	n=80	n=182
Extremely often	11 (10.8%)	9 (11.3%)	20 (11.0%)
Often	19 (18.6%)	16 (20.0%)	35 (19.2%)
Sometimes	23 (22.5%)	18 (22.5%)	41 (22.5%)
Rarely	24 (23.5%)	17 (21.3%)	41 (22.5%)
Never	25 (24.5%)	20 (25.0%)	45 (24.7%)
During the past week how often did you sneeze?	n=102	n=80	n=182
Extremely often	7 (6.9%)	6 (7.5%)	13 (7.1%)
Often	20 (19.6%)	23 (28.8%)	43 (23.6%)
Sometimes	36 (35.3%)	27 (33.8%)	63 (34.6%)
Rarely	26 (25.5%)	18 (22.5%)	44 (24.2%)
Never	13 (12.7%)	6 (7.5%)	19 (10.4%)
During the past week how often did you have watery eyes?	n=102	n=80	n=182
Extremely often	7 (6.9%)	4 (5.0%)	11 (6.0%)
Often	12 (11.8%)	15 (18.8%)	27 (14.8%)
Sometimes	27 (26.5%)	29 (36.3%)	56 (30.8%)
Rarely	18 (17.6%)	16 (20.0%)	34 (18.7%)

	Intervention	Comparator	Overall
Never	38 (37.3%)	16 (20.0%)	54 (29.7%)
During the past week to what extent did your nasal or other allergy symptoms interfere with your sleep?	n=102	n=80	n=182
All the time	1 (1.0%)	2 (2.5%)	3 (1.6%)
A lot	7 (6.9%)	6 (7.5%)	13 (7.1%)
Somewhat	15 (14.7%)	9 (11.3%)	24 (13.2%)
A little	19 (18.6%)	22 (27.5%)	41 (22.5%)
Not at all	60 (58.8%)	41 (51.3%)	101 (55.5%)
During the past week how often did you avoid any activities (e.g. visiting a house with a dog or cat or gardening) because of your nasal or other allergy symptoms?	n=102	n=80	n=182
Often	6 (5.9%)	6 (7.5%)	12 (6.6%)
Sometimes	11 (10.8%)	13 (16.3%)	24 (13.2%)
Rarely	12 (11.8%)	13 (16.3%)	25 (13.7%)
Never	73 (71.6%)	48 (60.0%)	121 (66.5%)
During the past week how well were your nasal or other allergy symptoms controlled?	n=102	n=80	n=182
Not at all	6 (5.9%)	4 (5.0%)	10 (5.5%)
A little	7 (6.9%)	9 (11.3%)	16 (8.8%)
Somewhat	32 (31.4%)	26 (32.5%)	58 (31.9%)
Very	24 (23.5%)	26 (32.5%)	50 (27.5%)
Completely	33 (32.4%)	15 (18.8%)	48 (26.4%)

APPENDIX P: ALLERGIC RHINITIS MANAGEMENT – INTERVENTION ARM ONLY

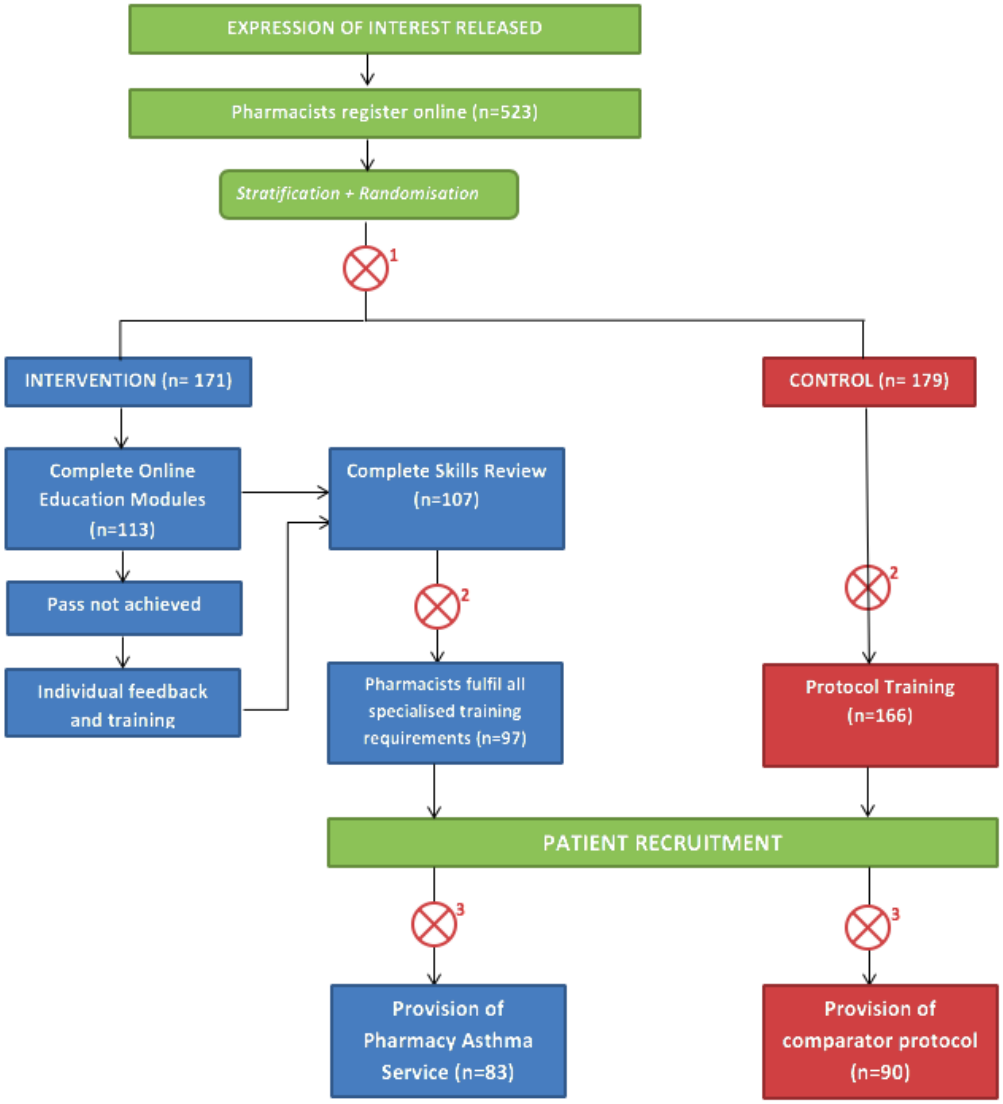
Appendix Table P-1: Allergic rhinitis management (Intervention arm only)

	Baseline (N=221)	Month 1 (N=190)
How bothersome are your current nasal symptoms [1]		
N	161	128
Mean (SD)	4.1 (3.27)	2.9 (2.62)
Median (Q1; Q3)	3.8 (1.0; 7.0)	1.9 (1.0; 4.8)
min max	0 10	0 10
How bothersome are your current eye symptoms[2]		
n	161	128
Mean (SD)	2.9 (3.09)	2.2 (2.54)
Median (Q1; Q3)	1.2 (1.0; 4.8)	1.1 (0.4; 3.0)
min max	0 10	0 10
Participant is taking anything for hay fever		
No	80/161 (49.7%)	43/128 (33.6%)
Yes	81/161 (50.3%)	85/128 (66.4%)
Oral decongestant	5/81 (6.2%)	2/85 (2.4%)
Oral antihistamine	68/81 (84.0%)	54/85 (63.5%)
Oral H antagonist	1/81 (1.2%)	0/85 (0.0%)
Intranasal decongestant	5/81 (6.2%)	4/85 (4.7%)
Intranasal antihistamine	1/81 (1.2%)	2/85 (2.4%)
Intranasal corticosteroid	34/81 (42.0%)	47/85 (55.3%)
Intranasal saline	9/81 (11.1%)	13/85 (15.3%)
Intraocular antihistamine	5/81 (6.2%)	6/85 (7.1%)
Intraocular saline	1/81 (1.2%)	1/85 (1.2%)

Note:

1. Nasal Symptom Severity VAS (How bothersome are your current NASAL symptoms?) Responses ranged from 1 (Not at all bothersome) to 10 (extremely bothersome)
2. Ocular Symptom Severity VAS (How bothersome are your current EYE symptoms?) Responses ranged from 1 (Not at all bothersome) to 10 (extremely bothersome)

APPENDIX Q: PHARMACIST PARTICIPATION AND RETENTION



	Withdrawal point	Reason
⊗	1	Pharmacist not selected or declined – Intervention and Comparator (n=173) *Reasons: Pharmacist not required, unable to contact, consent unreturned, unable to fulfil study requirements, no longer interested.*
⊗	2	Pharmacist did not fulfil training requirements – Intervention only (n=74). *Reasons: Lack of time, personal reasons, change of mind.*
⊗	3	Pharmacist withdrew from trial – Intervention and Comparator (n=71) *Reasons: Pharmacy withdrew, unable to recruit, no time/too busy, understaffed, technical difficulties, lack of interest, personal reasons, pharmacy sold, left workplace.*

Appendix Figure Q-1: Pharmacist participation

The pharmacists and their retention are described below:

Registration of interest: Between July 2018 and January 2019, an EOI form was sent out by the Pharmacy Guild of Australia to 2 597 Australian pharmacies in NSW, WA and Tasmania. From this, 523 pharmacists from 278 pharmacies within the 3 states registered online to participate.

Invitations and pharmacist consent: Following stratification based on state and remoteness, pharmacies were randomly allocated into intervention and comparator arms, provided consent

Training participation: Intervention pharmacists were given access to specialised training modules and comparator arm pharmacists received protocol training only. Amongst the intervention pharmacists, 113 pharmacists completed the online training modules and 107 pharmacists completed the skills assessment. Ninety-seven pharmacists fulfilled all specialised training requirements. 166 comparator arm pharmacists received protocol training.

Participant recruitment: Only 83 trained intervention pharmacists went on to recruit participants and deliver the Pharmacy Asthma Service and 90 pharmacists went on to deliver the comparator arm.

APPENDIX R: REMOTENESS DISTRIBUTION OF PARTICIPATING PHARMACIES

The remoteness distribution of active pharmacies is presented below. Targets numbers were set to match the distribution of the Australian population within the three states. Targets for all remoteness categories were met overall. There was an over representation of highly accessible pharmacies in both intervention and comparator arms and an over representation of accessible pharmacies in the intervention arm.

Appendix Table R-1: Remoteness distribution of intervention and comparator pharmacies

	NSW		WA		Tasmania		Total	
	Target	Achieved	Target	Achieved	Target	Achieved	Target	Achieved
INTERVENTION		**(% of target)**		**(% of target)**		**(% of target)**		**(% of target)**
Highly Accessible	15	23 (153)	7	7 (100)	7	5 (71)	29	35 (121)
Accessible	4	7 (175)	1	2 (200)	2	2 (100)	7	11 (157)
Moderately accessible, remote, and very remote	1	2 (200)	2	2 (100)	1	1 (100)	4	4 (100)
COMPARATOR								
Highly Accessible	15	22 (147)	7	8 (114)	7	3 (43)	29	33 (114)
Accessible	4	6 (150)	1	1 (100)	2	0 (0)	7	7 (100)
Moderately accessible, remote and very remote	1	3 (300)	2	1 (50)	1	0 (0)	4	4 (100)

APPENDIX S: PHARMACY BASELINE CHARACTERISTICS AND OTHER HEALTH SERVICE PROVISION

Data presented in Table 1 have been collected from pharmacies that recruited at least one participant into the trial. The great majority of pharmacies were in a shopping strip or small shopping centre (<50 shops) less than 1km from their nearest GP or neighbouring pharmacy.

- Rural pharmacies represent 14% of total 5,723 in Australia (our study 9, 10%) (8)
- Approximately 67% of pharmacies nationally are in a shopping strip (our study 50, 64%) (8)
- The national average for prescription dispensing is 1150 per week. Approximately 80% of our sample were similar to this average. (8)

Appendix Table S-1: Pharmacy baseline characteristics

		Intervention n (%)	Comparator n (%)	Total n (%)
Number of Pharmacies		51 (53.7)	44 (46.3)	95 (100.0)
State	*New South Wales*	32 (62.7)	31 (70.5)	63 (66.3)
	Western Australia	11 (21.6)	10 (22.7)	21 (22.1)
	Tasmania	8 (15.7)	3 (6.8)	11 (11.6)
Remoteness	*Highly Accessible*	35 (68.6)	33 (75)	68 (71.6)
	Accessible	11 (21.6)	7 (15.9)	18 (18.9)
	Moderately Accessible, Remote, Very remote	5 (9.8)	4 (9.1)	9 (9.5)
Comparability Data Available		50 (98.0)	44 (100.0)	94 (100.0)
Number of PTP-ARC trained pharmacists	*Range*	1.0 – 4.0 (3.0)	1.0 – 5.0 (4.0)	1.0 – 5.0 (4.0)
	Mean (± SD)	1.7 (±0.9)	2.1 (±0.9)	1.9 (±0.9)
	Median	1.0	2.0	2.0
	Q3, Q1 (IQR)	1.0, 2.0 (1.0)	1.0, 3.0 (2.0)	1.0, 2.0 (1.0)
Pharmacy Location	*Shopping strip*	25 (50.0)	28 (63.6)	53 (56.4)
	Small shopping centre with less than 50 shops	10 (20.0)	5 (11.4)	15 (16.0)
	Isolated (1-4 shops together)	6 (12.0)	5 (11.4)	11 (11.7)
	Small medical centre with less than 8 prescribers	2 (4.0)	4 (9.1)	9 (9.6)
	Large shopping centre with 50 or more shops	5 (10.0)	1 (2.3)	6 (6.4)
	Large medical centre with 8 or more prescribers	2 (4.0)	3 (6.8)	5 (5.3)
	Hospital	1 (2.0)	0 (0.0)	1 (1.1)
	Nursing Home	0 (0.0)	1 (2.3)	1 (1.1)

		Intervention	Comparator	Total
		n (%)	n (%)	n (%)
Distance to closest GP practice	*Co-located on premises/adjacent premises*	19 (38.0)	13 (29.5)	32 (34.0)
	Less than 1km	23 (46.0)	28 (63.6)	51 (54.3)
	1 km to 5km	7 (14.0)	3 (6.8)	10 (10.6)
	11km to 50km	1 (2.0)	0 (0.0)	1 (1.1)
Distance to the closest other Pharmacy	*Less than 1km*	24 (48.0)	20 (45.5)	44 (46.8)
	1 km to 5km	17 (34.0)	16 (36.4)	33 (35.11)
	6 to 10km	0 (0.0)	2 (4.5)	2 (2.13)
	11 to 50km	7 (14.0)	5 (11.4)	12 (12.8)
	More than 50km	2 (4.0)	1 (2.3)	3 (3.2)
Average number of scripts per day	*Less than 100*	10 (20.0)	2 (4.5)	12 (12.8)
	101-200	14 (28.0)	18 (40.9)	32 (34.0)
	201-300	17 (34.0)	14 (31.8)	31 (33.0)
	More than 300	9 (18.0)	10 (22.7)	19 (20.2)
Type of private consultation area	*Defined consultation room*	41 (82.0)	33 (75.0)	74 (78.7)
	Private counselling area	14 (28.0)	21 (47.7)	35 (37.2)
	No private room or area	1 (2.0)	2 (4.5)	3 (3.2)
Number of fulltime equivalent pharmacists	*Range*	1.0 – 5.0	1.0 – 12.0	1.0 – 12.0
	Mean (± SD)	2.4 (± 1.1)	3.0 (± 2.2)	2.7 (± 1.7)
	Median	2.0	2.0	2.0
	Q3, Q1 (IQR)	3.0, 1.9 (1.1)	3.9, 1.9 (2.0)	3.0, 1.9 (1.1)
Number of hours considered full time	*Range*	33.0 – 49.5	32.0 – 55.0	32.0 – 55.0
	Mean (± SD)	38.9 (± 2.5)	39.5 (± 4.1)	39.2 (± 3.3)
	Median	38.0	38.0	38
	Q3; Q1 (IQR)	40.0, 38.0 (2.0)	40.0, 38.0 (2.0)	40.0, 38.0 (2.0)
Average number of Pharmacists working at any one time	*Range*	1.0 – 3.0	1.0 – 4.0	1.0 – 4.0
	Mean (± SD)	1.9 (± 0.5)	2.1 (± 0.7)	2.0 (± 0.6)
	Median	2.0	2.0	2.0
	Q3; Q1 (IQR)	2.0, 1.5 (0.5)	2.9, 1.5 (1.4)	2.0, 1.5 (0.5)
Number of non-pharmacist staff employed	*Range*	0.0 – 30.0	1.0 – 35.0	0.0 – 35.0
	Mean (± SD)	10.4 (± 7.2)	10.4 (± 7.9)	10.4 (± 7.5)
	Median	9.5	7.5	8.5
	Q3; Q1 (IQR)	16.0, 4.8 (11.3)	15.8, 3.3 (12.5)	16.0, 4.0 (12.0)
	Range	0.0 – 27.0	0.0 – 24.0	0.0 – 27.0

		Intervention n (%)	Comparator n (%)	Total n (%)
Number of non-pharmacist staff S2/S3 trained	*Mean (± SD)*	8.6 (± 6.2)	7.7 (± 5.6)	8.2 (± 6.0)
	Median	7.0	6.0	6.0
	Q3; Q1 (IQR)	13.0, 4.0 (9.0)	11.0, 3.0 (8.0)	12.0, 3.8 (8.3)
Average number of non-pharmacist staff working at any one time	*Range*	0.0 – 15.0	1.0 – 16.0	0.0 – 16.0
	Mean (± SD)	4.8 (± 3.2)	4.9 (± 3.5)	4.8 (± 3.3)
	Median	4.0	3.8	4.0
	Q3; Q1 (IQR)	6.0, 2.0 (4.0)	7.0, 2.0 (5.0)	6.5, 2.0 (4.5)
Total floor area of pharmacy (m^2)	*Range*	25.0 – 600.0	40 – 800	25.0 – 800.0
	Mean (± SD)	251.7 (± 143.7)	220.3 (± 153.5)	236.9 (± 148.4)
	Median	250.0	200.0	200.0
	Q3; Q1 (IQR)	350.0, 130.0 (220.0)	270, 100 (170.0)	315.0, 128.0 (187.0)
Area of private counselling room or area (m^2)	*Range*	1.5 – 30.0	2.0 – 30.0	1.5 – 30.0
	Mean (± SD)	8.2 (± 5.5)	9.8 (± 6.8)	9.0 (± 6.2)
	Median	6.1	8.0	7.5
	Q3; Q1 (IQR)	10.0, 5.0 (5.0)	11.0, 5.0 (6.0)	100, 5.0 (5.0)
Average number of Asthma prescription medications dispensed per week (self report)	*Range*	10.0 – 390.0	10.0 – 646.0	10.0 – 646.0
	Mean (± SD)	61.7 (± 74.9)	74.1 (± 104.7)	67. 7 (± 90.4)
	Median	45.0	40.0	42.5
	Q3; Q1 (IQR)	70.0, 20.0 (50.0)	95.0, 21.5 (73.5)	78.8, 20.3 (58.5)
Average number of asthma relievers sold per week on average (via POS system)	*Range*	5.0 – 300.0	5.0 – 649.0	5.0 – 649.0
	Mean (± SD)	52.5 (± 47.9)	68.2 (± 105.6)	60.2 (± 81. 2)
	Median	42.0	36.0	42.0
	Q3; Q1 (IQR)	67.0, 22.0 (45.0)	65.0, 20.0 (45.0)	65.3, 20.0 (45.3)
Pharmacy currently provides Asthma service outside of trial		13 (26.0)	10 (22.7)	23 (24.5)
Pharmacy provides other health programs and services		49 (98.0)[1]	36 (81.8)	85 (90.4)
Are pharmacists required to undertake formal training for any of the services provided by the pharmacy (Apart from HMR's or RMMR's)		39 (78.0)	28 (63.6)	67 (71.27)

		Intervention n (%)	Comparator n (%)	Total n (%)
Previous involvement in Research studies		29 (58.0)	24 (54.5)	53 (56.4)
Use of resources and processes to deliver professional services:	*Software platforms to guide delivery of the service (e.g. GuildCare)*	43 (86.0)	35 (79.5)	78 (83.0)
	Systems to manage participant appointments and follow up (electronic or manual)	36 (72.0)[2]	22 (50.0)	58 (61.7)
	Participant files in the pharmacy (electronic or manual) to document participant management or test	40 (80.0)[3]	23 (52.3)	63 (67.0)
	Written documentation of participant management or test results provided to participants	34 (68.0)	21 (47.7)	55 (58.5)
	Direct communication of participant management or test results to GPs	38 (76.0)	25 (56.8)	63 (67.0)
	Written/electronic protocols/policies for your pharmacists/staff outlining criteria for referral	33 (66.0)	21 (47.7)	54 (57.5)
	Setting target numbers for participant recruitment to professional services	29 (58.0)	21 (47.7)	50 (53.2)
	Monitoring of performance around professional services	22 (44.0)	20 (45.5)	42 (44.7)
	Pharmacist/Staff meetings to review and improve quality of professional services	31 (62.0)	25 (56.8)	56 (59.6)
	Pharmacy-based training for pharmacists/staff to implement services	45 (90.0)[4]	26 (59.1)	71 (75.5)
	Incentives/rewards to encourage pharmacist performance in delivering services	15 (30.0)	10 (22.7)	25 (26.6)
	Dedicated periods of service delivery (i.e. non-dispensing) allocated to pharmacists	26 (52.0)[5]	10 (22.7)	36 (38.3)

		Intervention n (%)	Comparator n (%)	Total n (%)
	Collaboration or agreement with local GPs, individually or with a representative organization	28 (56.0)	19 (43.2)	47 (50.0)

Note:

1. Intervention pharmacies were more likely to offer other professional services at time of commencement.
2. Intervention pharmacies were more likely to report use of a system to manage appointments
3. Intervention pharmacies were more likely to keep patient files in the pharmacy (electronic or manual) to document participant management or tests.
4. Intervention pharmacies were more likely to undertake pharmacy-based training for all staff to implement services.
5. Intervention pharmacies were more likely to report the use of dedicated periods of service delivery

One-quarter of active pharmacies already provided an asthma service within the pharmacy prior to their involvement in the trial. Most of these services were run by employee pharmacists all year, and most often included inhaler technique checks and medication counselling. A smaller proportion provided access to spirometry, an asthma educator, control support and asthma action plan review.

Appendix Table S-2: Other asthma services currently provided by pharmacies outside of the trial

	Frequency n (%)
Number of pharmacies who currently provide Asthma services outside of trial	23 (24.5)
Number of weeks of the year this service is offered:	
All year	19 (82.6)
16 weeks or less per year	4 (17.4)
Personnel that conduct asthma service:	
Employee pharmacist	19 (82.6)
Pharmacy owner	9 (39.1)
Employee Intern pharmacist	5 (21.7)
Other health professional (employed or funded by the pharmacy)	1 (4.3)
Health professional (not paid/funded by the pharmacy)	1 (4.3)
Pharmacy student (under supervision)	1 (4.3)
Personnel that counsel, explain the results and provide recommendation to participants after administering the asthma service:	
Employee pharmacist	18 (78.3)
Pharmacy owner	11 (47.8)
Employee intern pharmacist	5 (21.7)
Pharmacy student (under supervision)	2 (8.7)
Employee pharmacy assistant	1 (4.3)
Other health professional (employed or funded by the pharmacy)	1 (4.3)
Components of service provided:	
Inhaler technique check	16 (69.6)
Medication counselling	6 (26.1)
Spirometry	4 (17.4)
Asthma education	3 (13.0)
Assessment of control	1 (4.3)
Asthma action plan review	1 (4.3)

92.4% of pharmacies involved (98.0% of intervention pharmacies and 81% of comparator pharmacies) provide other professional services. On average each pharmacy provided access to at least 5 other services, the most reported being blood pressure monitoring, vaccinations, MedChecks, dose administration aids (DAA) and diabetes clinics.

Appendix Table S-3: Other professional services provided by pharmacies

		Frequency n (%)
Other Health service provision		85 (92.4)
Number of health services provided	*Range*	0.0 – 12.0
	Mean	5.4 (± 2.6)
	Median	5.0
	Q3; Q1 (IQR)	6.3, 4.0 (2.3)
Other health services provided by participant pharmacies (Self-reported)	*Blood pressure monitoring*	47 (55.3)
	Vaccinations	42 (49.4)
	MedChecks	40 (47.1)
	Dose Administration Aids (DAA)	33 (38.8)
	Diabetes clinic (HbA1c and blood glucose testing)	31 (36.5)
	Home Medicines Review (HMR)	23 (27.1)
	Sleep apnoea services	22 (25.9)
	Diabetes MedsChecks	17 (20.0)
	Weight loss service	17 (20.0)
	Cholesterol checks	14 (16.5)
	Pain clinic	10 (11.8)
	Opioid substitution	9 (10.6)
	Staged supply	7 (8.2)
	Naturopath	6 (7.1)
	Compounding	6 (7.1)
	First aid	6 (7.1)
	Iron checking	5 (5.9)
	Hearing checks	5 (5.9)
	Compression stockings	5 (5.9)
	Medication Management Review	4 (4.7)
	Nursing home servicing	4 (4.7)
	My DNA	4 (4.7)
	Health checks	4 (4.7)
	COPD screening	3 (3.5)
	Equipment hire	3 (3.5)
	Lice clinic	3 (3.5)
	Respiratory check	2 (2.4)
	Diabetes educator	2 (2.4)
	Nicotine Replacement Therapy	2 (2.4)

Needle exchange program	2 (2.4)
Stroke assessment	2 (2.4)
Baby nurse	2 (2.4)
Unspecified POC testing	2 (2.4)
Nutritionist	2 (2.4)
Skin care	1 (1.2)
Kidney health	1 (1.2)
Cardiovascular risk assessment	1 (1.2)
Women's clinic	1 (1.2)
INR checks	1 (1.2)
Digestive health	1 (1.2)
Oligoscans	1 (1.2)

APPENDIX T: PHARMACIST BASELINE CHARACTERISTICS – INTERVENTION AND COMPARATOR

Characteristics of participating pharmacists are shown below. Participating pharmacists represent a mix of proprietors and salaried pharmacists, of ranging age, gender, and years in practice. Pharmacists delivering the intervention and comparator protocol were comparable in age, experience, further accreditation, employment status, employment position and prior involvement in research. There were significantly more comparator pharmacists involved in delivering the protocol from the pharmacy (this could be due to the fact that training requirements were minimal and so more pharmacists could be trained from each participating pharmacy) and there was an overrepresentation of pharmacists from NSW and from highly accessible pharmacies in the comparator arm.

Appendix Table T-1: Pharmacist baseline characteristics

		Intervention n (%)	Comparator n (%)	Total n (%)
Number of Pharmacists		83 (40.3)	123 (59.7)	206 (100.0)
State	*New South Wales*	50 (60.2)	88 (71.5)	138 (67.0)
	Western Australia	18 (21.7)	27 (22.0)	45 (21.8)
	Tasmania	15 (18.1)	8 (6.5)	23 (11.2)
Remoteness	*Highly Accessible*	54 (65.1)	98 (79.7)	152 (73.8)
	Accessible	21 (25.3)	15 (12.2)	36 (17.5)
	Moderately Accessible, Remote, Very remote	8 (9.6)	10 (8.1)	18 (8.7)
Comparability data available		71 (85.5)	83 (67.5)	154 (74.8)
Age	*20 – 39 years of age*	40 (58.8)	54 (68.4)	94 (63.9)
	40 – 59 years of age	25 (36.8)	22 (27.8)	47 (32.0)
	60 years or greater	3 (4.4)	3 (3.8)	6 (4.1)
	Mean (SD)	38.7 (± 10.6)	36.9 (±10.7)	37.7 (±10.7)
	Min Max	22.8 64.7	24.1 74.6	22.8 74.6
	Median	37.1	34.3	35.7
	Q3; Q1 (IQR)	46.4, 30.7 (15.7)	43.3, 28.2 (15.1)	44.6, 29.1 (15.5)
Years registered	*Mean (SD)*	15.9 (±11.2)	14.0 (±11.1)	14.9 (±11.1)
	Min Max	1.0 44.0	1.0 46.0	1.0 46.0
	Median	14.0	11.0	13.0
	Q3; Q1 (IQR)	24.0, 7.0 (17.0)	21.0, 5.0 (16.0)	22.0, 5.8 (16.3)
Employment status	*Full time*	51 (71.8)	71 (85.5)	122 (79.2)
	Part time	16 (22.5)	10 (12.0)	26 (16.9)
	Casual	4 (5.6)	2 (2.4)	6 (3.9)
Employment position	*Owner*	30 (42.3)	34 (41.0)	64 (41.6)
	Manager	7 (9.9)	7 (8.4)	14 (9.1)

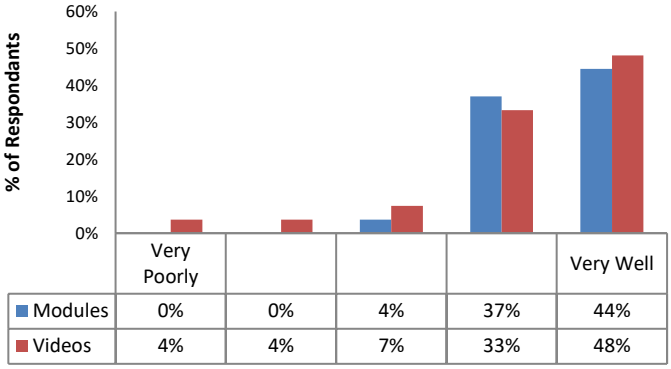
		Intervention	Comparator	Total
		n (%)	n (%)	n (%)
	Pharmacist in charge	9 (12.7)	19 (22.9)	28 (18.2)
	Employee registered Pharmacist	25 (35.2)	23 (27.7)	48 (31.2)
Education	*Bachelors*	56 (78.9)	66 (79.5)	122 (79.2)
	Masters	14 (19.7)	17 (20.5)	31 (20.1)
	Doctoral	1 (1.4)	0 (0.0)	1 (0.6)
Further Accreditation	*Yes*	29 (40.8)	27 (32.5)	56 (36.4)
	No	42 (59.2)	56 (67.5)	98 (63.6)
Prior Involvement in research	*Yes*	22 (31.0)	32 (38.6)	54 (35.1)
	No	49 (69.0)	51 (61.4)	100 (64.9)
Involvement in trial	*Pharmacy preparation and staff training*	48 (67.6)	60 (72.3)	108 (70.1)
	Recruitment	61 (85.9)	62 (74.7)	123 (79.9)
	Conducting sessions	63 (88.7)	56 (67.5)	119 (77.3)
	Was not involved	1 (1.4)	5 (6.0)	6 (3.9)

APPENDIX U: PHARMACIST ONLINE MODULE EVALUATION

CONTENT

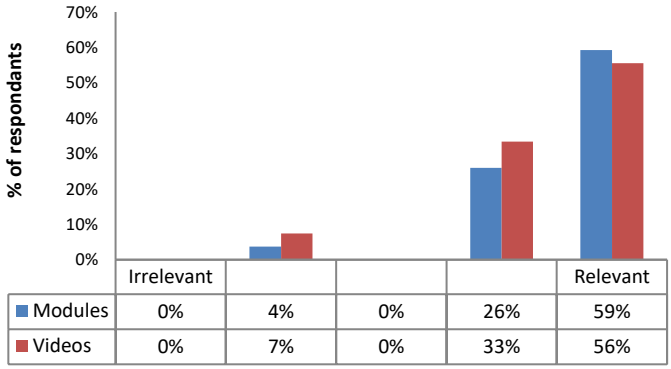
Over 80% of the pharmacists who completed feedback reported that the modules and videos achieved the learning objectives and met their expectations. Over 55% of the pharmacists reported that the modules and videos were relevant to the management of their asthma participants. Most pharmacists rated the format of the modules and videos highly and that the modules presented neither too little nor too much information with a smaller percentage reporting that there was too much content. Responses are outlined in Figure U-1.

Criteria 1: Achieving the learning objectives and meeting your expectations (n=27)

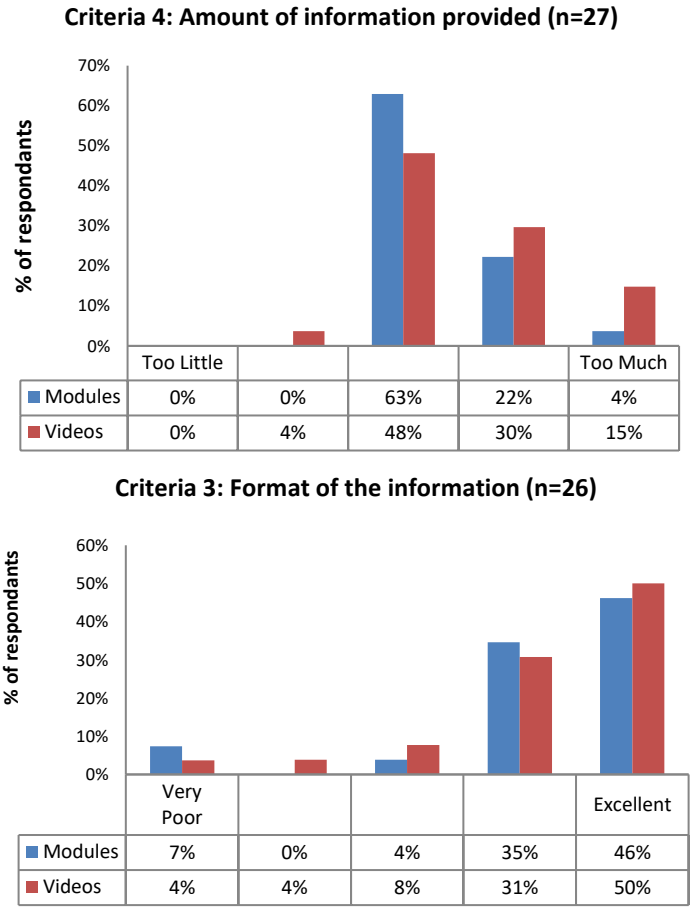


	Very Poorly				Very Well
Modules	0%	0%	4%	37%	44%
Videos	4%	4%	7%	33%	48%

Criteria 2: Relevance to management of your asthma patients (n = 27)



	Irrelevant				Relevant
Modules	0%	4%	0%	26%	59%
Videos	0%	7%	0%	33%	56%

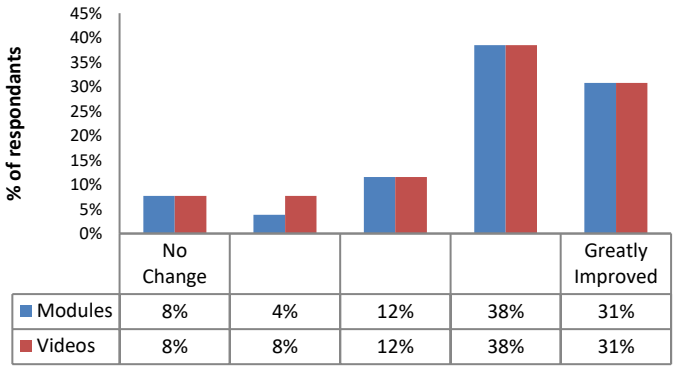


Appendix Figure U-1: Training content evaluation by participant pharmacists

EFFICACY

Most pharmacists reported that the training modules and videos improved their knowledge about adherence, inhaler technique and allergic rhinitis, and improved their confidence in assisting participants in these areas. There was greater variability in pharmacists reporting on the allergic rhinitis module with a larger proportion of pharmacists stating neutrality or that the modules had led to minimal change in knowledge or confidence than in the other learning areas.

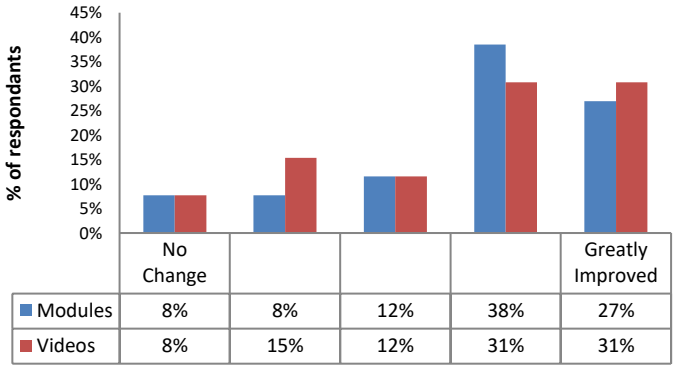
Improving confidence in assisting patients to improve their adherence (n=26)



	No Change				Greatly Improved
Modules	8%	4%	12%	38%	31%
Videos	8%	8%	12%	38%	31%

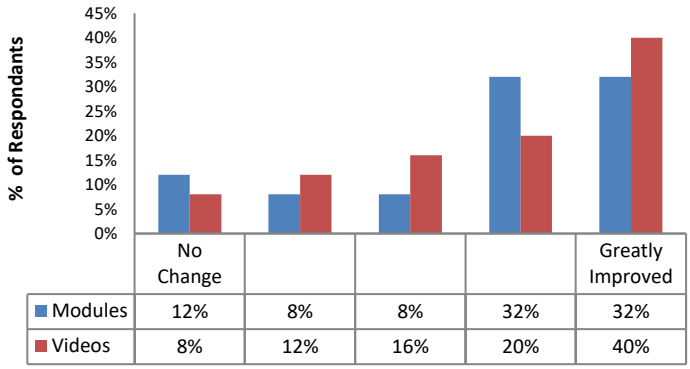
-

Improving knowledge about adherence to asthma medicines (n=26)



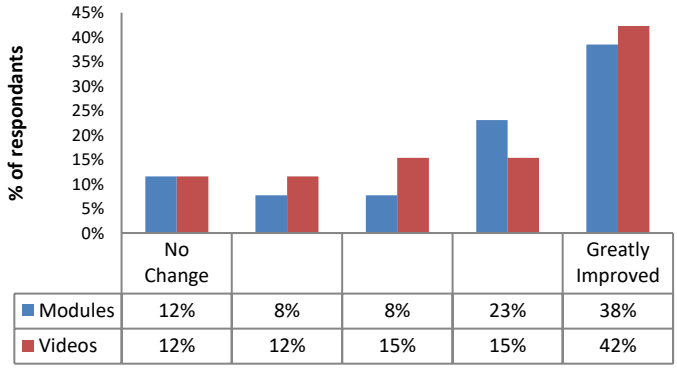
	No Change				Greatly Improved
Modules	8%	8%	12%	38%	27%
Videos	8%	15%	12%	31%	31%

Improving confidence to help patients improve their inhaler technique (n=25)

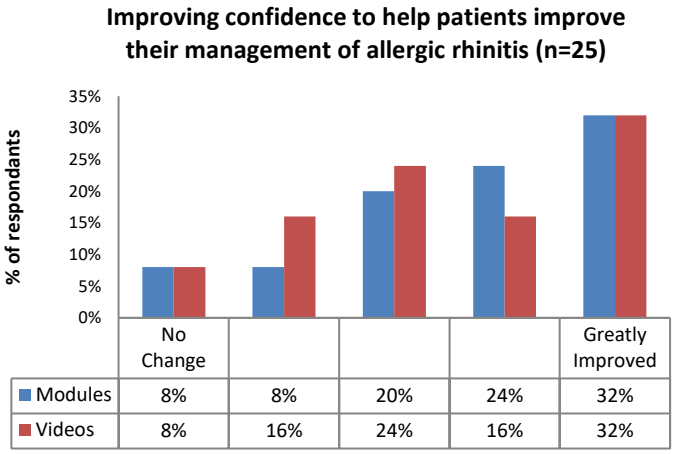


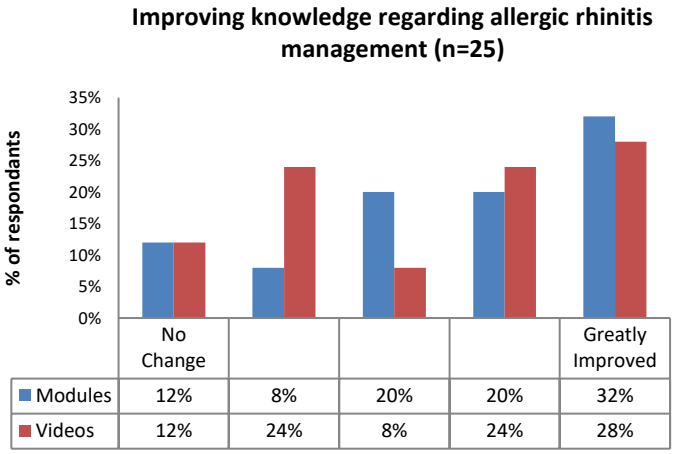
	No Change				Greatly Improved
Modules	12%	8%	8%	32%	32%
Videos	8%	12%	16%	20%	40%

Improving knowledge/skills regarding inhaler technique (n=26)



	No Change				Greatly Improved
Modules	12%	8%	8%	23%	38%
Videos	12%	12%	15%	15%	42%





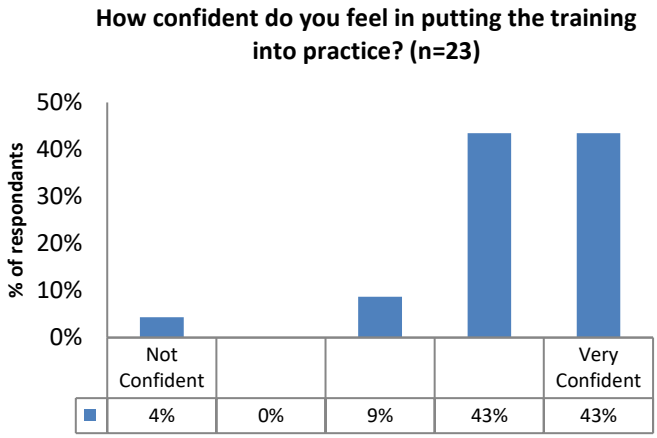
Appendix Figure U-1: Training efficacy evaluation by participant pharmacists

In terms of feedback, 71% of pharmacists reported that continual and regular evidence-based refresher training would help to further enhance their knowledge. To a lesser extent more time (14%) and practice (14%) were also mentioned to enhance their knowledge.

Practice and real-world experience were the main driver to improve pharmacist's skills-based knowledge for 56% of responding pharmacists. Clearer software instruction (11%), more time (11%) and follow up device training (22%) was also reported.

PRACTICAL APPLICATION

Most pharmacists reported that they were confident in putting the training into practice with very few (4%) reporting that they were not confident about implementing the training in practice.



Appendix Figure U-1: Practical application evaluation

When pharmacists were asked what would improve their ability to apply skills in the workplace 75% reported more time and resources. 12.5% of pharmacists also reported having their own set of placebo inhaler devices (which were later provided to all intervention pharmacist as a part of the study resources) and confidence in knowledge and products.

APPENDIX V: SESSIONS CONDUCTED BY PARTICIPATING PHARMACIES

Appendix Table V-1: Sessions conducted by participating pharmacies in study arms

	Number of sessions conducted by pharmacies		
	Intervention (n=51)	Comparator (n=44)	Combined (n=95)
Total	736	402	1137
Mean (± SD)	14.43 (± 12.42)	9.14 (± 6.09)	11.98 (±10.30)
Median	12.00	8.00	9.00
Min Max	0.00 58.00	0.00 21.00	0.00 58.00
Q1 Q3 (IQR)	4.00; 20.00 (16.00)	3.00; 14.25 (11.25)	4.00; 16.00 (12.00)

APPENDIX W: PARTICIPANT REPORTED MEDICATION CHANGES

Appendix Table W-1: Patient reported medication changes by visit

	Intervention (N=190)	Comparator (N=131)	Odds Ratio1	p-value1
1 MONTH FOLLOW-UP VISIT				
Updates regarding your asthma medications or therapy			1.19 (0.47, 3.03)	0.7191
No	163/190 (85.8%)	115/131 (87.8%)		
Yes	27/190 (14.2%)	16/131 (12.2%)		
Medication ceased			0.20 (0.00, 32.63)	0.5312
No	189/190 (99.5%)	125/129 (96.9%)		
Yes	1/190 (0.5%)	4/129 (3.1%)		
New medication			1.07 (0.34, 3.32)	0.9127
No	177/190 (93.2%)	121/130 (93.1%)		
Yes	13/190 (6.8%)	9/130 (6.9%)		
Dose increase			1.06 (0.32, 3.45)	0.9271
No	181/190 (95.3%)	121/127 (95.3%)		
Yes	9/190 (4.7%)	6/127 (4.7%)		
Dose decrease			1.28 (0.00, 775.01)	0.9386
No	188/190 (98.9%)	127/128 (99.2%)		
Yes	2/190 (1.1%)	1/128 (0.8%)		
Other			3.11 (0.65, 14.75)	0.1527
No	181/190 (95.3%)	125/127 (98.4%)		
Yes	9/190 (4.7%)	2/127 (1.6%)		
12 MONTHS FOLLOW-UP VISIT				
Was a GP referral required?			0.73 (0.34, 1.59)	0.4316
No	113/143 (79.0%)	83/111 (74.8%)		
Yes	30/143 (21.0%)	28/111 (25.2%)		
Seen doctor in regard to your asthma since your last visit			1.18 (0.52, 2.68)	0.6960
No	48/143 (33.6%)	40/107 (37.4%)		
Yes	95/143 (66.4%)	67/107 (62.6%)		
Updates regarding your asthma medications or therapy[2]			1.14 (0.49, 2.63)	0.7559
No	112/143 (78.3%)	88/107 (82.2%)		
Yes	31/143 (21.7%)	19/107 (17.8%)		
Medication ceased[2]			1.55 (0.50, 4.78)	0.4438
No	130/143 (90.9%)	98/104 (94.2%)		
Yes	13/143 (7.7%)	6/104 (5.8%)		
New medication[2]			0.62 (0.24, 1.63)	0.3286
No	132/143 (92.3%)	94/106 (88.7%)		
Yes	11/143 (7.7%)	12/106 (11.3%)		
Dose increase[2]			0.56 (0.14, 2.15)	0.3951
No	139/143 (97.2%)	97/102 (95.1%)		
Yes	4/143 (2.8%)	5/102 (4.9%)		

	Intervention (N=190)	Comparator (N=131)	Odds Ratio1	p-value1
Dose decrease[2]			2.32 (0.00, 1453.71)	0.7973
No	136/143 (95.1%)	101/102 (99.0%)		
Yes	7/143 (4.9%)	1/102 (1.0%)		
Other[2]			0.59 (0.00, 148.85)	0.8527
No	134/137 (97.8%)	99/101 (98.0%)		
Yes	3/137 (2.2%)	2/101 (2.0%)		

APPENDIX X: COMPARATOR (CONTROL) ARM FINDINGS

QUALITATIVE EVALUATION

A characteristic profile of interviewed comparator pharmacists is presented in Appendix Table X-1.

Appendix Table X-1: Respondent characteristics – Comparator pharmacists

	Frequency n (%)
Pharmacy state	
NSW	15 (75)
WA	3 (15)
TAS	2 (10)
Pharmacy remoteness	
Highly Accessible	13 (65)
Accessible	4 (20)
Moderately Accessible, Remote, Very remote	3 (15)
Age (years)	
Mean (SD)	39 (± 7.96)
Median (Q1; Q3)	38 (33; 45)
Min Max	25 53
Gender	
Male	10 (50)
Female	10 (50)
Work situation	
Full-time employed	20 (100)
Years registered	
Mean (SD)	17 (± 9.00)
Median (Q1; Q3)	17 (11; 23)
Min Max	2 33
Number of participants recruited	
Mean (SD)	4 (± 2.07)
Median (Q1; Q3)	4 (2; 6)
Min Max	2 9
Number of participants completed	
Mean (SD)	4 (± 1.72)
Median (Q1; Q3)	3.5 (3; 5)
Min Max	2 7

EXPECTATIONS AND MOTIVATIONS OF PHARMACISTS AND PARTICIPANTS

Recruitment of people with asthma into the trial had been challenging. This was explored by the investigative team in a published paper titled *Recruiting patients to asthma services in pharmacy – a key frontier in the transition from product supply to service provision (128)*. Over one-quarter of comparator pharmacists interviewed described recruitment as more difficult than expected.

> *"I found it really hard to recruit people, and when we first thought, 'Okay. These are the type of people we can target. This shouldn't be too bad,' it ended up being a lot harder than we anticipated, so that was a bit of a frustration, because we thought, 'We're set up to do this quite well. We've got three pharmacists on most days, and there's that time and opportunity to have those conversations'" but it just didn't really pan out that way." (WA638NC)*

Just under half of the respondents stated that participant lack of time, interest and the eligibility criteria were significant barriers to recruitment.

> *"I mean, we didn't actually get that many people to agree. I think a lot of people were not big fans of doing these sorts of studies." (NSW3013MH)*

> *"That was hard – so we do have a lot of people on inhalers, but they just didn't meet the criteria that was – to do the trial." (NSW2360AW)*

Only a few pharmacists explained they had no problem with recruitment.

> *"... based on having a pretty good rapport with them [patients], we had pretty good success when we applied ourselves." (NSW2967JM)*

> *"I think that invariably they all agreed. I think I only had one person who was a bit too busy to do it." (TAS743AH)*

The comparator arm pharmacists described numerous methods to recruit participants, the most popular being searching medication profiles and flagging potential participants on dispense software, approaching patients upon presentation of prescriptions for respiratory medicines or salbutamol requests, or simply just asking.

> *"We would do a history search on [the] dispense software as to who has got a preventor medicine in the last three to six months, and then we kind of highlighted them and just put little pop-up notes in their system just saying when they came in, that we just wanted to have a word with them, and so then we would fill out that initial questionnaire, and if they met the criteria, we essentially asked them at that stage." (NSW2967JM)*

> *"I think anybody who was ... asking for Ventolin® over-the-counter, or if they handed in any sort of asthma prescription." (NSW2656PO)*

Almost one-quarter of respondents mentioned they selectively chose patients with whom they had good rapport.

> *"That was the best way. That's it. Just find people you like and ask them. That was it. That's my basic strategy." (NSW2184JY)*

"... one of the lines that I would use with some of them was, 'You're doing me a favour,' and I just basically banked on the fact that I have a pretty good relationship with them and hopefully got some return on that, but some of them will outright kind of say, 'No, I haven't got time for this,' but we find that because we're pretty good at creating those relationships we have pretty good return on that." (NSW2967JM)

"Basically, they were people that we thought were probably more likely to say yes, so that would be happy to be part of a trial." (NSW2806CA)

Almost all of those who explained the phrases they used to recruit participants mentioned to the patient that the trial would benefit them, improve understanding of asthma, medications or improve asthma control.

"Just by having a brief conversation with them about how their asthma was going and would they be interested in being involved in a study that may help them to understand their asthma and control it better." (NSW1094SF)

"'Then just ask if they would like to participate in the survey that would help with asthma medications or controlling their asthma." (NSW2663LW)

So, it clear that in some cases a misrepresentation of what the participant should expect had been communicated by the pharmacist, whether this was due to an insufficient understanding of the trial and their role within the protocol or a way to persuade people to join the trial because of the difficulties that arose during recruitment.

Pharmacists were asked to discuss their participants' motivations to join the trial. Over three-quarters of pharmacists believed that participants entered the trial seeking personal benefit, most notably to improve asthma control, which was mentioned by over half of respondents. Other motivations mentioned included to learn more about asthma, improve management and treatment, to improve inhaler technique or get feedback on their condition.

"If their asthma wasn't very good, and they wanted to see some improvement ... that would be pretty much their only motivation." (NSW3032TV)

"I think it would have varied from person to person, but probably mostly improving asthma control." (NSW3146AR)

"Improvement. Improving the asthma management and treatment." (NSW2089AT)

In addition, over half of the respondents mentioned other participant motivations including participant curiosity, interest in asthma and research, and the potential for people living with asthma to help others, while close to one-third of pharmacists stated that participants took part because the pharmacist had asked.

"Half the people just like to participate in this sort of thing, and the other half of my participants felt that they weren't necessarily getting adequate control of their symptoms, so they thought this may be a way of getting some better control." (TAS743AH

"Some that actually thought about themselves in terms of directly getting benefit from it and the others where it was more just a happy to help and be part of the study that might help others." (WA638NC)

"... if we were saying that it was something good to be involved in that they would usually just do it." (TAS5347KH)

PROTOCOL DELIVERY

PROTOCOL QUESTIONS

Some pharmacists had both positive and negative views of the protocol questions utilised in the trial. Just under half of respondents made a negative comment regarding the protocol questions, describing them as irrelevant, too comprehensive, long winded, repetitive and/or confusing, in particular the focus on mental health in the quality of life surveys.

> *"… the questionnaires ... were possibly too comprehensive. I don't know what kind of data was meant to be gathered exactly from those questionnaires, but some of them, yes, were quite in-depth, and I wasn't sure if it was necessary." (NSW3032TV)*

> *"There was one part there was about feeling – I think, mental health as well … I think that got a bit too personal … and I think people didn't understand what the relationship between asthma and mental health was." (WA4412PN)*

> *"They [the questionnaires] were very repetitive … it was very lengthy and repetitive." (NSW3091AO)*

Almost three-quarters of respondents made positive comments about protocol questions, stating that they were an advantageous tool which prompted conversations, highlighted problem areas for participants, created an organised flow and allowed for effective follow-up. One pharmacist also mentioned the protocol questions enabled them to learn more about the participant's backstory, and another said it directly impacted rapport building, which was mentioned as the most prominent benefit of the trial.

> *"I think it was a tool for us to connect with our patients about their asthma." (NSW11305KP)*

> *"So, for maybe a third of them, the questions themselves created a discussion at that point about their health, which was positive." (NSW2089AT)*

> *"I think the questions might have seemed odd for some people, but for other people where it was relevant it made perfect sense." (NSW2967JM)*

> *"It actually worked out quite well, because it basically allowed me – it gave structure to the whole process, and basically gave the impression that everything was smooth and under control." (TAS743AH)*

> *"So, it just sort of triggered some personal stories that I wouldn't have known." (NSW2663LW)*

PROBLEM IDENTIFICATION

Most pharmacists reported that the trial enabled them to identify asthma-related management issues among their participants. The most commonly reported included poor asthma control, poor compliance with medication taking, overuse of relievers, poor inhaler technique and the effects of other co-morbidities.

> *"I think it sort of helped them probably understand their asthma better as well, you know, highlighting a few areas that they might be struggling with or areas that need to be improved." (NSW2656PO)*

"… there was one patient who was quite poorly controlled. From what I recall, she was on, you know, pretty much the steroids already, but she found that she was using the Ventolin® still quite often … So, yes, she obviously wasn't really happy with the way it was being controlled, but she had felt that there was nothing that she could do about it." (NSW3032TV)

"I believe they were more seasonal asthmatics, so they weren't using preventor inhalers all the time. It was sort of on and off." (WA638NC)

"I have two [patients] in the trial, and they ... mainly use reliever. They didn't use the preventor." (WA638NC)

"The most common thing was just over-use of reliever medication." (NSW2930AW)

"And then another patient who had very poor inhaler technique, and it was, yes, causing significant mental health issues as well." (NSW3146AR)

Only one of the interviewed pharmacists stated there were no significant problems raised by the single participant he had managed. Thus, the protocol questions facilitated discussions in which pharmacists were exposed firsthand to a range of participant issues that were affecting their health, in particular their asthma management.

PHARMACIST ACTIONS

Three-quarters of respondents performed at least one supplementary intervention beyond the scope of the research protocol, to address participant issues or concerns. Over half of the respondents reviewed inhaler technique or made recommendations to improve technique such as the addition of a spacer, while one-quarter of pharmacists reviewed preventer compliance and discussed participant understanding of their medicines.

"So sometimes there was a discussion about technique. Other times, it was a referral to the GP. It just depends on the circumstances … just remind them that there's lot of people who take shortcuts with their inhalers and may not be getting the best effect from them, to reinforce the correct technique if that seemed to be necessary." (NSW1094SF)

"So, one person in the initial survey ... didn't use their inhaler correctly, so that was corrected." (NSW3146AR)

"I think two of them I actually taught them how to use it [inhaler] properly, so that was good. Compliance was probably better … I think one of them didn't have a spacer, so I recommended the spacer." (NSW2663LW)

"I demonstrated it [inhaler technique] for her, and I got her to demonstrate it for me, and improved slightly." (NSW3146AR)

"I provided spacers where necessary, and so able to sell them the spacer and also give them the counselling as to what they could reasonably expect from their asthma management." (TAS743AH)

"There was one that really just didn't get the use of the – the basic interaction between we will say call it a blue and a brown puffer. So, we just said to them, 'Look, guys, you're just going to use your brown. Be consistent. Don't worry what the weather is like.' You know, so a lot of them thought the brown one was just for a particular time of year when they were asthmatics and needed it all the time. So that was – probably came out a lot." (NSW2184JY)

"I was just really drilling it into their head that they've got to use it [their preventer medication] all the time. That's just ground floor. They've just got to use their puffers. ...just getting that through to them sometimes can take you three months." (NSW2184JY)

"One was sort of using the Symbicort®– not regularly, and she was getting quite puffy, so I said to her it's actually better to use it on a daily basis, so she started doing that. So, she ... stopped having nocturnal asthma attacks, which was great." (NSW2663LW)

"... making sure they really understand that taking the preventor is preventing the symptoms from happening." (TAS5347KH)

"... she didn't realise that she had to use it regularly. She only used it when she needs it … So, after using the Symbicort® combined with Ventolin® regularly, at least that side of the asthma is under control, so she feels better that she's actually getting a full night's sleep and not waking up out of breath." (NSW2663LW)

Other interventions mentioned included recommending management strategies for allergic rhinitis, reviewing reliever use, addressed underlying co-morbidities including smoking and mental health issues, discussed lifestyle improvements, conducted a MedsCheck, initiated the creation of an asthma action plan and providing educational materials.

"We also give the MedsCheck as well. Well, after the review, we discovered he was hopeless with his medications, so we did a MedsCheck, and then we ended doing a HMR and going through everything, and like now he's here all the time. Any questions, and he's straight back." (NSW309AO)

"And if they were having like other lifestyle issues ... we've got a fair few people that have allergies, like seasonal allergy issues, and trying to get that under control as well." (TAS5347KH)

"He was also suffering from hay fever … I believe we gave him Telfast® … He then came back in for a second box of 10, so it must have helped." (NSW2656PO)

"…he's a pretty heavy smoker… that's why I referred him to the doctor… I think he has given up now." (NSW3146AR)

Many of the interventions undertaken by comparator pharmacists have strong evidence in improving asthma management and control. Some pharmacists claimed these interventions were already part of their everyday practice. Three-quarters of respondents checked inhaler technique or made suggestions to improve participant inhaler technique such as addition of a spacer as part of usual practice. Almost half checked reliever usage and counselled about different medications and checked compliance to preventer medications regularly. This was not part of the protocol for the comparator arm.

Participants in the comparator arm were expected to receive a referral to their GP at the end of their baseline consultation. Over three-quarters of respondents were able to recollect the pharmacist's referral either verbally or in written form. The remaining one quarter could not recall how their pharmacy managed the GP referrals and did not provide comment. Almost half of the pharmacists mentioned that participants benefited directly from GP referrals, as it was the trigger for participant asthma reviews and monitoring by their doctor, the doctor-initiated medication changes to more appropriate therapy and participant asthma action plan were updated.

> *"I think just in the fact that my patients actually went and got followed up by their GPs … it's just they've always had asthma, they've always used that puffer, they don't get it reviewed, they go for other problems to their GP … So, [the baseline consultation] actually actively made them go back and talk about their asthma." (NSW11305KP)*

> *"I think [the baseline consultation] definitely got them thinking about their asthma and their management, and I think it hopefully got them to sort of engage with their doctor, whether or not they sort of told us about it or they did it a bit later ... I think it was just greater awareness." (NSW3013MH)*

> *"She has been put on a new puffer now, and she's not using her Ventolin® as much." (NSW3013MH)*

> *"I believe that she did get put on a different type of medication, and that she found it to be more effective." (NSW3032TV)*

> *"Most of them were our regular customers, and so I got some feedback saying, "Yes, I've had a chat to my doctor," and couple of them even sort of came in with brand new asthma action plans." (TAS743AH)*

Two pharmacists acknowledged within their interviews that they were part of the comparator arm of the trial. One of them still carried out supplementary interventions.

> *"I don't think I was in a group that would have spoken about inhaler technique or any of that kind of gear, so I didn't get much of a chance to go over that." (NSW2967JW)*

> *"We've done a couple of trials, yes, but we just weren't as the control group, I think…Well, after the review, we discovered he was hopeless with his medications, so we did a MedsCheck, and then we ended doing a HMR and going through everything, and like now he's here all the time. Any questions, and he's straight back." (NSW3091AO)*

PERCEIVED BENEFIT

BENEFIT TO PARTICIPANTS

Almost all pharmacists perceived that some, if not all participants, benefited from the trial, most notably by improving participants' understanding of asthma, and their medications, management and adherence. These improvements were mentioned by over half of the respondents.

> *"A better understanding … if you have to live with asthma, you can actually have a quality of life if you actually control your symptoms." (NSW2663LW)*

"They understand more about their condition … they can keep an eye on that, how and what they use ... to prevent asthma attacks." (NSW2092CN)

"I would like to think that we started for the non-compliant increasing compliance." (NSW2806CA)

Several mentioned that participants' symptom control improved, as well as reliance on their reliever.

"And so, the follow-up interview, they said it made a whole difference, and they didn't need to use their salbutamol anymore." (WA4412PN)

"Basically, we had one lady who was really using a lot of Ventolin®. It was just more the belief that because she had got that instant sort of relief from her Ventolin®, she should be using it all the time and just taking it routinely before bed, etc, etc – just got her to … only use it when required … Started to use her preventor medication regularly, and then she was symptom free." (NSW2930AW)

Pharmacists also perceived that participants benefited by encouraging smoking cessation, improving participant inhaler technique and addressing allergic rhinitis management. These changes were mentioned by a couple of respondents.

"We have two smokers, actually, in the trial…well, one of them – he's quite motivated actually, so he has ended up quitting anyway, not – like he was cutting down through the trial…I'm not sure if it's anything that we specifically did, but it was more reinforcement and encouragement from us, like telling, 'Doing a really good job' and encouraging him, and, you know, he was like starting to exercise as distraction and that sort of thing… the management of allergic rhinitis, just helping people to understand how important that is, and just showing them the range of products that are available and not to settle for having symptoms." (TAS5347KH)

Several pharmacists s perceived that the trial made participants more aware of their conditions and benefited from someone checking in on them.

"Anything where a patient gets one-on-one time with the doctor or pharmacist around their asthma is definitely a benefit." (NSW2930AW)

"... he could come back to and talk to about how well he was doing and [I was] just encouraging him to continue with that." (TAS5347KH)

"So, it was the increased sort of patient contact time. A lot of people – because we were specifically making a time to go through their asthma specifically in a sit-down setting, I think they felt a lot more valued and felt like they were getting a lot more out of their visit." (TAS743AH)

Despite the number of pharmacists reporting participant benefit, almost half also stated that for some, the trial was not beneficial. Most notably, this was because the pharmacist believed the participants to be already well managed, and it was hard to overcome participant barriers such as loss of interest or perception that they knew everything already. Other reasons included that pharmacists were limited to what they could do within the trial, and participants did not follow up referrals and remained poorly controlled.

"A third weren't interested. They were just, "Yes, I know what I'm doing" … like most asthmatics." (NSW2089AT)

"Some, yes. Some, no. Some don't want help at all." (NSW2930AW)

"I feel like there wasn't so much I could do for her, anyway, because she was under a specialist, she was under a GP, she's an ex-RN." (NSW2967)

BENEFIT TO PHARMACISTS

Almost all pharmacists reported that being involved in the trial, albeit the comparator (usual care) arm, was beneficial. Over half of the pharmacists reported that it strengthened their relationship with their participants. One pharmacist mentioned that it allowed them a better understanding of the patient experience.

"I think any interaction we have with our patients, with our doctors is improving our relationships with those people, and that goes a long way." (NSW11305KP)

"There were two sides to it. So, there's one, the customer interaction, and there's, two, just building up systems in the shop to do these sorts of things." (NSW2184JY)

"I mean, for us, generally, it's just building that relationship further with the patient and making sure that they know that we're obviously here to help look after them and their health." (NSW3032TV)

"From a pharmacy in general and as a pharmacist, you get to know your patient condition in a lot more depth, so, yes, you can talk to them about their asthma sort of on the fly, but you don't necessarily get an idea of how it affects them day-to-day or what any sort of potential causes are." (TAS743AH)

One-quarter of pharmacists acknowledged learning more about asthma and medicines, despite there being no formal educational materials provided to these pharmacists apart from protocol training. One pharmacist mentioned that it improved their research literacy.

"Well, I brushed up on my inhaler thing, as well as my medication and my clinical knowledge. And also, I think the greatest benefit was building that rapport with patients." (WA4412PN)

Several pharmacists mentioned that the trial helped to change role perceptions of pharmacists, which, as another pharmacist mentioned, promotes the service focus and allows the building of service delivery systems.

"... it portrays the image we're service based. We're not here just to hand out medication, which at some point in the future a vending machine will do. We're a clinic-based pharmacy." (NSW2089AT)

"... we're more than a vending machine, and so any opportunity to kind of prove that to the other healthcare professionals and just show them we can be relied upon, we're useful, and we're relevant, and we're helping to keep people out of hospital, I'm all for." (NSW2967JM)

Other mentioned benefits included that it was good for business and was professionally satisfying.

"... it also maintains consistent or recurrent business." (NSW2663LW)

Only two pharmacists mentioned that the trial provided no benefit to the pharmacist, with one stating that it was what they did already, but just lengthened the administrative time because of the paperwork required.

> *"... it probably didn't really benefit us to much extent, because it just meant a bit more effort to what we would normally do." (WA504BS)*

QUANTITATIVE EVALUATION

PARTICIPANT CHARACTERISTICS

A baseline comparison of participant characteristics is presented in Appendix Table X-2. The only characteristics significantly associated with adherence to the protocol were state (NSW) and location (Highly Accessible).

Appendix Table X-1: Baseline characteristics for comparator participants (asthma patients) from adherent and non-adherent pharmacies.

	Adherent pharmacies	Non-adherent pharmacies	Overall	*p*-value
Pharmacy state	n=31	n=69	n=100	0.0284*
NSW	28 (90.3%)	48 (69.6%)	76 (76.0%)	
WA	3 (9.7%)	8 (11.6%)	11 (11.0%)	
TAS	0 (0.0%)	13 (18.8%)	13 (13.0%)	
Pharmacy remoteness	n=31	n=69	n=100	0.0052*
Highly Accessible	22 (71.0%)	32 (46.4%)	54 (54.0%)	
Accessible	9 (29.0%)	19 (27.5%)	28 (28.0%)	
Moderately Accessible, Remote, Very remote	0 (0.0%)	18 (26.1%)	18 (18.0%)	
Age (years)	n=31	n=69	n=100	0.2526
18 to 25	1 (3.2%)	8 (11.6%)	9 (9.0%)	
26 to 35	3 (9.7%)	6 (8.7%)	9 (9.0%)	
36 to 45	4 (12.9%)	2 (2.9%)	6 (6.0%)	
46 to 55	5 (16.1%)	10 (14.5%)	15 (15.0%)	
> 55	18 (58.1%)	43 (62.3%)	61 (61.0%)	
Sex	n=31	n=69	n=100	0.7755
Male	9 (29.0%)	22 (31.9%)	31 (31.0%)	
Female	22 (71.0%)	47 (68.1%)	69 (69.0%)	
Work situation	n=31	n=69	n=100	0.4661
Full-time employed	7 (22.6%)	12 (17.4%)	19 (19.0%)	
Home duties	4 (12.9%)	7 (10.1%)	11 (11.0%)	
Part-time/casual	6 (19.4%)	15 (21.7%)	21 (21.0%)	
Retired/Pensioner	7 (22.6%)	27 (39.1%)	34 (34.0%)	

	Adherent pharmacies	Non-adherent pharmacies	Overall	*p*-value
Unemployed or seeking work	3 (9.7%)	3 (4.3%)	6 (6.0%)	
Full-time carer	1 (3.2%)	0 (0.0%)	1 (1.0%)	
Other	3 (9.7%)	5 (7.2%)	8 (8.0%)	
Level of education	n=31	n=69	n=100	0.2012
No formal education	0 (0.0%)	3 (4.3%)	3 (3.0%)	
Primary school	2 (6.5%)	2 (2.9%)	4 (4.0%)	
High school	15 (48.4%)	38 (55.1%)	53 (53.0%)	
Tertiary non-university (e.g. TAFE)	5 (16.1%)	18 (26.1%)	23 (23.0%)	
University	7 (22.6%)	7 (10.1%)	14 (14.0%)	
Post-graduate	2 (6.5%)	1 (1.4%)	3 (3.0%)	
Age at asthma onset	n=31	n=69	n=100	0.0592
0-5 years of age	12 (38.7%)	14 (20.3%)	26 (26.0%)	
6-15 years of age	2 (6.5%)	15 (21.7%)	17 (17.0%)	
16-34 years of age	9 (29.0%)	17 (24.6%)	26 (26.0%)	
35-55 years of age	7 (22.6%)	12 (17.4%)	19 (19.0%)	
> 55 years	1 (3.2%)	11 (15.9%)	12 (12.0%)	
Ever had a lung function test	n=31	n=69	n=100	0.4821
No	9 (29.0%)	25 (36.2%)	34 (34.0%)	
Yes	22 (71.0%)	44 (63.8%)	66 (66.0%)	
Last lung function test	n=22	n=44	n=66	0.3611
<12 months ago	6 (27.3%)	17 (38.6%)	23 (34.8%)	
≥12 months ago	16 (72.7%)	27 (61.4%)	43 (65.2%)	
Active smoker	n=31	n=69	n=100	0.8322
No	26 (83.9%)	59 (85.5%)	85 (85.0%)	
Yes	5 (16.1%)	10 (14.5%)	15 (15.0%)	
History of hay fever	n=31	n=69	n=100	0.2027
No	12 (38.7%)	18 (26.1%)	30 (30.0%)	
Yes	19 (61.3%)	51 (73.9%)	70 (70.0%)	
RCAT score[1]				0.3095
Mean (SD)	18.7 (3.50)	20.0 (5.26)	19.7 (4.85)	
Median (Q1; Q3)	18.0 (16.0; 20.0)	20.0 (17.0; 24.0)	20.0 (16.0; 24.0)	
Min Max	14 26	7 28	7 28	
IAQLQ score[2]				0.3500
Mean (SD)	3.4 (1.90)	3.0 (2.17)	3.1 (2.09)	

	Adherent pharmacies	Non-adherent pharmacies	Overall	*p*-value
Median (Q1; Q3)	3.4 (1.8; 4.5)	2.4 (1.4; 4.1)	2.7 (1.5; 4.3)	
Min Max	1 8	0 10	0 10	
ACQ score[3]				0.4410
Mean (SD)	2.6 (0.91)	2.4 (0.88)	2.5 (0.89)	
Median (Q1; Q3)	2.5 (1.7; 3.2)	2.2 (1.7; 3.0)	2.3 (1.7; 3.0)	
Min Max	2 5	2 5	2 5	
SF-12 mental health score[4]				0.8078
Mean (SD)	46.4 (8.31)	45.9 (9.67)	46.1 (9.23)	
Median (Q1; Q3)	47.1 (43.0; 52.3)	47.4 (42.3; 53.3)	47.3 (42.4; 53.1)	
Min Max	19 60	12 62	12 62	
SF-12 physical health score[4]				0.4583
Mean (SD)	44.4 (8.05)	43.1 (8.49)	43.5 (8.33)	
Median (Q1; Q3)	45.4 (40.8; 51.3)	44.2 (36.7; 49.6)	44.9 (37.9; 50.0)	
Min Max	24 56	26 58	24 58	

Note:

* significant result

1. Rhinitis Control Assessment Test scores lie between 6 and 30. The lower the score, the more severe the allergic rhinitis; the higher the score, the less severe the allergic rhinitis. Participants scoring ≤21 are considered clinically "symptom uncontrolled"; those scoring > 21 are considered "symptom controlled" (81).
2. The Impact of Asthma on Quality of Life Questionnaire (IAQLQ) scores lie between 0 and 10. Higher scores represent a greater impact of asthma on quality of life (55).
3. Asthma Control Questionnaire (ACQ) scores lies between 0 (Totally controlled) and 6 (Extremely poorly controlled). A score of 1.5 or greater is considered an indication of poorly controlled asthma (79).
4. SF-12 MH and SF-12 PH scores lie between 0 and 100, where a zero score indicates the lowest level of health measured by the scales and 100 indicates the highest level of health.

COMPARATOR ARM INTERVIEW GUIDE: PHARMACISTS

My name is ……. from the Woolcock Institute. Last year, your pharmacy took part in the asthma rhinitis control study funded under the Sixth Community Pharmacy Agreement.

We are calling you, given your involvement in the study, to obtain feedback on your perception of the trial and how it worked out in your pharmacy. The interview can be done at any time to suit you and we were wondering if you might have 10-15 minutes to provide this valuable feedback now or we can book in a day/time that suits you better?

Once date is set ask if it is OK for Interview to be recorded for transcription purposes only and once transcribed it will be destroyed. Any feedback provided is confidential and all identifying features removed.

1. We know it was a while ago, but just as a summary your pharmacy recruited X asthma patients into the trial between X to Y 2019. Of course, it is difficult to remember in detail, but would you please describe, just generally – how your pharmacy approached these patients?

- As you invited patients into the trial, what did you feel were patient's motivations to agree (or disagree) to participate
- After the initial approach what happened next?

2. Can you describe what happened during a typical initial visit with your patients in the trial?
    - How do you feel the protocol questions helped you with your patients, if at all?
    - Can you recall examples of any problems with your patients' asthma? Can you describe them?
3. Do you remember any clinical actions you took at that initial visit?
        - Pharmacists may mention things like – Discussing medication use, inhaler technique, problems with their asthma or medication, asthma actions plans, differences between relievers and preventers, other related conditions etc) – It is important not to prompt this but if they did these things we need to know.
4. The trial processes suggested that a referral letter be provided to the patient for their GP to action. How did this work in your pharmacy?
    - If you were aware that the referral was acted upon, what did the GP do?
5. So apart from the referral letter, was they any particular action you took/or something the patient wanted help with etc?
    - at the initial visit or whenever they came in for a script afterwards? (could be yourself or from another staff member)
6. How did your pharmacy manage the follow up phone calls, can you describe what happened on a typical follow-up phone call?
    - How do you feel the protocol questions helped you with your patients, if at all?
    - Do you remember any clinical actions you took?
        - Pharmacists may mention things like – Discussing medication use, inhaler technique, problems with their asthma or medication, asthma actions plans, differences between relievers and preventers, other related conditions etc) – It is important not to prompt this but if they did these things we need to know.
7. Can you describe your usual practice/interaction when meeting with a patient with asthma?
    - Were you able to use your usual practice in our protocol? If yes, what aspects did you include?
8. Do you believe there were any benefits for your patients in the trial? If yes, can you give me any specific examples? Was there anything you did in particular that you believe helped your patients?
9. Do you believe there were any benefits for you? If yes, what were they?
10. Would you like to add anything further about your involvement, the trial or interactions with your asthma patients?

APPENDIX Y: COST PER ARM COMPARISON BY PARTICIPANT CHARACTERISTICS

While the mean total annual costs were mostly similar in both arms, the distribution of costs significantly differed with regard to some characteristics (Appendix Table Y-1). Even though the mean total costs were not statistically different in both arms, on average, costs were higher in the intervention arm ($4035) compared with the comparator arm ($3943). Across the categories of educational levels, having less than a high school education was associated with the highest mean total costs in both arms with the highest observed in the comparator arm ($5592) compared to the intervention arm ($5383). Regarding employment status, the average costs were highest among those who were unemployed, with the highest costs observed in the intervention arm ($5599). The distribution of annual total costs was significantly different between intervention and comparator arms for age (p <0.001), education (p=0.026), employment (p <0.001), the number of hospital admissions (p=0.003), IAQLQ score (p=0.004), and self-reported depression and anxiety (p=0.006). MBS and PBS cost summaries by participant characteristics are presented in Appendix Table Y-2.

Appendix Table Y-1: Total annual cost summary by characteristics for the study participants.

Spearman's rank correlation coefficients *p*-values are reported for continuous variables (intervention// comparator) and two-sample Wilcoxon rank-sum test with exact *p*-values, for categorical variables.

Characteristic	Total costs (MBS+PBS) Intervention Mean (SD)	Comparator Mean (SD)	*p*-value
Age, years	4035 (5238)	3943 (4024)	< 0.001// < 0.001
Gender			
Male	4077 (4920)	4054 (4312)	0.834
Female	4017 (5383)	3894 (3911)	
Education			
< High school (%)	5383 (3894)	5592 (4192)	
High school (%)	4268 (4881)	4161 (4219)	0.026
> High school (%)	3701 (5707)	5427 (4463)	
Employment status			
Full-time	2461 (5050)	1547 (1573)	
Parttime or casually employed	2511 (3139)	1912 (1564)	< 0.001
Unemployed	5599 (5652)	3528 (3783)	
Location n (%)			
NSW	4247 (5422)	3944 (4315)	
TAS	2906 (3771)	3907 (2853)	0.394
WA	3806 (5199)	3963 (3144)	
Current smoker			
No	4183 (5496)	3856 (3729)	0.684

Characteristic	Total costs (MBS+PBS) Intervention Mean (SD)	Comparator Mean (SD)	*p*-value
Yes	3015 (2743)	4388 (5361)	
Age of asthma onset			
< 35 years	3899 (5414)	3541 (4173)	0.101
³35 years	4377 (4789)	4881 (3523)	
Hospital admissions	4034 (5238)	3943 (4024)	0.002// 0.271
Emergency Department visits	4034 (5238)	3943 (4024)	0.421// 0.544
ACQ score (≥1.5)	4034 (5238)	3943 (4024)	0.012// 0.037
Baseline RCAT score	4034 (5238)	3924 (3992)	0.153// 0.555
Baseline IAQLQ score	4034 (5238)	3943 (4024)	0.004// 0.012
Hay fever			
No	5517 (6533)	4605 (3628)	
Yes	3518 (4618)	3697 (4151)	0.048
Yes	5368 (5976)	-	

Appendix Table Y-2: MBS and PBS Cost summaries by characteristics for the study participants.

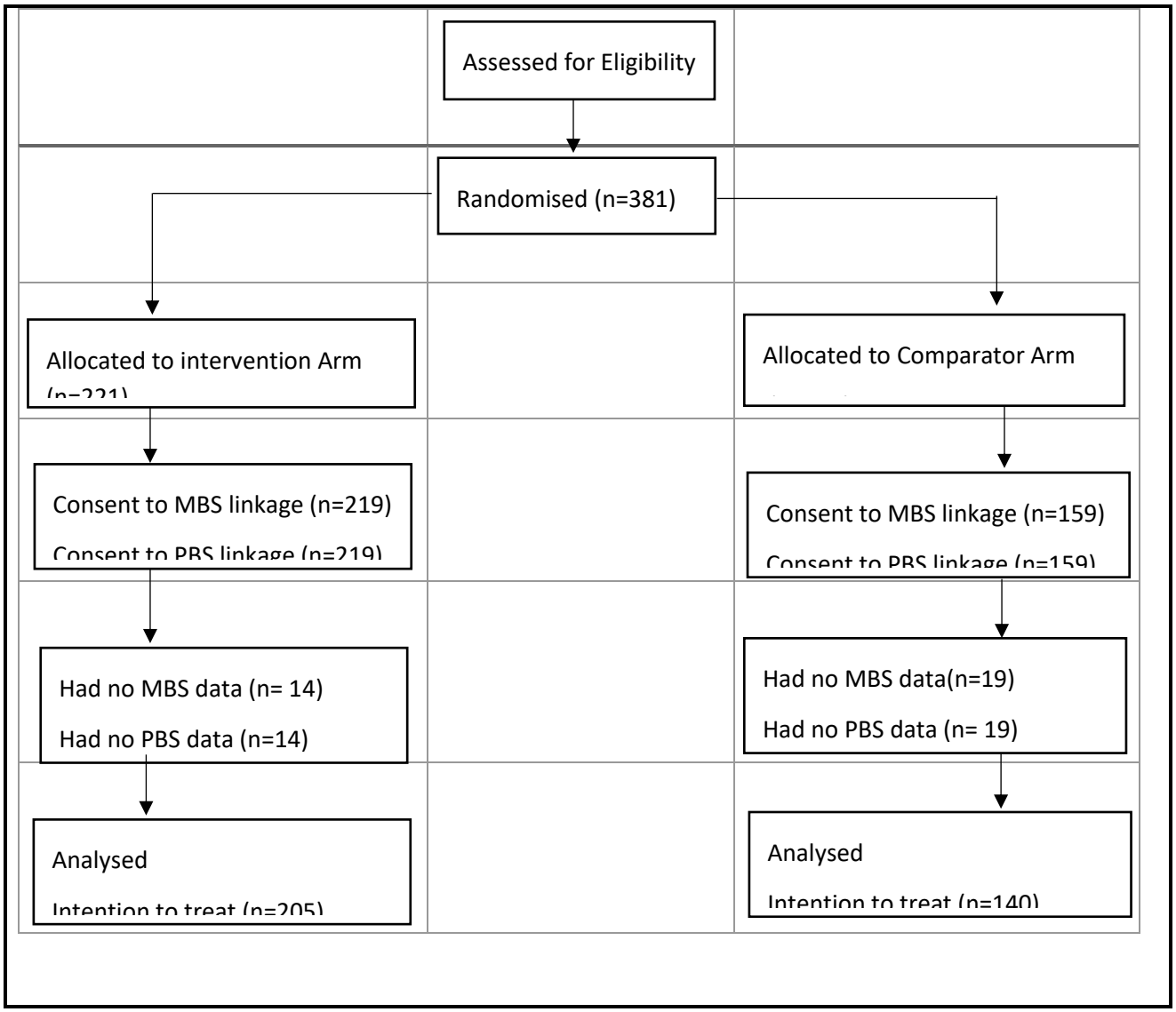
Spearman's rank correlation coefficients p-values are reported for continuous variables (intervention// comparator) and Wilcoxon matched-pairs signed-rank test exact p-values, for categorical variables.

Characteristic	MBS-Schedule Treatment Mean (SD)	Comparator Mean (SD)	*p*-value	PBS-Benefits Treatment Mean (SD)	Comparator Mean (SD)	*p*-value
Age, years	2436 (3126)	2495 (2750)	< 0.001// < 0.001	1599 (3148)	1448 (2103)	< 0.001// < 0.001
Gender						
Male	2283 (2698)	2430 (2975)	0.566	1794 (3310)	1624 (2271)	0.297
Female	2501 (3297)	2525 (2660)		1516 (3086)	1369 (2031)	
Education						
< High school (%)	1452 (2149)	1151 (1086)		2317 (2278)	2127 (1949)	
High school (%)	1900 (2363)	1424 (1116)	0.088	1762 (3194)	1706 (2283)	0.006
>High school (%)	3210 (3660)	3307 (3193)		1384 (3178)	1095 (1875)	
Employment status						
Full-time	3066 (2065)	3465 (3363)	< 0.001	1009 (3384)	396 (680)	< 0.001
Part time or casually employed	2506 (2707)	2455 (2455)		612 (953)	488 (709)	

Characteristic	MBS-Schedule Treatment Mean (SD)	Comparator Mean (SD)	*p*-value	PBS-Benefits Treatment Mean (SD)	Comparator Mean (SD)	*p*-value
Unemployed	2316 (3550)	2433 (2913)		2388 (3520)	2120 (2438)	
Location n (%)						
NSW	2594 (3281)	2492 (2950)		1653 (1652)	1451 (2254)	
TAS	1716 (2374)	2668 (2417)	0.226	1190 (2676)	1239 (869)	0.528
WA	2203 (2841)	2404 (1827)		1603 (3795)	1558 (1887)	
Current smoker						
No	2552 (3275)	2484 (2552)	0.237	1631 (3315)	1372 (2065)	0.318
Yes	1639 (1617)	2554 (3668)		1375 (1603)	1834 (2295)	
Age of asthma onset						
<35 years	2400 (3300)	2153 (2588)	0.232	1499 (2993)	1388 (2340)	0.011
≥35 years	2527 (2658)	3295 (2976)		1850 (3528)	1586 (1416)	
Hospital admissions	2436 (3126)	2495 (2750)	0.001// 0.323	1598 (3148)	1448 (2103)	0.004//0.232
Emergency Department visits	2436 (3126)	2495 (2750)	0.406// 0.772	1598 (3148)	1448 (2103)	0.283//0.171
ACQ score (≥1.5)	2436 (3126)	2495 (2750)	0.044// 0.318	1599 (3149)	1448 (2103)	0.008//0.017
Baseline RCAT score	2436 (3126)	2504 (2798)	0.303// 0.707	1598 (3148)	1420 (2023)	0.107// 0.234
Baseline IAQLQ score	2436 (3126)	2495 (2750)	0.018// 0.263	1598 (3148)	1448 (2103)	0.003// 0.001
Hay fever						
Yes	3456 (4378)	-		1912 (2860)		

APPENDIX Z: PARTICIPANTS FLOW AND BASELINE CHARACTERISTICS – MBS AND PBS DATA

Data on a total number of 381 participants were collected in this randomised control trial (RCT) (Appendix Figure Z-1). Two-hundred and twenty-one were randomised into the intervention arm while the rest formed the comparator arm. Of these, 378 consented to data linkage, and 345 had full trial, MBS and PBS data. Thus, 32 participants did not have MBS and PBS data while one did not have trial data. Therefore, the final analytical sample included 205 (59%) participants from the intervention and 140 (41%) from the comparator arms.



Appendix Figure Z-1: Flow chart summarising the Medicare Benefits Schedule (MBS) and Pharmaceutical Benefits Scheme (PBS) costs data collection for trial participants.

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