Commonwealth Department of Health

Sixth Community Pharmacy Agreement Pharmacy Practice Incentive Program:

Clinical Interventions

Initial Evaluation - Final Report

17th November 2016

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Abbreviations

3CPA	Third Community Pharmacy Agreement
4CPA	Fourth Community Pharmacy Agreement
5CPA	Fifth Community Pharmacy Agreement
6CPA	Sixth Community Pharmacy Agreement
ABS	Australian Bureau of Statistics
ADR	Adverse Drug Reaction
ATSI	Aboriginal and Torres Strait Islander
CALD	Culturally and Linguistically Diverse
CI	Clinical Intervention
CMI	Consumer Medicine Information
CUA	Cost-Utility Analysis
DAA	Dose Administration Aid
DOCUMENT	Drug selection, Overdose, Compliance, Undertreated, Monitoring, Education, Not classifiable, and Toxicity
DRP	Drug-Related Problem
GPCIs	GuildCare Program Clinical Interventions
GP	General Practitioner
HMR	Home Medicines Review
HRU	Health Resource Utilisation
HTA	Health Technology Assessment
ICT	Information and Communications Technology
MSAC	Medical Services Advisory Committee
NPS	National Prescribing Service
PBS	Pharmaceutical Benefits Scheme
PHN	Primary Health Network
PICO	Population, Intervention, Comparator, Outcome
PPI	Pharmacy Practice Incentives

PROMISe	Pharmacy Recording of Medication Incidents and Services electronically
PSA	Pharmaceutical Society of Australia
PwC	PricewaterhouseCoopers
QCPP	Quality Care Pharmacy Program
QALY	Quality-adjusted life years
QoL	Quality of life
QUM	Quality Use of Medicines
QUMAX	Quality Use of Medicines Maximised (for Aboriginal and Torres Strait Islander People)
RACF	Residential Aged Care Facility
RMMR	Residential Medication Management Reviews
SS	Staged Supply

EXECUTIVE SUMMARY

On the 28th June 2016, the Department of Health engaged HealthConsult to evaluate the three Pharmacy Practice Incentives (PPI) Program initiatives: Clinical Interventions (CIs), Staged Supply (SS), Dose Administration Aids (DAAs). The initial evaluation of CI involved:

- a literature review to identify data to inform the comparative clinical and cost-effectiveness of the CI initiative and 'like' programs internationally; and
- an examination of Australian utilisation data from the CI initiative since its start under earlier Community Pharmacy Agreements (CPAs).

Background

The CI priority area was established under the Better Community Health Initiative of the Fourth Community Pharmacy Agreement (4CPA) and Fifth Community Pharmacy Agreement (5CPA) between the Pharmacy Guild of Australia and the Commonwealth Government. The CI initiative was continued under the Sixth Community Pharmacy Agreement (6CPA), as part of the PPI Program directed at improving medication compliance through community pharmacies in Australia.

The Pharmaceutical Society of Australia (PSA) *Standard and Guidelines for Pharmacists Performing Clinical Interventions* (March 2011) defines a CI to be a 'specific intervention by a pharmacist, involving identifying, and making a recommendation in an attempt to prevent or resolve, a drug-related problem (DRP)'.

It is intended that CIs complement other professional services offered by community pharmacists, such as the provision of Consumer Medicine Information (CMI), Home Medication Review (HMR), Residential Medication Management Review (RMMR), MedsCheck services (also known as Medicines Use Review), and the provision of DAAs.

It is recognised that defining and monitoring CIs is complex, as CIs refer to 'any professional activity by the pharmacist directed towards improving the quality use of medicines (QUM) and resulting in a recommendation for a change in the patient's medication therapy, means of administration or medication-taking behaviour' (PSA, 2011).

Participating pharmacists are required to record CIs for the purposes of the PPI Program using DOCUMENT, a classification system with eight main categories for type of DRP: Drug selection, Overdose, Compliance, Undertreated, Monitoring, Education, Not classifiable, and Toxicity. However, incentive payments are not made for interventions under the MEN (Monitoring, Education, and Not classifiable) components of the classification system.

Eligible community pharmacies are entitled to claim incentive payments four times a year for performing and recording CIs using the DOCUMENT classification system. Pharmacies must also demonstrate that they participate in delivering CIs through regular claiming to Medicare Australia. It is important to note that the incentive payment calculation is based on a formula that takes into account the number of CIs provided as well as the number of PBS scripts dispensed. Therefore, there is only an indirect relationship between the amount of the incentive payment and the volume of CI services provided by a given pharmacy.

Methodology

Literature search

A systematic literature review was undertaken in August 2016 to identify studies that provide evidence relating to the effectiveness, costs and cost-effectiveness of CI or similar programs provided by pharmacists to individuals living in the community. The grey literature was also searched, as were the reference lists of included studies. Table ES.1 presents the evidence selection criteria.

Table ES.1 Selection criteria for evidence relating to CI services provided by community pharmacies

Criteria	Description
Population	Community patients taking one or more self-administered medications (prescribed or over-the-counter). 'Self-administered' refers to the administration of a medication without the active assistance of a health care professional. It allows for medication administered by a family member or carer.
Intervention	Any professional activity undertaken by a community pharmacist directed towards improving QUM and resulting in a recommendation for a change in a consumer's medication therapy, means of administration or medication-taking behaviour. Note: The 'professional activity' may involve a recommendation for a change of therapy, referral, provision of information, or monitoring in relation to a drug-related problem. A drug-related problem may include: • drug selection (the choice of drug prescribed or taken) • over- or under-dosing (the prescribed dose or schedule of a drug) • compliance (the way the consumer takes the medication) • under-treatment (actual or potential conditions that require management or prevention) • monitoring the efficacy or adverse effects of a drug • education or information about a drug or disease (at the consumer's request) • toxicity or adverse reaction to a medication • not classifiable
Comparator	Community patients in the absence of the intervention.
Outcomes	• adherence/compliance/concordance with prescribed dose schedule (e.g. pill count, self-report) • change in patient management • clinical outcomes (e.g. BP in patients with hypertension, HbA_{1c} in patients with diabetes) • adverse drug events/reactions and medication-related problems • mortality • health care resource use (ED attendance, hospitalisation, GP visits, specialist visits, pathology or other investigations) • patient acceptance/satisfaction • health-related quality of life • costs and cost-effectiveness
Study design	Comparative studies (randomised or non-randomised controlled trials, cohort studies, case control studies) or systematic reviews of comparative studies. Applicability to the Australian context will be considered.
Publication type	Full English-language publications or reports. Conference abstracts are excluded.
Search period	No year restrictions

Abbreviations: BP, blood pressure; CI, clinical intervention; ED, emergency department; GP, general practitioner; HBA_{1c}, glycated haemoglobin; QUM, quality use of medicines.

The literature search identified four Australian studies of CIs funded by the Commonwealth. One was an Australian randomised controlled trial (RCT) comparing CI rates after providing pharmacist education and/or remuneration (or neither) for these services. Different aspects of the study,

including an economic impact analysis, were reported in three separate publications (Benrimoj et al, 2000; Benrimoj et al, 2003a and 2003b). Three CPA-funded CI projects related to the DOCUMENT classification system were also identified (PROMISe I, PROMISe II, and PROMISe III). In addition, the targeted search of the websites of relevant pharmacy organisations and the Commonwealth Department of Health identified one GuildCare report on the CI initiative, and one previous evaluation of the CI initiative funded under the 5CPA.

By agreement with the Department, as all the identified studies (even those published in the peer reviewed literature) were funded by the Department, either directly or under 3CPA, 4CPA or 5CPA, the findings are reported as previous work conducted to design and evaluate the CI program. In fact, only the Benrimoj et al (2003) study met the agreed selection criteria, and this study was a key input into the initial CI program design.

The primary challenge of identifying studies of pharmacists' CIs that resemble those provided by Australian pharmacists under the PPI Program is the lack of a widely accepted term for the intervention, risking the sensitivity of any literature search. Furthermore, many studies refer to other professional pharmacy services as a CI, when in the Australian context such interventions fall outside the CI initiative (e.g. Home Medicines Review, MedsCheck or DAA). The specificity of the literature search undertaken for this Review was substantially reduced by this lack of specificity in the search terms, with most studies excluded due to the CI in question being more similar to other professional pharmacy services or enhanced service provision models or programs (e.g. asthma medication optimisation and adherence programs) rather than a CI in the PPI Program context.

Given the limitations in conducting a systematic literature review for an intervention of this nature, it is not possible to assert with absolute confidence that a potentially relevant study has not been missed. However, a lack of empirical research evaluating the clinical and economic value of CIs performed within the community pharmacy setting is not unexpected given that the intervention is already part of standard practice in some countries (such as Australia) where pharmacists have a professional obligation to check for potential DRPs and intervene to prevent them. This introduces difficulties in conducting a study with a suitable comparator when assessing the potential outcomes of CIs.

Utilisation analysis

Although DOCUMENT data is held by the Pharmacy Guild of Australia, the only data available for inclusion in the utilisation analysis were claims payment data held by the Department of Health. These data have been analysed in the context of geographical factors that have been inferred from the postcode of each pharmacy. Those factors included remoteness; overall population and chronic disease prevalence by Primary Health Network (PHN) geographic areas. These factors were used to assess whether the growth in CI services has occurred in line with any of these factors. Key metrics in the analysis are limited to the amount of claims paid and the number of patient CI services provided. No data that enabled descriptive data by specific interventions was available at the time of undertaking the analysis.

Results of the literature review

The key research questions for the literature review of CI services primarily relate to the potential advantages to consumers that are outlined in the PSA Guidelines (2011). As a departure from normal practice, to provide MSAC with additional information, a summary of the answers to the posed questions is provided that draws on the Commonwealth funded (either directly or through the CPAs) studies. In so doing, it is acknowledged that the reported studies (most of which are not published in peer reviewed literature) would normally be regarded as low quality and/or excluded.

Had this approach not been adopted the conclusion with respect to all questions would have been that no relevant evidence was identified.

Is there evidence that a CI service provided by community pharmacies provides benefits to consumers, compared with no CI service provided by community pharmacies, in terms of: improved symptom control and therapeutic response; decreased incidence of adverse events related to medicines; decreased emergency visits and hospitalisations due to DRPs; improved adherence to and concordance with the prescribed medicine regimen; and enhanced knowledge of medicines and disease states?

The most relevant study was PROMISe III (Petersen et al, 2009), which examined the number and nature of DRPs detected and CIs performed, over a three-month period in a sample of 210 community pharmacies using DOCUMENT. It included 531 pharmacists who recorded 6,230 CIs from 2,013,923 prescriptions for 486,147 patients.

Peterson reported that the most common interventions were related to drug selection problems (31%) and educational issues prompted by patient requests (24%). Pharmacists made an average of 1.6 recommendations for each intervention. Referral to the prescriber and an education or a counselling session accounted for over 70% of the recommendations made by pharmacists. Change in therapy was reported as the most common type of recommendation (40%), followed by provision of information (34%).

Whilst the study outlines a fairly robust framework, the determination of patient outcomes was made by an Expert Clinical Panel, and not corroborated by any kind follow up with the patient to determine actual outcomes. The Panel merely assigned a predicted consequence (probabilistically) based on patient characteristics collected at the time of the CI service. Also, whilst 6,230 interventions were documented during the twelve week study, only 200 were selected to be analysed by the Panel to feed into the cost effectiveness analyses. On this basis, it is considered that there is insufficient evidence to answer the research question.

Is there evidence that a CI service provided by community pharmacies results in cost offsets or cost savings through rationalisation of medication therapy and avoidance of DRPs?

By extrapolation of the PROMISe III Panel's judgements for the 200 interventions to the full study population, Peterson and colleagues concluded that there were significant savings in terms of reductions in GP visits, specialist visits, investigations, duration of hospital visits and medications. When extrapolating to the Australian population, Peterson and colleagues reported potential net savings of some $289 million. As discussed in a subsequent publication (Stafford et al, 2012), expert opinion provides a relatively low level of evidence but may nonetheless be useful in the absence of studies that provide higher levels of evidence. Taking this view into account, it is concluded that there is insufficient evidence to make a determination on the research question.

What costs are associated with a CI service provided by community pharmacies?

Benrimoj et al (2000) reported the cost of providing a CI intervention in terms of pharmacist time and telephone calls was in the range from $2.50 to $3.16 per proactive CI (defined as a CI that would have not been necessary to dispense the medication). These figures are based on 1997 data. PROMISe III reported that, based on 2009 data, the incremental costs of implementing PROMISe III practice across Australia would be of the order of $95 million. It is considered that these estimates are not likely to reflect current community pharmacy practice and it is probably best to update them by undertaking a contemporary costing study.

Is there evidence that a CI service provided by community pharmacies is cost-effective, compared with no CI service provided by community pharmacies?

Again, the PROMISe III study is the most relevant, as it included a cost utility analysis. The impact on QoL of a CI was determined by the Expert Panel for each of the 200 cases subject to detailed review and then extrapolated to the population. Using these judgements in combination with the predictions of impact on healthcare resource utilisation, Peterson et al, 2009 reported that, in terms of cost-effectiveness, CI dominated the comparator (no CI). As discussed by Stafford et al, 2012 this expert judgement methodology represents a low level of evidence, and the systematic literature was unable to identify and corroborating studies. It is thus concluded that the level of uncertainty in the available findings is too high to make an evidence based determination regarding the cost effectiveness of the CI service.

Results of the utilisation analysis

The available data show that the volume of the claims for patient CIs provided has increased substantially between 2012 and 2015 nationally, and that the number of participating pharmacies has also increased, especially in more remote regions.

In the absence of knowing what patient groups are receiving CI services or the types of CIs that are being provided to different patient groups, CI claims payment data for 2015 were analysed in the context of geographical factors that have been inferred from the postcode of each pharmacy. Those factors included are remoteness[1] and chronic disease prevalence (mental health or diabetes) by PHN geographic areas. These factors were used to assess whether the growth in CI services had any relationship to these populations. This analysis identified no significant relationships between any of the investigated population groups and the take up rates for the CI services.

Conclusions

Other than work funded by the Department of Health, there were no studies identified that assessed the clinical and cost effectiveness of providing funding incentives to community pharmacists to deliver CI services. There is a larger body of evidence for more comprehensive and multi-faceted pharmacy-led interventions focused on patient care, but findings from these studies cannot be extrapolated to CIs.

There are difficulties involved in estimating the clinical and economic outcomes of CIs performed by community pharmacies given that CIs are routinely undertaken by community pharmacists as part of standard practice in Australia. Another complexity lies in the broad definition of each consequence resulting from a CI (i.e. clinical significance), and the assumptions that a given consequence will result in the same level of disability and health resource utilisation in every patient, regardless of age and co-morbidities.

As the Benrimoj work funded by the Commonwealth was used in the design of the program, it is not considered as independent evidence. That said, it did not directly address the questions of clinical and cost effectiveness. The Peterson work (PROMISe I, II, and III) is the most relevant, but it only provided a relatively low level of evidence for cost-effectiveness and no corroborating studies could be found. Thus it is concluded that to make a robust assessment of the clinical and cost effectiveness of CIs, further research is required. Such research would best take the form of a study that included:

[1] ABS postcode to remoteness.xls available from http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1270.0.55.006July%202011?OpenDocument (accessed 5th October, 2016)

- a high-quality study of adequate size (number of patients) and duration that assessed who utilised the CI service (a discrete type(s) of CI service not part of standard practice) delivered through community pharmacies on medication adherence, clinical outcomes, health care utilisation, patient satisfaction (through primary data collection and linkage to secondary datasets, (e.g. MBS, PBS, hospital utilisation, and so on));
- a robust costing study that measured the unit cost of providing a discrete CI service (not part of standard practice) in a variety of settings across the community pharmacy sector (could also be used to inform fee-setting);
- a translational study that takes the results of the unit cost and outcome measurement work and calculates cost effectiveness (no further primary data collection would be required).

However, it would be imperative that any future study is focused on gathering data about discrete well defined CIs that are not part of standard practice provided by pharmacists otherwise it would produce results that are also confounded.

1 INTRODUCTION

On the 28th June 2016, the Australian Government Department of Health engaged HealthConsult to evaluate the Sixth Community Pharmacy Agreement (6CPA) Pharmacy Practice Incentives (PPI) Program: Clinical Interventions. The initial evaluation of CI involved:

- a literature review to identify data to inform the comparative clinical and cost-effectiveness of the CI initiative, including a review of the international literature to determine whether results for 'like' programs can be extrapolated to be considered as evidence for the CI initiative in Australia; and
- an examination of Australian utilisation data from the CI initiative since its start under earlier CPAs, with an emphasis on elucidating the characteristics and volumes of:
  - pharmacy services delivered via the program;
  - pharmacists and pharmacies delivering these services; and
  - individuals receiving these services.

1.1 Sixth Community Pharmacy Agreement

In May 2015, the Australian Government and Pharmacy Guild of Australia entered into the 6CPA, which provides around $18.9 billion in remuneration for community pharmacy, as well as support to the pharmaceutical supply chain (with a further $372 million provided for chemotherapy compounding fees). Up to $1.26 billion in funding is available under the 6CPA for evidence-based, patient-focused professional pharmacy programs and services. This consists of:

- $613 million for the continuation of a number of programs and services from 5CPA;
- $50 million for a new pharmacy trial program; and
- up to $600 million for new and expanded community pharmacy programs.

The 6CPA includes three key funding elements:

- community pharmacy remuneration;
- ensuring that all Australians have timely access to the Pharmaceutical Benefits Scheme (PBS) medicines they require regardless of the cost of the medicine or where they live; and
- community pharmacy programs directed at improving consumer management of their medications and delivering primary healthcare services through community pharmacy.

1.2 Pharmacy Practice Incentives Program

The 6CPA PPI Program provides a financial incentive to pharmacists to deliver compliance initiatives. As part of the 6CPA, there are several continuing PPI Programs directed at improving medication compliance through community pharmacies in Australia. The continuing programs include:

- Medication Adherence Programs
  - Dose Administration Aids (DAAs)
  - Clinical Interventions (CIs)
  - Staged Supply (SS)
- Medication Management Programs
  - Home Medicines Reviews (HMR)
  - Residential Medication Management Reviews (RMMR)
  - MedsCheck and Diabetes MedsCheck

- Rural Support Programs
  - Rural Pharmacy Workforce Program
  - Rural Pharmacy Maintenance Allowance
- Aboriginal and Torres Strait Islander (ATSI) Programs
  - Quality Use of Medicines Maximised for ATSI People (QUMAX)
  - S100 Pharmacy Support Allowance
  - ATSI Workforce Program (Pharmacy Assistant Traineeship Scheme and Pharmacy Scholarships Scheme)
- eHealth:
  - Electronic Prescription Fee

Under 6CPA, all programs and services need to be reviewed by the Medical Services Advisory Committee (MSAC) for clinical and cost-effectiveness and the health benefits they offer to the community. This process is being used to ensure pharmacy programs and services are assessed against the same standards of evidence as for other health professions. It supports a consistent approach to informing investment that delivers the greatest benefit to consumers.

2 CLINICAL INTERVENTIONS

This Section describes the CI initiative, which falls under the broader Medication Adherence Program within 6CPA.

2.1 Background

The CI priority area was established under the Better Community Health Initiative of the Fourth Community Pharmacy Agreement (4CPA) and Fifth Community Pharmacy Agreement (5CPA) between the Pharmacy Guild of Australia and the Commonwealth Government. The CI initiative was continued under the Sixth Community Pharmacy Agreement (6CPA), as part of the PPI Program directed at improving medication compliance through community pharmacies in Australia. The Pharmaceutical Society of Australia (PSA) *Standard and Guidelines for Pharmacists Performing Clinical Interventions* (March 2011) defines a CI to be a 'specific intervention by a pharmacist, involving identifying, and making a recommendation in an attempt to prevent or resolve, a drug-related problem (DRP)'.

It is recognised that defining and monitoring CIs is complex as CIs refer to 'any professional activity by the pharmacist directed towards improving the quality use of medicines (QUM) and resulting in a recommendation for a change in the patient's medication therapy, means of administration or medication-taking behaviour' (PSA, 2011).

2.2 Drug related problems and clinical interventions

A DRP is defined in the literature as an event or circumstance involving drug treatment that actually or potentially interferes with the patient experiencing an optimum outcome of medical care. Terms used to describe a DRP or subtype include medication-related problem, medication error, adverse drug event, adherence issues and adverse drug reaction (PSA, 2011).

DRPs occur frequently both in hospital and in community settings, and are responsible for a significant proportion of hospital admissions and health expenditure (Elliot and Booth, 2014). A literature review by Roughead et al (2009) examined medication safety in the Australian acute care setting. It found that 2%–4% of all hospital admissions are drug-related, and up to three-quarters of those admissions are potentially preventable. The review also found that medication incidents remain the second most common type of incident reported in Australian hospitals. Another literature review by the National Prescribing Service (NPS, 2009) reported that adverse drug events were responsible for up to 30% of hospital admissions in the older age group (>75 years). A study by Miller et al (2006) investigated the frequency, cause and severity of adverse drug events among general practice patients. The study found that nearly 10% (852 of 8,215) of patients visiting their general practitioners (GPs) had experienced a DRP (predominantly recognised from side effects) within the past six months, with 23% of the events classified as preventable.

There are various pharmacy-led programs and interventions aimed at reducing DRPs where pharmacists conduct a formal review of a patient's medications, or carry out other professional services as an extension of their normal daily activities (i.e. other than dispensing and counselling). These additional processes and services increase the information available to the pharmacist concerning the patient, and thereby present increased opportunities to detect and resolve DRPs.

2.3 Objectives of the CI initiative

According to the PSA standard and guidelines for pharmacists performing CIs (PSA, 2011), the aims of CIs are to:

- encourage pharmacists to work in partnership with consumers and other healthcare providers to reduce the occurrence of DRPs;
- encourage communication between pharmacists, consumers, prescribers and other healthcare providers;
- increase the number of beneficial clinical interventions performed by pharmacists; and
- develop a quality system for the documentation of clinical interventions performed by pharmacists.

It is intended that CIs complement other professional services offered by community pharmacists, such as the provision of Consumer Medicine Information (CMI), Home Medication Review (HMR), Residential Medication Management Review (RMMR), MedsCheck services (also known as Medicines Use Review), and the provision of DAAs. Collectively, these services and activities uphold the QUM principles:

- selecting management options wisely;
- choosing suitable medicines if a medicine is considered necessary; and
- using medicines safely and effectively.

2.4 DOCUMENT DRP classification system

Participating pharmacists are required to record CIs for the purposes of the PPI Program using DOCUMENT, a classification system with eight main categories for type of DRP: Drug selection, Overdose, Compliance, Undertreated, Monitoring, Education, Not classifiable, and Toxicity (Petersen et al, 2009). However, incentive payments are not made for interventions under the MEN (Monitoring, Education, and Not classifiable) components of the classification system.

Table 2.1 shows the eight types of DRPs classified in the DOCUMENT system. The subcategories were determined following testing of the DOCUMENT system on the information provided from a previous community pharmacist intervention documentation project (McKenzie and Peterson, 2002). The process of identifying and resolving DRPs is initiated by the pharmacist's decision on the type of problem they are dealing with (using DOCUMENT categories), followed by investigation to determine if the problem exists or is an issue. The pharmacist then makes a recommendation to resolve the issue (either to the doctor or the patient) and the recommendation is either accepted or not (outcome). Consideration of the potential severity of the situation (significance) is also undertaken (PSA, 2011).

Table 2.1 Types and subcategories of DRPs in the DOCUMENT system

Category/type	Definition	Subcategories/subtypes of DRP
Drug selection (D)	Problems relating to the choice of drug prescribed or taken	Duplication, drug interaction, wrong drug, incorrect strength, inappropriate dosage form, contraindications apparent, no indication apparent, other drug selection problem.
Over or under dose (O)	Problems relating to the prescribed dose or schedule of a drug	Prescribed dose too high, prescribed dose too low, incorrect or unclear dosing instructions, other dose problem

Category/type	Definition	Subcategories/subtypes of DRP
Compliance (C)	Problems relating to the way the consumer takes the medication	Under-use by consumer, over-use by consumer, erratic use of medication, intentional drug misuse (including non-prescription medicines, difficulty using dosage form, other compliance problem
Undertreated (U)	Problems relating to actual or potential conditions that require management or prevention)	Condition undertreated, condition untreated, preventive therapy required, other untreated indication problem
Monitoring (M)	Problems relating to monitoring the efficacy or adverse effects of a drug	Laboratory monitoring, non-laboratory monitoring, other monitoring problem
Education or information (E)	Consumer requests further information about a drug or disease state	Consumer requests drug information, consumer requests disease management advice, other education or information problem
Not classifiable (N)	Problems that cannot be classified under another category	Clinical Interventions that cannot be classified under another category
Toxicity (T)	Problems relating to the presence of signs or symptoms that may be attributed to a drug	Toxicity, allergic reaction or adverse effect present

Source: Standard and guidelines for pharmacists performing clinical interventions (PSA, 2011), p.25
Abbreviations: DRP, drug-related problem.

CIs are classified under four levels of clinical significance. A brief description of the clinical significance codes as used in DOCUMENT are outlines in Table 2.2. A nil significance indicated a DRP with no consequence to the patient.

Table 2.2 Clinical significance categories for DRPs in the DOCUMENT classification system

Clinical significance	Brief description
Low	Consequences to the patient are related to costs or information only
Mild	Consequences to the patient are that they have improved a minor sign or symptom, or if the intervention had not occurred they would have developed a minor symptom. The sign or symptom should be such that it does not require a doctor's visit or treatment.
Moderate	When, if the intervention did not occur, it was likely that patient could have had to go to the doctor because of the consequences. Also, covers the situation where the pharmacist refers the patient to the doctor because of the seriousness of the situation.
High	When, if the intervention did not occur, it was likely that the patient would have had to go to a hospital because of the consequences. Also covers the situation where the pharmacist refers the patient to a hospital because of the seriousness of the situation. When, if the intervention did not occur, it was likely that the patient would have had to receive assistance from a regular nurse visit, or would have had to been placed into residential care of some sort. Also includes the situation where the intervention prevents the additional nursing care or delays the admission to residential care.

Source: Peterson et al (2009), Table 1.12, p. 57
Abbreviations: DRP, drug-related problem.

In addition to using the DOCUMENT classification system for DRPs, pharmacists are also required to record the following information:

- date of the intervention;
- drugs involved, including those central to the DRP, and any recommendations for the resolution of the DRP (strengths and doses of medicines should also be recorded where possible);
- consumer details, including age range and gender;
- any communication with the consumer's prescriber; and
- consumer history (clinical) notes, including any follow-up, outcomes or resolution details.

2.5 Participation in the CI initiative

To be eligible to receive incentive payments for the CI initiative, a community pharmacy must:

- be a Section 90 Pharmacy;
- be accredited by an approved Pharmacy Accreditation Program such as the Quality Care Pharmacy Program (QCPP);
- agree to publicly display and comply with the Community Pharmacy Service Charter and Customer Service Statement;
- register for the CIs priority area via the 6CPA Registration and Claiming Portal;
- continue to meet the above eligibility criteria while participating in the CIs priority area; and
- deliver CI services in accordance with the PPI Program Specific Guidelines.

Eligible community pharmacies are entitled to claim incentive payments four times a year for performing and recording CIs using the DOCUMENT classification system. Pharmacies must also demonstrate that they participate in delivering CIs through regular claiming to Medicare Australia.

The 2011 PSA guidelines provide a standardised best practice process for pharmacists to classify and document DRPs and their CIs. The dimensions of this system include:

- electronic or paper based system linked to dispensing system;
- date of intervention;
- drugs involved including strengths and dosages;
- consumer details, including age range and gender;
- any communication with the consumer's prescriber;
- DOCUMENT and recommendation codes to classify the DRP and CI; and
- consumer history (clinical) notes, including any follow-up, outcomes or resolution details.

2.6 Skills development

The 2011 PSA guidelines mention that training programs may be established to support the development of pharmacists' skills to increase the performance of clinical interventions, and the subsequent documentation of DRPs and clinical interventions. Areas in which pharmacists may identify a need for enhanced skills may include:

- assistance in identifying DRPs and performing clinical interventions (including up-to-date clinical knowledge);
- education about the DOCUMENT classification system for DRPs;
- instruction on how to document DRPs and clinical interventions; and
- advice on methods to improve their rate of DRP detection.

3 REVIEW METHODOLOGY

This Section describes the methodology used to identify and assess the evidence relating to CIs or similar pharmacy-led programs. The evaluation encompasses a systematic literature review of Australian and international evidence for the effectiveness and cost-effectiveness of CI services provided by pharmacists to individuals living in the community, and an analysis of available data on the utilisation of the service provided under the PPI Program.

3.1 Systematic literature review

3.1.1 Research questions and PICO criteria

The key research questions for the evaluation of CI services relate to the potential benefits to consumers that are outlined in the PSA standard and guidelines for pharmacists performing CIs (PSA, 2011).

- Is there evidence that a CI service provided by community pharmacies provides benefits to consumers, compared with no CI service provided by community pharmacies, in terms of:
  - improved symptom control and therapeutic response;
  - decreased incidence of adverse events related to medicines;
  - decreased emergency visits and hospitalisations due to DRPs;
  - improved adherence to and concordance with the prescribed medicine regimen; and
  - enhanced knowledge of medicines and disease states?

- Is there evidence that a CI service provided by community pharmacies results in cost offsets or cost savings through rationalisation of medication therapy and avoidance of DRPs?

Additional research questions of relevance to the evaluation relate to the costs and cost-effectiveness of the service:

- What costs are associated with a CI service provided by community pharmacies?
- Is there evidence that a CI service provided by community pharmacies is cost-effective, compared with no CI service provided by community pharmacies?

Table 3.1 presents the selection criteria for evidence relating to CI services.

Table 3.1 Selection criteria for evidence relating to CI services provided by community pharmacies

Criteria	Description
Population	Community patients taking one or more self-administered medications (prescribed or over-the-counter). 'Self-administered' refers to the administration of a medication without the active assistance of a health care professional. It allows for medication administered by a family member or carer.
Intervention	Any professional activity undertaken by a community pharmacist directed towards improving QUM and resulting in a recommendation for a change in a consumer's medication therapy, means of administration or medication-taking behaviour. Note: The 'professional activity' may involve a recommendation for a change of therapy, referral, provision of information, or monitoring in relation to a drug-related problem. A drug-related problem may include: • drug selection (the choice of drug prescribed or taken) • over- or under-dosing (the prescribed dose or schedule of a drug) • compliance (the way the consumer takes the medication) • under-treatment (actual or potential conditions that require management or prevention) • monitoring the efficacy or adverse effects of a drug • education or information about a drug or disease (at the consumer's request) • toxicity or adverse reaction to a medication • not classifiable
Comparator	Community patients in the absence of the intervention.
Outcomes	• adherence/compliance/concordance with prescribed dose schedule (e.g. pill count, self-report) • change in patient management • clinical outcomes (e.g. BP in patients with hypertension, HbA1c in patients with diabetes) • adverse drug events/reactions and medication-related problems • mortality • health care resource use (ED attendance, hospitalisation, GP visits, specialist visits, pathology or other investigations) • patient acceptance/satisfaction • health-related quality of life • costs and cost-effectiveness
Study design	Comparative studies (randomised or non-randomised controlled trials, cohort studies, case control studies) or systematic reviews of comparative studies. Applicability to the Australian context will be considered.
Publication type	Full English-language publications or reports. Conference abstracts are excluded.
Search period	No year restrictions

Abbreviations: BP, blood pressure; CI, clinical intervention; ED, emergency department; GP, general practitioner; HBA_{1c}, glycated haemoglobin; QUM, quality use of medicines.

3.1.2 Search strategy

A comprehensive search of peer-reviewed scientific literature was conducted in September 2016 to identify studies that provide evidence relating to the effectiveness and cost-effectiveness of CIs or similar programs provided by pharmacists to individuals living in the community. Four electronic databases were searched for original research papers describing systematic reviews, meta-analyses, or comparative studies, as shown in Table 3.2. The Medline databases, Embase and International Pharmaceutical Abstracts were searched on 20th September 2016 and the Cochrane Library was searched on 22nd September 2016 and publication date was unrestricted. The specific search terms used to identify relevant literature are outlined in Appendix 3.

The Health Systems Evidence database (McMaster Health Forum) and databases maintained by Health Technology Assessment (HTA) agencies[2] were also searched to identify relevant literature. In addition, the reference lists of relevant systematic reviews, selected narrative reviews, primary articles and reports were examined to identify studies not otherwise found in the literature searches.

A search of pharmacy organisations[3] and the grey literature was also performed to identify previous evaluations of the CI initiative in Australia, and similar community pharmacist-led programs from other jurisdictions.

Table 3.2 Databases searched

Database	Search period
Embase via Ovid	Up to 20 September 2016
Medline via Ovid (1946 to September, Week 1, 2016; Daily update; Most Recently Published; Epub Ahead of Print September 19, 2016)	Up to 20 September 2016
International Pharmaceutical Abstracts via Ovid	Up to 20 September 2016
The Cochrane Library (includes Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, Cochrane Central Register of Controlled Trials, NHS Economic Evaluation Database, Health Technology Assessment, Cochrane Methodology Register)	Up to 22 September 2016
Health Systems Evidence	Up to 22 September 2016
HTA websites and databases	Up to 22 September 2016

3.1.3 Selection of relevant evidence

The literature search outlined above identified 1937 records (1184 unique citations), a further three citations were identified by hand searching reference lists of other studies, and five records were identified in targeted website searches and the grey literature. The following exclusion criteria were applied:

- Wrong publication or study type– excludes narrative reviews, conference abstracts and editorials, and non-comparative studies (i.e. single arm, observational studies)
- Wrong population – excludes pharmacists practicing in pharmacies other than community pharmacies (i.e. in clinic or hospital pharmacies)
- Wrong intervention – excludes studies of interventions that do not align with CIs as described in Section 3.1.1 (e.g. structured medication reviews, services exceeding 15 minutes duration, specific interventions or programs requiring protocol training)
- Wrong comparator – excludes studies that do not include a comparator group of delivery of services without the CI
- Wrong outcomes – excludes studies that do not assess one of the outcomes outlined in Section 3.1.1
- Not in English – excludes studies not published in English language or those that do not include at least some information (e.g. a summary) in English

The exclusion of citations from the searches is presented in Table 3.3.

[2] Agency for Healthcare Research and Quality (AHRQ) at AHRQ; Canadian Agency for Drugs and Technologies in Health (CADTH) at CADTH Reports; National Institute for Health and Care Excellence (NICE) at NICE, UK

[3] Including Pharmacy Guild of Australia; Pharmaceutical Society of Australia; and Australian Association of Consultant Pharmacy.

Table 3.3 Summary of the process used to identify relevant studies and reports

Description	Embase, Medline, International Pharmaceutical Abstracts, Cochrane Library	Health System Evidence	Hand searched references	Targeted websites and grey literature
Records retrieved	1887	50	3	5
Total number of citations	1945			
Duplicates within and across sets removed	753			
Total number of citations screened	1192			
Excluded at title/abstract review: Wrong publication type Wrong population Wrong intervention Wrong comparator Wrong outcome Not English *Total citations excluded at title/abstract review*:	 340 198 496 0 33 9 1076			
Citations screened at full text review	116			
Excluded at full text review: Wrong publication type Wrong population Wrong intervention Wrong comparator Wrong outcome *Total citations excluded at full text review:*	 5 6 97 0 0 *108*			
Total included studies or reports	**8**			
Included citations from database searches	*3*			
Total included CPA reports	*4*			
Other included citations from grey literature searches	*1*			

Abbreviations: CPA, Community Pharmacy Agreement.

The systematic literature search of the databases identified three relevant studies. Two studies are a pair of publications reporting on an Australian randomised controlled trial (RCT) comparing CI rates after providing pharmacist education and/or remuneration (or neither) for these services, and exploring the potential impact of these CIs in terms of clinical significance (Benrimoj et al, 2003a and 2003b). The same group has also published an economic impact analysis based on the same RCT (Benrimoj et al, 2000). The citations are provided in Table 3.4.

Of the 116 records reviewed at full text, 50 were systematic reviews, meta-analyses or overviews of systematic reviews. Of these, examination of the study inclusion criteria revealed that nine systematic reviews did not include studies of relevance to the current Review, and these were excluded. Of the remaining 41 systematic reviews, all included some studies that were out of scope of the current Review, and so were excluded during screening. However, the studies included in these systematic reviews were screened for potential inclusion in the current Review. In addition, the three identified overviews of systematic reviews were also checked for relevant systematic reviews not identified in the database searches, and the included studies within these reviews were, in turn, checked for eligible studies. (Members of the Working Group for the evaluation of the

medication adherence PPI Programs in Appendix 4 lists the systematic reviews checked for eligible included studies.) Searching within systematic reviews identified only one relevant study – the Australian RCT mentioned above (Benrimoj et al, 2003a).

The targeted search of the websites of relevant pharmacy organisations and the Commonwealth Department of Health identified three CPA-funded CI projects undertaken by Peterson and colleagues: PROMISe I reported in 2004; PROMISe II reported in 2007; and PROMISe III reported in 2009. The citations are provided in Table 3.4. The most recent of these reports included a (non-systematic) review of the international literature relating to CIs conducted in community pharmacies. A total of 25 studies were included in the report; with the exception of Benrimoj et al (2003), none of these studies met the selection criteria in Table 3.1. Most of the included studies were observational in nature, with DRPs and their resolution being reported, but without a control group.

The targeted search of the websites of relevant pharmacy organisations and the Commonwealth Department of Health also identified one GuildCare report on the CI initiative, and one previous evaluation of the CI initiative funded under the 5CPA. The citations are provided in Table 3.4.

Section 3.2 provides a summary of the findings of the Australian CI projects and evaluations.

Table 3.4 Citation details for projects and evaluations funded under a CPA

Study ID	Citation
Benrimoj (2003a)	Benrimoj SI, Langford JH, Berry G, Collins D, Lauchlan R, Stewart K, et al. (2003a). Clinical intervention rates in community pharmacy: a randomised trial of the effect of education and a professional allowance. Int J Pharm Pract; 11:71-80.
Benrimoj (2003b)	Benrimoj SI, Langford JH, Berry G, Collins D, Lauchlan R, Stewart K, et al. (2003b). Clinical significance of clinical interventions in community pharmacy: a randomised trial of the effect of education and a professional allowance. Int J Pharm Pract; 11:81-7.
Benrimoj (2000)	Benrimoj SI, Langford JH, Berry G, Collins D, Lauchlan R, Stewart K, et al. (2000). Economic impact of increased clinical intervention rates in community pharmacy. Pharmacoeconomics 2000; 18:459-68.
Peterson (2004)	Peterson G, Tenni P, et al. (2004). Community Pharmacy Medication Incident Reporting and Management Systems (CPMIRMS) also known as PROMISe: Pharmacy Recording of Medication Incidents and Services electronic documentation system: Final Report 2004 available at http://6cpa.com.au/resources/third-agreement/community-pharmacy-medication-incident-and-reporting-management-system-cpmirms-promise/
Peterson (2007)	Peterson G, Tenni P, et al. (2007). Evaluation of clinical interventions within community pharmacy: PROMISe II. Final Report available at http://guild.org.au/docs/default-source/public-documents/services-and-programs/research-and-development/Third-Agreement-R-and-D/2003-519/final-report.pdf?sfvrsn=0
Peterson (2009)	Peterson G, Tenni P, Jackson S, Bereznicki L, Hughes J, et al. (2009). Documenting clinical interventions in community pharmacy: PROMISe III. Final Report available at http://6cpa.com.au/wp-content/uploads/Documenting-Clinical-Interventions-in-Community-Pharmacy-PROMISe-III-Final-Report-.pdf
Ortiz (2012)	Ortiz M, Cecere R, Gallagher R (2012). Pharmacy practice incentives increase clinical interventions in community pharmacies: the first seven months of the 5CPA stimulus. Australian Pharmacist, 31: 581-584.
PwC (2015)	PricewaterhouseCoopers (2015). Combined Review of Fifth Community Pharmacy Agreement Medication Management Programmes (Final Report). Retrieved from https://www.health.gov.au/internet/main/publishing.nsf/Content/6EF022DE87761986CA257EC80013198B/$File/combined-review-5cpa-medication-management-programmes-final-report-and-appendices.pdf

Abbreviations: CPA, Community Pharmacy Agreement; PwC, PricewaterhouseCoopers.

By agreement with the Department, as all identified studies (even those published in the peer reviewed literature) were funded by the Department, either directly or under 3CPA, 4CPA or 5CPA,

the findings are reported in Chapter 4, under previous work conducted to design and evaluate the CI program. As mentioned, only the Benrimoj et al (2003) study met the selection criteria, and this study was a key input into the initial CI program design.

3.1.4 Limitations of the search strategy

The primary challenge of identifying studies of pharmacists' CIs that resemble those provided by Australian pharmacists under the PPI Program is the lack of a widely accepted term for the intervention, risking the sensitivity of any literature search. Furthermore, many studies refer to other professional pharmacy services as a CI, when in the Australian context such interventions fall outside the PPI Program definition of a CI (e.g. HMR, MedsCheck or DAA interventions). The specificity of the literature search undertaken for this Review was substantially reduced by this lack of specificity in the search terms, with most studies excluded due to the CI in question being more similar to other professional pharmacy services or focused programs (e.g. asthma medication optimisation and adherence programs) than a CI in the PPI Program setting.

The original search strategy reviewed by the Working Group included terms for adverse outcomes, such as DRP and adverse drug reaction, as well as terms relating to the intervention. The approved search was executed and the records were investigated, but this search was found to be too insensitive and non-specific, generating a large number of records while failing to identify relevant studies or systematic reviews. Consequently, the search strings were developed further to improve both sensitivity and specificity.

The search strings for the final search focused more on terms to capture pharmacist CIs, broadening the scope of terms to capture references to non-dispensing roles, pharmaceutical care and prescription review. Searched fields were narrowed to title or keywords only, as searching abstracts and other fields increased the record yield and decreased the specificity considerably, and it seemed highly likely that relevant studies would refer in some way to the intervention in at least one of these fields.

CIs, as defined in the PSA standard and guidelines for pharmacists (PSA, 2011), includes patient education. However, as explained in Section 2.4, reimbursement is not available for this aspect of CI services. Nonetheless, the literature search included an exploded term for patient education. This approach was an attempt to capture any potentially relevant studies of any CIs, with the intention of determining the applicability of the study during the screening process.

In order to supplement the process of direct screening for relevant studies, the search string was augmented with a very broad search for any records with pharmacy terms in the title, in combination with a simple search string for systematic reviews (or RCTs). The consequent inclusion of a large number of systematic reviews provided an additional avenue of study identification as all included studies in each of these reviews were screened.

Despite this approach, only the three studies known to be eligible prior to the search were identified in this systematic review of the literature databases (Benrimoj et al, 2000; Benrimoj et al, 2003a and 2003b), and only one of the 63 systematic reviews (Patwardan et al, 2014) included one of the Benrimoj publications.

In light of the lack of evidence identified by this extensive and focused search, it would appear that no additional eligible studies have been published other than those known to have been published prior to the search. Due to the nature of the CI under investigation in this Review, being practiced by pharmacists as part of their typical service delivery, all other studies of community pharmacist interventions were excluded on the basis of being too involved (i.e. specific protocols with regular

patient follow up), too specified (i.e. requiring training for particular populations) or taking too long (i.e. over 15 minutes) and, in fact, most intervention exclusions failed on all three of these criteria.

Given the limitations in conducting a systematic literature review for an intervention of this nature, it is not possible to assert with absolute confidence that a potentially relevant study has not been missed. However, a lack of empirical research evaluating the clinical and economic value of CIs performed within the community pharmacy setting is not unexpected given that the intervention is already part of standard practice in some countries (such as Australia) where pharmacists have a professional obligation to check for potential DRPs and intervene to prevent them. This introduces difficulties in conducting a study with a suitable comparator when assessing the potential outcomes of CIs.

3.2 CI utilisation analysis

Utilisation was calculated from the CI claims payment data made by individual pharmacy, covering claims paid on dates between 5th January, 2012 and 26th May, 2016.

In the absence of knowing what patient groups are receiving CI services or the types of CIs that are being provided to different patient groups, CI claims payment data for 2015 have been analysed in the context of geographical factors that have been inferred from the postcode of each pharmacy. Those factors included are remoteness[4] and chronic disease prevalence by Primary Health Network (PHN) geographic areas. These factors were used to assess whether the growth in CI services has any relationship to the included populations.

The claims payments administration system changed in March 2014. Before the change, payments to pharmacies were annotated with the 'Pharmacy ASN' identifier. After the change claims payments were annotated using the 'Organisation Number' identifier. Both identifying codes are used in Section 90 registers to identify individual pharmacies. These codes were used to assist in locating each pharmacy within its postcode.

Postcodes were mapped to remoteness using the Australian Bureau of Statistics (ABS) mapping table and to PHAs and PHN areas via Statistical Areas Level 2 (SA2), ABS Australian Statistical Geography Standard (ABS ASGS) 2011.

Key metrics in the analysis are limited to claims paid and the number of patients receiving CIs in the claim period (these metrics are recorded in the claims payment administration systems pre and post the system change). Claims paid and the volumes of patients receiving CIs are not closely related since the payment formula relates to volume at the level of individual pharmacies, as well as overall.

[4] ABS postcode to remoteness.xls available from http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1270.0.55.006July%202011?OpenDocument (accessed 5th October, 2016)

4 PREVIOUS DEPARTMENT-FUNDED WORK ON THE DESIGN AND EVALUATION OF THE PPI PROGRAM

This Section summarises the findings of the pilot, and 3CPA and 4CPA projects that preceded subsidised funding of CI services by community pharmacies, as well as an evaluation of the CI initiative funded by the Commonwealth under the 5CPA. The intention of these summaries is to provide MSAC with an understanding of the approaches taken to develop the CI initiative in Australia, as well as a high level overview of the findings of previous evaluations in relation to effectiveness and cost-effectiveness of the service.

4.1 Study of remuneration for CIs, 1996, published 2003

In 2003, Benrimoj and co-authors published the results from a RCT that examined the effect of providing fee-for-service professional remuneration and education on the rates and clinical significance of CIs (Benrimoj 2003a, 2003b). The trial, which was conducted during November and December 1996, was funded by the Commonwealth Department of Human Services and Health. Pharmacists from 30 community pharmacies in New South Wales were randomly allocated to one of the following three groups: Group A pharmacies served as a control group and received neither education nor remuneration; Group B received education and professional remuneration; and Group D received professional remuneration with no education. Pharmacists in the fourth group (Group C; n=10) were selected from the 30 pharmacies containing pharmacists known to have previously attended a minimum of six weekends of professional education over a two-year period, and now received advanced education and professional remuneration. The professional fee-for-service was $10 per intervention.

Pharmacists documented CIs for a one-week baseline period, and for a further two weeks with a one week break between recordings following the educational component and remuneration intervention. The methods of documenting and quantifying CI rates in community pharmacies were based on those developed and tested in a 1996 pilot study by Caleo et al (1996). Interventions were categorised as ‘reactive’ or ‘proactive’ by a panel comprising a community pharmacist and a hospital pharmacist. ‘Proactive’ interventions were defined as those where dispensing could have occurred without further consultation with the patient or the medical practitioner but for which the pharmacist identified a clinical problem and intervened, resulting in a change to the patient’s regimen intended to optimise therapy and/or minimise the risk of adverse effects (e.g. incorrect dosage and drug/drug interactions). ‘Reactive’ interventions were defined as those where dispensing could not have occurred without further consultation with the prescriber (e.g. where the strength of a medication had been omitted from the prescription). Reactive interventions were predominantly related to errors or omissions in required information on the prescription and would not usually be regarded as clinical in nature. The CI rate was defined as the number of CIs/number of PBS prescription items dispensed.

The study reported a total of 762 CIs resulting from 87,130 prescriptions (CI rate of 0.87%) during the study period (see Table 4.1). Of the total, 375 (0.43%) were proactive and 387 (0.44%) were reactive. Of note, there were significant differences amongst the four pharmacy groups in terms of proactive intervention frequency at baseline, which were considered in subsequent statistical analyses. Over the study period, Group D had statistically significant reductions from baseline in both proactive and reactive intervention rates (P =0.02 and P =0.04, respectively). In the control group, there was a decrease over time in the proportion of reactive and proactive interventions but only the reactive interventions achieved statistical significance (P =0.02). There were no significant differences between Group D and the control group. On the other hand, Groups B and C (the groups

that had educational and remuneration programs provided) showed increases in CI rates (both proactive and reactive) immediately after the educational intervention (during Week 1), but these rates decreased to near baseline levels at Week 2.

Table 4.1 Interventions documented in community pharmacies at three time points

Pharmacy group	Time (week)	Prescriptions (n)	Number of proactive CIs (rate %)	Number of reactive CIs (rate %)	Total number of CIs (%)
Group A: Control group, no education or remuneration	0 (baseline)	7,847	16 (0.20%)	38 (0.48%	54 (0.68%)
	1	7,293	16 (0.22)	18 (0.25%)	34 (0.47%)
	2	8,545	12 (0.14%)	13 (0.15%)	25 (0.29%)
Group B: Remuneration plus basic education	0 (baseline)	5,061	24 (0.47%)	36 (0.71%)	60 (1.19%)
	1	5,216	35 (0.67%)	50 (0.96%)	85 (1.63%)
	2	7,438	21 (0.28%)	39 (0.52%)	60 (0.80%)
Group C: Remuneration plus advanced education	0 (baseline)	6,894	57 (0.83%)	51 (0.74%)	108 (1.57%)
	1	6,717	84 (1.25%)	48 (0.71%)	132 (1.96%)
	2	7,543	57 (0.76%)	53 (0.70%)	110 (1.46%)
Group D: Remuneration without education	0 (baseline)	7,574	24 (0.32%)	21 (0.28%)	45 (0.59%)
	1	8,119	20 (0.25%)	15 (0.18%)	35 (0.43%)
	2	8,883	9 (0.10%)	5 (0.06%)	14 (0.16%)
Total	-	**87,130**	**375 (0.43%)**	**387 (0.44)**	**762 (0.87%)**

Source: Benrimoj (2003a), Table 1, p. 74
Abbreviations: CIs, Clinical Interventions

In the same RCT, Benrimoj et al (2003b) assessed the clinical significance of clinical interventions undertaken by community pharmacists. A validated method was developed by an expert panel to assess the clinical significance of proactive CIs. Analysis of consensus revealed that 52% (196/375) of proactive CIs were deemed to be clinically significant and 2% (9/375) were deemed to be either clinically very significant or potentially life-saving. However, 22% (81/375) of proactive interventions were deemed to be not applicable for assessment, although the reasons for this were not reported in the publication. The authors reported that if these figures were extrapolated to national Australian prescribing figures (1995/1996 financial year), a mean of 3,752 potentially life-saving interventions by community pharmacists could be expected per year (95% CI 454 to 13,554).

Assessment of the clinical significance of CIs showed that there was no significant difference between levels of clinical significance of interventions undertaken by the four study groups ($P < 0.05$). When considering the clinical significance of proactive interventions undertaken before and after the study intervention, pharmacists in Groups B and C (i.e. those groups receiving the educational intervention) showed an increased proportion of interventions rated as significant, very significant or potentially life-saving after the study intervention; however, this increase was not statistically significant. The opposite trend was observed in Groups A and D, where the proportion of such interventions decreased over time.

The authors concluded that payment of a fee-for-service remuneration alone is unlikely to change community pharmacists' practice in relation to CIs. Although provision of a specific educational program together with a fee-for-service remuneration led to a short-term increase in intervention

rates, there are concerns relating to the sustainability of any impact of education on CI rates. A major limitation of this trial was the presence of inter-group variability, which was attributed to the lower rates of CIs at baseline. The reasons for the difference in CI rates between individual pharmacists at baseline were not known. The authors speculated that the clinical knowledge shared by pharmacists in Group C may have contributed to the high baseline proactive CI rate in this group; however, no attempts were made by the authors to actively identify factors that may predispose towards CIs.

4.2 Study on economic impact of CI remuneration, 2000

An analysis of the economic impact of CI remuneration was published by Benrimoj et al (2000). It drew on the same RCT conducted during November and December 1996, which was the subject of the Benrimoj 2003a, 2003b papers. Only the proactive interventions were included in the analysis as the authors considered reactive interventions to have been necessary for a prescription to be dispensed rather than to alter health outcomes.

The analysis was based on savings attributable to healthcare costs avoided (based on a five-member clinical panel's opinion on the probable course of treatment and the probability that the intervention would prevent an adverse outcome), healthcare costs incurred by the pharmacists' actions (including referrals to a GP or emergency department), changes in medication costs (calculated as a 'once-only' cost or saving based on 1997 PBS figures, not extrapolated to long term therapy), pharmacy time (minutes spent on the intervention multiplied by the appropriate wage rate) and telephone calls made by the pharmacist. Proactive interventions were costed by summing these individual components.

Table 4.2 shows the proactive CI savings assessed at baseline and after implementation of the educational and remuneration strategies. The proactive CIs in Group D incurred an additional cost of $1.18 per 1000 prescriptions after the introduction of the remuneration fee. However, pharmacies in Group C achieved savings of $85.35 per 1000 prescriptions, which was nearly four times greater than savings generated by pharmacies in Group B and six times greater than control (Group A) pharmacies.

Table 4.2 Proactive CIs costs/savings per 1000 prescriptions assessed before and after education/ remuneration interventions

Pharmacy groups	Randomised arm	Mean costs/saving per 1,000 prescriptions	Net change[a]
Group A: Control group, no education or remuneration	Baseline	$6.29	-$20.08
	Post-intervention	-$13.78	
Group B: Remuneration plus basic education	Baseline	-$6.43	-$19.22
	Post-intervention	-$25.65	
Group C: Remuneration plus advanced education	Baseline	$3.55	-$88.89
	Post-intervention	-$85.35	
Group D: Remuneration without education	Baseline	-$162.95	$164.13
	Post-intervention	$1.18	

Source: Benrimoj et al (2000), Table I, p. 462
Abbreviations: CIs, Clinical Interventions.
a Difference between the baseline and post-intervention savings for each group.

Table 4.3 shows the net savings calculated in the 375 proactive CIs reported by the four groups of pharmacies. There was a wide variation in the mean baseline value of a proactive intervention, ranging from a saving of $51.42 in Group D to a cost incurred of $3.09 in the control group (Group A). Further, there were significant changes in the estimates after the education and remuneration components of the study were introduced, including in the control group. The authors estimated that Group D pharmacies increased costs after the intervention, whereas there was an increase in savings in Groups B, C and the control group.

Table 4.3 Component costs/savings ($) per proactive CI

Pharmacy groups	Study period	Healthcare costs avoided[a]	Healthcare costs incurred[b]	Changes in medication costs[c]	Pharmacy time[d]	Phone calls[e]	Mean total	Net change[f]
Group A: Control	Baseline	-$4.96	$6.22	-$1.33	$2.63	$0.53	$3.09	$10.89
	Post-intervention	-$12.01	$1.19	$0.09	$2.46	$0.47	-$7.80	
Group B: Fee plus basic education	Baseline	-$4.11	$1.38	-$1.37	$2.27	$0.47	-$1.36	$4.39
	Post-intervention	-$13.43	$3.97	$0.98	$2.28	$0.45	-$5.75	
Group C: Fee plus advanced education	Baseline	-$4.88	$2.91	-$0.24	$2.24	$0.44	$0.47	$9.12
	Post-intervention	-$13.76	$3.53	-$0.92	$2.04	$0.46	-$8.65	
Group D: Fee without education	Baseline	-$61.14	$6.91	-$0.28	$2.62	$0.47	-$51.42	-$52.12
	Post-intervention	-$3.19	$1.14	$0.01	$2.28	$0.46	$0.70	

Source: Benrimoj et al (2000), Table III, p. 464
Abbreviations: CIs, Clinical Interventions.
Note: The cost of training and the professional fee of $10 per intervention were formally excluded in the costing analyses.
a Avoided costs were based on a five-member clinical panel's opinion on the probable course of treatment and the probability that the intervention would prevent an adverse outcome.
b Incurred costs included referral for an urgent visit to the GP or ED.
c Changes in medication costs were calculated using the 'dispensed prices' from the PBS, February 1997. These changes were calculated as a 'once-only' cost or saving and were not extrapolated to long term therapy.
d Pharmacy time was calculated by the number of minutes spent on the intervention multiplied by the appropriate wage rate.
e Calculated by multiplying the number of telephone calls by the unit cost of the call.
f Difference between the baseline and post-intervention savings for each group.

Table 4.4 shows the healthcare costs/savings with proactive CIs per 1000 prescriptions. This analysis takes into account the volume of interventions undertaken by each group of pharmacists. At baseline, the healthcare costs avoided per 1000 prescriptions was $193.74 in Group D (remuneration without education) compared to $10.12 in the control group. This substantially decreased by 35-fold in Group D post intervention (saving of $5.45). However, Groups B and C (where education was provided to pharmacists) would have the greatest impact on healthcare costs with savings of $59.45 and $136.01 per 1000 prescriptions, respectively.

Table 4.4 Healthcare costs avoided with the proactive CIs per 1000 prescriptions

Pharmacy groups	Randomised arm	Mean costs avoided per 1000 prescriptions	Net change[a]
Group A: Control group, no education or remuneration	Baseline	-$10.12	$11.11
	Post-intervention	-$21.23	

Pharmacy groups	Randomised arm	Mean costs avoided per 1000 prescriptions	Net change[a]
Group B: Remuneration plus basic education	Baseline	-$19.47	$39.989
	Post-intervention	-$59.45	
Group C: Remuneration plus advanced education	Baseline	-$40.36	$95.65
	Post-intervention	-$136.01	
Group D: Remuneration without education	Baseline	-$193.74	-$188.29
	Post-intervention	-$5.45	

Source: Benrimoj et al (2000), Table IV, p. 465
Abbreviations: CIs, Clinical Interventions
a Difference between the baseline and post-intervention savings for each group.

4.3 3CPA and 4CPA PROMISe trials, 2004-2009

The Pharmacy Recording of Medication Incidents and Services electronically (PROMISe) projects were funded under 3CPA and 4CPA. The overall aim of the most recent of these studies, PROMISe III, was to establish the viability of, and requirements for, national implementation of an electronic documentation system for the recording of clinical interventions identified in community pharmacies. PROMISe III borrows and expands on two previous PROMISe studies – PROMISe I and PROMISe II – undertaken in 2004 and 2005, respectively, by the same research group.

The PROMISe I pilot study was conducted predominantly to develop the DOCUMENT DRP classification system (described in Section 2.4). The pilot study demonstrated that the DOCUMENT classification system could adequately record and transfer information relating to CIs from a pharmacy interface to a central repository. There were a small number of pharmacists involved (n=14), and a total of 352 CIs were undertaken with 9,012 prescriptions (CI rate of 3.9%). Approximately one-third of the CIs documented were related to patient education and counselling about disease or medication management, and 20% of CIs were considered 'non-clinical'. Both of these documented CIs were related to nil, mild or low significance. Approximately one-third of CIs were classified as either moderately or highly significant.

The PROMISe II project used the DOCUMENT system in a wider sample of pharmacies and estimated the economic value of the CIs undertaken. The frequency of CI was reported to be 0.55 CIs per 100 prescriptions. The majority of documented CIs belonged to one of three categories: drug selection problems (22.7%), dosage problems (19.4%), or education problems (17.4%). Almost one-third of CIs were classified as either moderate or severe level of clinical significance. The report claimed that the value of Australian community pharmacists CIs related to prescription medication is in the order of $200 million each year in direct costs avoided. In addition, it was claimed that 170,000 hospitalisations are avoided and 25 million days of adverse health impact are avoided each year.

The PROMISe III project consisted of four phases:

- Phase 1 consisted of a review of the available software used to record CIs. Focus groups were conducted with key stakeholders to determine the requirements for an intervention documentation system.
- Phase 2 examined three levels of the PROMISe software over a 12-week period. It involved a representative sample of 210 community pharmacies from across Tasmania, Victoria and New South Wales. Results were compared to a group of pharmacies that did not have the PROMISe software (this control group also provided baseline data). Findings from Phase 2 were then used in the economic analysis and business case modelling performed in Phases 3 and 4. The

frequency and type of CIs captured in the PROMISe III trial and the GuildCare Pharmacy CIs program are presented in Section 4.3.1.

- Phase 3 involved evaluation of the PROMISe trial. The frequency, type and determinants of CIs were evaluated and an economic analysis was performed using a sample of 200 CIs. This included determining the average economic value of CIs at each of four levels of clinical significance (S1, S2, S3, and S4), and conducting a cost-utility analysis (CUA). Results of the health resource utilisation and quality of life (QoL) changes by CIs are presented in Section 4.3.2.
- Phase 4 involved the construction of a business case and implementation plan for a national rollout of an electronic documentation system for recording CIs in community pharmacies. Five remuneration options and an additional phased implementation model were developed and assessed.

4.3.1 Documentation of the nature of CIs

The PROMISe III study (Petersen et al, 2009) examined the number and nature of DRPs detected and CIs performed, over a three-month period in a sample of 210 Australian community pharmacies using DOCUMENT. It included 531 participating pharmacists that recorded 6,230 CIs from 2,013,923 prescriptions for 486,147 patients. The overall rate of prescription-related documented CI across the three months was 3.1 CIs per 1000 prescriptions.

However, this included CIs documented using the Monitoring, Education, and Non-classifiable (MEN) interventions, which do not attract incentive payments but represented 28% of CIs documented. Exclusion of the MEN documented CIs results in 2.2 CIs per 1000 prescriptions. The most common interventions were related to drug selection problems (31%) and educational issues prompted by patient requests (24%). Multiple recommendations were common, with pharmacists making an average of 1.6 recommendations for each intervention. Referral to the prescriber and an education or a counselling session accounted for over 70% of the recommendations made by pharmacists. Change in therapy was reported as the most common type of recommendation (40%), followed by provision of information (34%). Drug groups most commonly subject to an intervention included antibiotics, glucocorticoids, nonsteroidal anti-inflammatory drugs, and opioids.

4.3.2 Economic analysis

The PROMISe III study provided an estimate of expected improvement in patients' QoL and reduced healthcare expenditure, both by patients and by the Government, as a result of the CIs performed by community pharmacists. The economic evaluation undertaken involved a number of steps listed below:

- The clinical consequences that are likely to be avoided or caused by CIs in community pharmacies were determined.
- Health resource utilisation (HRU) of each clinical consequence were estimated using the available literature or consultation with expert panels. These included the number and cost of GP and specialist visits, cost of additional investigations, the duration and costs of any hospital admissions, and the impact on QoL. The expert panels consisted of 14 GPs and five consultant physicians.
- A sample of 200 suitable CIs were selected for assessment by an expert panel consisting of five specialists, nine pharmacists and 10 GPs. The selected CI sample was assessed to determine which clinical consequences were likely to occur, the probability of each identified clinical consequence with and without the CI, and the likelihood that the pharmacist would have been the only health professional to detect the DRP and intervene. The expert estimates of probability

and the attribution to the pharmacist were combined to determine an attributed change in probability.

- The attributed change in probability and the associated values for each consequence were combined to determine the economic impact of each intervention in terms of utility and HRU.
- The change in medication costs (based on PBS costs) were added for each intervention and the cost of performing CIs (based on the pharmacists' time in screening prescriptions and performing interventions) was calculated to determine the average economic value of documented CIs at each of four levels of clinical significance.
- A CUA was conducted to determine the average cost utility of interventions, and was extrapolated to the Australian perspective. A second CUA was performed in order to determine the incremental cost utility of avoided CIs performed in PROMISe that would otherwise not have been performed in current practice.

Based on the observed frequency of interventions collected during Phase 2 of the PROMISe III study, 20% of CIs were classified as S1 interventions[5], 40% were classified as S2 interventions[6], 34% were classified as S3 interventions[7], and 5% were classified as S4 interventions[8]. The average values that resulted from the economic evaluation are shown in Table 4.5 for each of the four levels of clinical significance (S1, S2, S3, and S4). The results showed a significant incremental benefit of the PROMISe program above that of current practice in terms of cost savings from healthcare utilisation avoided. As shown, the majority of the avoided healthcare utilisation was from approximately 260,000 avoided days in hospital, and almost two million avoided visits to GPs and specialists. The authors noted that these estimates were based on 100% uptake of the CI program by all pharmacies in Australia, and do not include the costs for implementing the program.

Table 4.5 Health resource utilisation and QoL changed by CIs, by clinical significance classifications

Parameter	S1	S2	S3	S4
QALY (days)	0.009 (3.28)	0.0077 (2.80)	0.0113 (4.12)	0.020 (7.29)
Number of GP visits	1.3103	1.1554	1.7468	2.4479
Cost of GP visits	-$43.96	-$38.76	-$58.60	-$82.13
Number of specialist visits	0.2987	0.3278	0.4590	0.9390
Cost of specialist visits	-$16.71	-$18.61	-$26.26	-$50.21
Cost of investigations	-$23.91	-$38.67	-$36.99	-$68.21
Duration of hospital admissions	0.1382	0.2412	0.2683	0.6060
Cost of hospital admissions	-$137.57	-$224.35	-$274.17	-$555.00
Cost of medications	-$9.04	$15.93	-$58.95	$24.46
Total health resource utilisation	**-$231.19**	**-$304.47**	**-$454.97**	**-$731.09**

Source: Peterson (2009), PROMISe III, Table 8-11, p.270
Abbreviations: CIs, Clinical Interventions; GP, general practitioner; QALY, quality-adjusted life year; QoL, quality of life.
Note: S1 refers to CIs with consequences to the patient related to costs or information only. S2 refers to CIs that prevented mild symptom or improved compliance. S3 refers to CIs that prevented or required a GP visit. S4 refers to CIs that prevented or required a hospital admission.

The PROMISe III study also captured the level of CIs occurring in community pharmacies but without documentation using the PROMISe software (i.e. CIs in current practice). Table 4.6 presents the difference in benefits and costs between current practice and the practice in PROMISe software pharmacies extrapolated to a year of activity across Australia.

[5] S1 – Consequence related to costs or information only.
[6] S2 – Prevented a mild symptom (that would not require a doctor's visit) or improved compliance.
[7] S3 – Prevented or required a GP visit.
[8] S4 – Prevented or required a hospital admission.

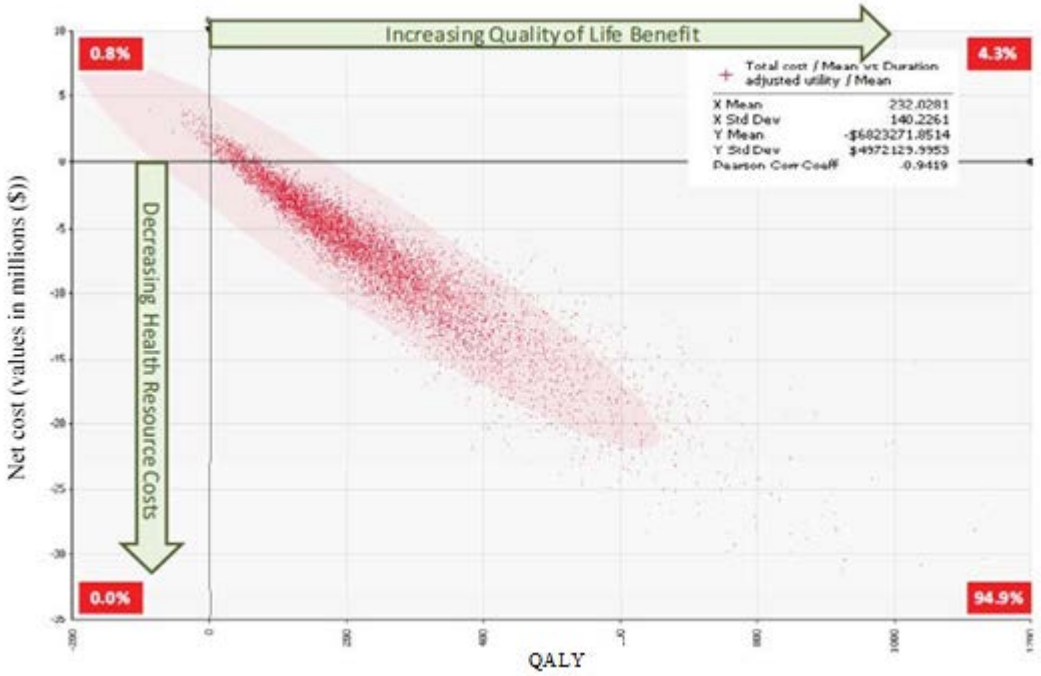
Table 4.6 Incremental benefit of PROMISe software extrapolated to a year of activity across Australia

Parameter	Current practice	PROMISe practice	Incremental difference
QALY	10404	20814	10410
Number of GP visits	1,542,766	3,087,717	1,544,952
Cost of GP visits	-$51.759,794	-$103,592,919	-$51,833,125
Number of specialist visits	423,997	845,292	412,295
Cost of specialist visits	-$23,916,420	-$47,684,619	-$23,768,199
Cost of investigations	-$39,640,435	-$77,747,909	-$38,107,474
Duration of hospital admissions	267,440	527,365	259,925
Cost of hospital admissions	-$258,310,961	-$511,196,761	-$252,885,799
Cost of medications	-$12,384,956	-$29,995,569	-$17,610,613
Total healthcare utilisation cost	-$386,012,566	-$770,217,777	-$384,205,211
Total cost to pharmacies	$47,883,135	$142,634,788	$94,751,653
Net cost	**-$338,129,431**	**-$627,582,989**	**-$289,453,557**

Source: Peterson (2009), PROMISe III, Table 8-11, p.270
Abbreviations: CIs, Clinical Interventions; GP, general practitioner; QALY, quality-adjusted life year; QoL, quality of life.

Figure 4.1 shows the cost-effectiveness plane for the incremental difference between PROMISe practice and current practice (per week of activity across Australia). The majority of re-samplings resulted in, on average, a 'dominant' finding, where the documented CI had a negative cost (that is, saved health resources) and a positive benefit (increased QoL). Approximately 94.9% resulted in the incremental benefit being dominant, with a further 4.3% positioned in the 'improves QoL yet costs money to implement' (north-east quadrant), although many of these are under the generally accepted threshold of $50,000 per QALY (98.9% of all outcomes were under the $50,000 cost per QALY threshold).

Figure 4.1 Cost-effectiveness plane for incremental difference between PROMISe practice and current practice (per week of activity across Australia)



Source: Peterson (2009), PROMISe III, Figure 8-10, p. 275
Abbreviations: QALY, quality-adjusted life year.

4.3.3 Limitations of the PROMISe methodology

A review article from Peterson and colleagues (published as Stafford et al, 2012) describes the issues and complexities involved in estimating the clinical and economic outcomes of CIs performed by community pharmacies. The article argues that it may be ethically questionable to conduct an RCT of CIs given that it is already part of standard practice in some countries (including Australia). The article acknowledges that expert opinion provides a relatively low level of evidence but may nonetheless be useful in the absence of studies that provide higher levels of evidence. The methodological framework used in the PROMISe studies is described, with reference to the shortcomings of previous studies that have used expert opinion to estimate the consequences of a patient not receiving the CI (i.e. counterfactual state).

Several limitations of the expert opinion approach are noted in the article. One limitation relates to the broad definition of each consequence and the values assigned to the parameters. It is assumed that a given consequence will result in the same level of disability and health resource utilisation in every patient, regardless of age and co-morbidities, which is a simplification of reality. A second limitation is that the methodology assumes total compliance with the outcomes of the CI for the intended duration of follow up, which will generate an over-estimate of the benefits resulting from the CI.

4.4 5CPA GuildCare study, 2012

The GuildCare study by Ortiz et al (2012) examined the number and nature of DRPs detected, and CIs performed, by Australian community pharmacists in the first seven months of the 5CPA incentives (July 2011 to January 2012). Approximately 230,000 GuildCare Program CIs (GPCIs) were documented in 2,571 enrolled pharmacies, with an average of 90 GPCIs per pharmacy. Table 4.7 shows the rates of GPCIs between July 2011 and January 2012.

Table 4.7 Number of GPCIs recorded by month, July 2011 – January 2012

Month	July	August	Sept	Oct	Nov	Dec	Jan	Total
CIs for the month	9,162	18,811	39,924	37,584	38,668	45,628	41,084	230,861
Active pharmacies	822	1,322	1,837	1,898	1,757	1,724	1,742	2,571
CIs/pharmacy	11.1	14.2	21.7	19.8	22.0	26.5	23.6	89.8
CIs/1000[a]	2.5	3.2	4.9	4.5	5.0	6.0	5.4	-

Source: Ortiz et al (2012), Table 1, p.583.
Abbreviations: CI, Clinical Interventions; GPCIs, GuildCare Pharmacy Clinical Interventions.
a Assumes 4,400 prescriptions per month per pharmacy.

Table 4.8 shows results when CI rates were adjusted based on the duration of program participation. When individual pharmacy activity was followed over time, GPCI rates increased with longer participation in the GuildCare Program, from around 9.8 CI/pharmacy (n=2,571) in their first month of participation to 35.1 per pharmacy (n=594) per month by the seventh month of participation. The CI rate increased from 2.2 per 1000 prescriptions in the first month to 8.0 per 1000 prescriptions in the seventh month.

Table 4.8 Change in GPCIs recorded over time

Month of participation	1	2	3	4	5	6	7
CIs/pharmacy/ month	9.8	18.4	24.1	23.1	23.9	30.3	35.1
CIs/pharmacy	2.2	4.2	5.5	5.2	5.4	6.9	8.0
Pharmacies included	2,571	1,936	1,786	1,660	1,477	1,077	594

Source: Ortiz et al (2012), Table 2, p.583.
Abbreviations: CI, Clinical Interventions; GPCIs, GuildCare Pharmacy Clinical Interventions.

All the GPCIs from the 2,571 pharmacies were divided into DOCUT categories. Table 4.9 shows that compliance was identified as the most frequent intervention in nearly 60% of the GPCIs, followed by drug selection and drug dose issues (17% and 13%, respectively).

Table 4.9 CIs by DOCUT classification system

Intervention category	Number	% of total
Drug selection	39,196	17.0%
Overdose/underdose	30,355	13.1%
Compliance	139,484	60.4%
Undertreated	11,804	5.1%
Toxicity	10,018	4.3%
Total	**230,861**	**100%**

Source: Ortiz et al (2012), Table 3, p.583.
Abbreviations: CIs, Clinical Interventions.
Note: DOCUT refers to Drug selection, Overdose/underdose, Compliance, Undertreated, and Toxicity.

A comparison between the GuildCare Program CIs and the CIs documented in the PROMISe III study is presented in Table 4.10.

Table 4.10 Comparison between PROMISe III and GuildCare

Intervention type	PROMISe III	GuildCare
Total DOCUT interventions	4,296	230,861
Participating pharmacies	210	2,571
Months (average)	3	5.5
CI/pharmacy/month	6.8	16.4
CI rate/1000 scripts	2.2[a]	5.5[b]

Source: Ortiz et al (2012), Table 3, p.583.
Abbreviations: CIs, Clinical Interventions.
Note: DOCUT refers to Drug selection, Overdose/underdose, Compliance, Undertreated, and Toxicity.
a Adjusted rate with the exclusion of MEN (Monitoring, Education, and Non-classifiable) CIs. PROMISe III 4,300 scripts/month/pharmacy.
b GuildCare 4,400 scripts/month/pharmacy for 3 months (November 2011-January 2012).

A comparison between the GuildCare Program CIs and the CIs documented in the PROMISe III study is presented in Table 4.11, by CI category. The type of GuildCare CIs differed significantly from those obtained in the PROMISe III study, especially for Compliance CIs (with 192% increase in the rates of CIs for Compliance). According to the authors, this substantial increase in Compliance CIs may be associated with the implementation of the Mirixa Australia compliance programs in 579 of the 2,571 participating community pharmacies.

Table 4.11 Comparison between PROMISe III and GuildCare by CI category

Intervention category	GuildCare (% of total)	PROMISe III (% of total)	GuildCare CI rate/ 1000 prescription[a]	PROMISe CI rate/ 1000 prescription	Rate difference
Drug selection	17.0%	42.8%	1.00	0.94	7%
Overdose/underdose	13.1%	27.6%	0.74	0.62	21%
Compliance	60.4%	13.0%	3.08	0.29	963%
Undertreated	5.1%	6.3%	0.41	0.14	192%

Intervention category	GuildCare (% of total)	PROMISe III (% of total)	GuildCare CI rate/ 1000 prescription[a]	PROMISe CI rate/ 1000 prescription	Rate difference
Toxicity	4.3%	10.4%	0.27	0.23	19%

Source: Ortiz et al (2012), Table 5, p.583.
Abbreviations: CIs, Clinical Interventions.
Note: DOCUT refers to Drug selection, Overdose/underdose, Compliance, Undertreated, and Toxicity.
a November 2011 to January 2012

The authors identified the lack of information about the number of prescriptions dispensed in each GuildCare pharmacy as a limitation in the study analysis. The intervention rates were calculated using a single monthly average prescription number and this may not reflect the dispensing rates of the active pharmacies over several months. Further, the occurrence of the CI or its categorisation as reported by the pharmacist was not validated.

4.5 5CPA Program Combined Review by PricewaterhouseCoopers, 2015

The CI program was evaluated as part of the Review of the PPI Program performed by PwC in 2015. The overall aim of the Review was to better inform how the 5CPA Medication Management programs and services (including PPI Program and MM Program) contribute to improving consumer health outcomes, in order to better inform future investment by the Australian Government in pharmacy programs and services. PwC evaluated the three priority areas in the PPI Program: CIs, DAAs and SS. The Review methodology involved an analysis of full program data in order to assess the uptake and volume of services delivered over the duration of the 5CPA (between 2011 and 2014), stakeholder consultations, consumer focus groups, practitioner focus groups, a practitioner survey and a consumer survey.

Table 4.12 summarises the main findings of the evaluation in relation to the CI initiative. A total of 767 primary health care practitioners, with the majority being pharmacists (94%), responded to the practitioner survey. More than half (60%) were involved in CIs. Results of consumer surveys are not discussed as none of the responders received a CI service, and thus results from the consumer surveys do not reflect consumers' satisfaction with CI services.

Table 4.12 Main findings of the 2015 5CPA combined review, 2011-2014

Measure/domain	Key findings
Program results	
PPI participating pharmacies	Overall, a total of 6,216 pharmacies (with unique registration numbers) submitted claims for PPI services
CI participating pharmacies and services	55,970 pharmacies submitted claims for 6,729,876 CI services
Total expenditure on PPI Program	$126,507,909
Total expenditure on CI initiative	$44,051,451 (35% of total funds allocated)
Practitioner focus group themes raised	
Addressing consumer need	The majority of participants commented that CIs, aside from being a screening tool, were not hugely valuable and presented more of an administrative burden compared to the financial and consumer benefits they bring.
Eligibility criteria and targeting	There were no specific marketing strategies or recruitment activities directed at those most in need of the 5CPA programs.

Measure/domain	Key findings
Program implementation	A multidisciplinary, collaborative approach to programs/services would aid in the implementation of the programs and benefit the impacts and outcomes for consumers. It was also suggested that funding should be allocated to support implementation to prevent inconsistencies in the way that programs are delivered.
Policy and strategy	Participants agreed that generally the 5CPA programs/services added value and should be part of the overall preventative strategy for consumers.
Practitioners/providers survey results	
Interaction between programs	Less than half (42%) of total survey respondents agreed or strongly agreed that the linkages/pathways between the programs/services were clearly identified. More than half (60%) agreed that there were gaps in the services provided, resulting in unmet needs of the consumer.
Factors influencing CIs decision making	The majority of providers agreed that the consumer needs assistance with their medicines (78%) and educating about medicines/health conditions (75%). The majority of pharmacists reported that the point at which they make the clinical decision to provide a particular service/intervention was: when a referral for service is received from a GP (76%), or during interaction with the consumer during the dispensing process (63%). Only half of responding pharmacists reported making clinical decisions about service provision through delivery of a CI (50%).
Screening/diagnostic/intervention tools	CIs were viewed as either predominantly medication management intervention tools or medication risk prevention tools. CIs were seen by the majority of participants (69%) to be quite distinct from advice given during routine counselling that occurs during dispensing.
Provider satisfaction	The majority (67%) reported being satisfied with their involvement in CI programs/ services. The majority (79%) reported being satisfied with the benefit their consumers receive through the CIs program.
Collaboration	There was very little collaboration between GPs and pharmacists for CIs, apart from brief phone calls or faxes to confirm a prescription or dosage.

Source: PricewaterhouseCoopers Combined Review of 5CPA Medication Management Programmes (2015)
Abbreviations: 5CPA, Fifth Community Pharmacy Agreement; CIs, Clinical Interventions; GP, general practitioner; PPI, Pharmacy Practice Incentives.
Note: Consumer survey results are not representative as there were no CI participants among survey respondents.

Overall, practitioners reported being reasonably satisfied with their involvement in the Medication Management programs and services. They also reported being satisfied with the benefit their consumers received through Medication Management programs and services, and they saw clear benefit in the suite of Medication Management programs and services as contributing towards improving the health outcomes of consumers.

However, stakeholders and practitioners indicated that 5CPA programs were difficult to access for consumers due to low consumer awareness, information on programs not being readily available to consumers, and low GP engagement and awareness to refer consumers to the relevant programs, particularly for Aboriginal and Torres Strait Islanders and culturally and linguistically diverse (CALD) peoples.

There were a number of limitations relevant to program data analysis. These included:

- Data collected as part of the claims process provided limited insight on uptake and volume of programs and services since multiple services could be submitted under one claim. The authors presented service level data where possible, merging accepted, rejected and claims datasets to conduct more accurate analyses.

- Consumer level data was de-identified and not linked to other data sources (e.g. Medicare and hospital data); therefore, it was not possible to determine the impact of participating in specific programs on consumer outcomes, outside of that particular episode of care.
- Consumer demographic data, such as age and gender, was not available for any of the PPI Program initiatives. Postcode was not captured at the consumer level within any program/service dataset, therefore analysis of the data could not be performed for socioeconomic indicator or remoteness.
- The number of medicines and health conditions of consumers was not captured in the PPI Program dataset, resulting in the inability to analyse trends over time and potential investment value, including impact, for other programs and services.
- Analysis of program data beyond 28th February 2014 was not performed, resulting in failure to capture the effects of administrative changes to programs and services implemented on 1st March 2014 on the uptake and volume of programs and services.

A cost-benefit analysis was not performed in this Review, thus direct and indirect benefits resulting from delivering medication management programs, such as the PPI Program, could not be inferred. The authors recommended that a baseline benefits analysis be conducted in a future review of the Program to inform the health, social and economic benefits that result from these program implemented as part of the 6CPA and evaluate the cost-benefits as a result of the 6CPA investment. A reliable cost-benefit analysis would require a more sophisticated approach towards collection of data, linking program data (multiple datasets, including at consumer level) combined with regular auditing and reporting requirements to enable consumer health outcomes to be more effectively monitored and measured over time.

5 CI UTILISATION ANALYSIS

5.1 CI initiative participating pharmacies and claims made

Between 2012 and 2016, 7,816 pharmacies have participated in the CI incentive program, peaking in 2014 at 5,931 pharmacies[9]. As 2016 is a part year, it is under-represented in the data and thus largely excluded in the analysis (Table 5.1).

Table 5.1 Summary of pharmacy CI claims 2012 – 2016

Claim year	No of pharmacies with claims	Value of claims	Volume of CIs received by patients	Average claim amount per CI	Average claim per participating pharmacy
2012	4,905	$26,204,044	2,013,377	$13.01	$5,342
2013	5,018	$12,426,350	3,764,365	$3.30	$2,476
2014	5,931	$20,003,906	3,514,910	$5.69	$3,373
2015	5,088	$19,640,278	4,477,088	$4.39	$3,860
2016	4,780	$4,926,953	1,449,043	$3.40	$1,031
Total	**7,816**	**$83,201,530**	**15,218,783**	**$5.47**	**$10,645**

Source: Claims payment data supplied in PPI Total Data Compilation_Copy.xls

Table 5.1 shows that the volume of patient CIs received by patients has increased 122.4% from 2.0 million in 2012 to 4.5 million in 2015, matched to corresponding increase of 3.7% in the number of participating pharmacies, indicating that participating pharmacies have substantially increased their volumes. Note that the 2012 average claim rates are higher due to the inclusion of an introductory base rate of $150 in the claim formula in the first year. Between 2013 and 2015 Table 5.1 shows that the average amount earned by pharmacies per patient CI has increased by 33.0%, going from $3.30 in 2013 to $4.39 in 2015, the average total annual amount claimed by participating pharmacies has also increased from $2,476 to $3,860 (55.9% increase), which has been driven primarily by proportionally higher volumes.

Table 5.2 deconstructs the same data by ABS remoteness. Pharmacies classified as Very Remote Australia have received disproportionately greater claims payments per patient CI than all of the other remoteness classifications (with an average of $5.97 in 2015). Remote Australia received the least per patient CI service supplied (with an average of $3.48). These variations are primarily a result of the inverse relationship between unit cost and the relative service volumes between regions.

Table 5.2 Summary of pharmacy CI claims 2012 – 2016 by ABS Remoteness

ABF Remoteness	Claim year	No of pharmacies with claims	Value of claims	Volume of CIs received by patients	Average claim amount per CI	Average claim per participating pharmacy
Inner Regional Australia	2012	999	$5,044,504	349,065	$14.45	$5,050
	2013	988	$2,200,353	551,757	$3.99	$2,227
	2014	1,218	$4,016,831	606,589	$6.62	$3,298
	2015	978	$4,017,911	772,869	$5.20	$4,108
	2016	924	$1,007,312	243,443	$4.14	$1,090
	Total	**1,634**	**$16,286,912**	**2,523,723**	**$6.45**	**$9,968**
Major Cities of Australia	2012	3,334	$18,567,671	1,480,857	$12.54	$5,569

[9] Pharmacies are counted according to unique S90 and /or Organisation Number identifiers.

ABF Remoteness	Claim year	No of pharmacies with claims	Value of claims	Volume of CIs received by patients	Average claim amount per CI	Average claim per participating pharmacy
	2013	3,436	$9,058,914	2,903,583	$3.12	$2,636
	2014	4,127	$14,056,887	2,581,683	$5.44	$3,406
	2015	3,484	$13,735,128	3,296,341	$4.17	$3,942
	2016	3,265	$3,422,533	1,079,505	$3.17	$1,048
	Total	**5,388**	**$58,841,134**	**11,341,969**	**$5.19**	**$10,921**
Outer Regional Australia	2012	478	$2,296,284	160,172	$14.34	$4,804
	2013	489	$1,026,653	270,691	$3.79	$2,099
	2014	621	$1,736,587	287,964	$6.03	$2,796
	2015	514	$1,698,759	360,375	$4.71	$3,305
	2016	483	$440,883	108,693	$4.06	$913
	Total	**803**	**$7,199,166**	**1,187,895**	**$6.06**	**$8,965**
Remote Australia	2012	64	$244,502	20,936	$11.68	$3,820
	2013	70	$114,244	34,420	$3.32	$1,632
	2014	86	$145,413	33,066	$4.40	$1,691
	2015	70	$132,637	38,149	$3.48	$1,895
	2016	71	$37,380	11,743	$3.18	$526
	Total	**122**	**$674,175**	**138,314**	**$4.87**	**$5,526**
Very Remote Australia	2012	30	$51,083	2,347	$21.77	$1,703
	2013	35	$26,185	3,914	$6.69	$748
	2014	51	$48,188	5,608	$8.59	$945
	2015	42	$55,843	9,354	$5.97	$1,330
	2016	37	$18,846	5,659	$3.33	$509
	Total	**65**	**$200,144**	**26,882**	**$7.45**	**$3,079**
Total		**7,816**	**$83,201,530**	**15,218,783**	**$5.47**	**$10,645**

Source: Claims payment data supplied in PPI Total Data Compilation_Copy.xls in conjunction with ABS postcode to remoteness.xls available from http://www.abs.gov.au/AUSSTATS/abs@.nsf/DetailsPage/1270.0.55.006July%202011?OpenDocument (accessed 5th October, 2016)
Abbreviations: ABS, Australian Bureau of Statistics; CI, Clinical Intervention.

The Very Remote Australia classification has experienced the highest relative increase in participating pharmacies, with numbers growing 40% (from 30 to 42) between 2012 and 2015 and the Remote Australia classification, growing 9% (from 64 to 70).

It is evident from the claims payment data that the volume of CI services received by patients has increased substantially between 2012 and 2015 nationally, and that the number of participating pharmacies has also increased, especially in the more remote regions. Growth in the program suggests it is considered effective, but the available data do not allow a determination of the reasons for growth (e.g. motivation for take-up of the incentive payment, or favourable patient feedback on the program, or both).

5.2 CI initiative reach to specific populations

The claims data do not include any information on the characteristics of the patients receiving the CI service or type of CI service provided, age of patient or indicators of frailty, mental faculties or health status; or indeed any other data that would assist in understanding what type of patient population are reached by the CI program and/or whether the program is effective.

In the absence of knowing what patient groups are receiving CI services or the types of CIs that are being provided to different patient groups, analysis into any relationship to chronic disease prevalence and the per-capita volumes of CIs claimed for pharmacies at geographic area level was examined.

To illustrate, Table 5.3 looks at the distribution across PHNs areas for CI service volumes against estimated diabetes (as an illustrative chronic disease) prevalence (i.e. proportion of the population in the PHN area with diabetes). Please note that the high, medium and low groupings in Table 5.3 are calculated by dividing the values for each of the metrics into three even segments between the highest and lowest values for all PHNs. Microsoft Excel is used to apply heat map colour coding to show where the range of values for each metric fall.

Table 5.3 Diabetes prevalence and CI service volumes and dollars claimed per capita, 2015

Primary Health Network	Diabetes prevalence	Diabetes prevalence range	Average CI services per capita	CI services /capita range	Average CI claim per capita	CI claim /capita range
Western Queensland	2.1%	Low	0.076	Low	$0.42	Low
Northern Queensland	2.8%	Low	0.184	Mid	$0.76	Mid
Eastern Melbourne	3.1%	Low	0.124	Low	$0.69	Low
Northern Territory	3.1%	Low	0.114	Low	$0.49	Low
Brisbane North	3.2%	Low	0.172	Low	$0.87	Mid
Country WA	3.2%	Low	0.144	Low	$0.62	Low
South Eastern Melbourne	3.2%	Mid	0.145	Low	$0.74	Mid
Australian Capital Territory	3.3%	Mid	0.272	High	$0.79	Mid
Murray	3.3%	Mid	0.204	Mid	$1.10	High
Northern Sydney	3.3%	Mid	0.201	Mid	$0.80	Mid
Western Victoria	3.3%	Mid	0.117	Low	$0.80	Mid
Perth North	3.4%	Mid	0.259	Mid	$0.92	Mid
Gippsland	3.5%	Mid	0.180	Mid	$0.98	Mid
Gold Coast	3.5%	Mid	0.209	Mid	$0.97	Mid
Perth South	3.5%	Mid	0.248	Mid	$0.80	Mid
Brisbane South	3.6%	Mid	0.177	Mid	$0.85	Mid
Darling Downs and West Moreton	3.6%	Mid	0.160	Low	$0.86	Mid
Nepean Blue Mountains	3.6%	Mid	0.199	Mid	$0.82	Mid
Western NSW	3.8%	Mid	0.232	Mid	$1.21	High
North Western Melbourne	3.9%	Mid	0.128	Low	$0.68	Low
Hunter New England and Central Coast	4.0%	Mid	0.365	High	$1.20	High
Murrumbidgee	4.0%	Mid	0.331	High	$1.37	High
Central Queensland, Wide Bay, Sunshine Coast	4.1%	Mid	0.210	Mid	$1.01	Mid
Central and Eastern Sydney	4.2%	Mid	0.230	Mid	$0.84	Mid
Tasmania	4.3%	Mid	0.273	High	$1.20	High
Western Sydney	4.3%	Mid	0.189	Mid	$0.82	Mid
North Coast	4.6%	High	0.249	Mid	$1.22	High
South Eastern NSW	4.8%	High	0.178	Mid	$0.89	Mid
Country SA	4.9%	High	0.134	Low	$0.87	Mid
Adelaide	5.2%	High	0.203	Mid	$0.87	Mid
South Western Sydney	5.5%	High	0.188	Mid	$0.86	Mid
Total	**3.8%**		**0.187**		**$0.82**	

Source: Claims payment data supplied in PPI Total Data Compilation_Copy.xls in conjunction with Phidu_data_pha_aust.xls available from http://www.phidu.torrens.edu.au/social-health-atlases/indicators-and-notes-on-the-data/social-health-atlases-of-australia-contents#population-projections (accessed 5th October, 2016)
Abbreviations: CI, Clinical Intervention.

Visual examination of Table 5.3 reveals a small degree of consistency in the relationships between diabetes prevalence and CI services provided and CI resources applied. It shows that 17 of 31 PHNs have the same banding for both disease prevalence, and average CI service volume per capita and average CI resources (claims) per capita. Of the six lowest prevalence diabetes PHNs, five feature as low CI services PHNs and four feature as low CI resources (claims) PHNs. There is considerably less consistency in the highest disease prevalence PHNs suggesting any underlying connections are relatively weak.

As another illustration, Table 5.4 looks at the distribution across PHNs areas for CI service volumes against estimated mental health issues prevalence (i.e. proportion of the population in the PHN area with a mental health issue). The same heat mapping approach is used.

Table 5.4 Mental health prevalence and CI service volumes and dollars claimed per capita, 2015

Primary Health Network	Mental health prevalence	Mental health prevalence range	Average CI services per capita	CI services /capita range	Average CI claim per capita	CI claim /capita range
Northern Territory	7.9%	Low	0.114	Low	$0.49	Low
Western Queensland	8.2%	Low	0.076	Low	$0.42	Low
Western Sydney	10.8%	Mid	0.189	Mid	$0.82	Mid
North Western Melbourne	11.1%	Mid	0.128	Low	$0.68	Low
Northern Queensland	11.1%	Mid	0.184	Mid	$0.76	Mid
Country WA	11.3%	Mid	0.144	Low	$0.62	Low
Eastern Melbourne	11.4%	Mid	0.124	Low	$0.69	Low
Northern Sydney	11.4%	Mid	0.201	Mid	$0.80	Mid
South Western Sydney	11.5%	Mid	0.188	Mid	$0.86	Mid
South Eastern Melbourne	11.7%	Mid	0.145	Low	$0.74	Mid
Central and Eastern Sydney	11.8%	Mid	0.230	Mid	$0.84	Mid
Perth North	11.8%	Mid	0.259	Mid	$0.92	Mid
Nepean Blue Mountains	11.9%	Mid	0.199	Mid	$0.82	Mid
Perth South	12.4%	Mid	0.248	Mid	$0.80	Mid
Western NSW	12.7%	Mid	0.232	Mid	$1.21	High
Brisbane South	12.8%	Mid	0.177	Mid	$0.85	Mid
Murrumbidgee	12.8%	Mid	0.331	High	$1.37	High
Brisbane North	13.3%	High	0.172	Low	$0.87	Mid
South Eastern NSW	13.3%	High	0.178	Mid	$0.89	Mid
Western Victoria	13.3%	High	0.117	Low	$0.80	Mid
Murray	13.4%	High	0.204	Mid	$1.10	High
Darling Downs and West Moreton	13.7%	High	0.160	Low	$0.86	Mid
Gold Coast	13.7%	High	0.209	Mid	$0.97	Mid
Hunter New England and Central Coast	13.7%	High	0.365	High	$1.20	High
Adelaide	14.0%	High	0.203	Mid	$0.87	Mid
Australian Capital Territory	14.0%	High	0.272	High	$0.79	Mid
Country SA	14.0%	High	0.134	Low	$0.87	Mid
Gippsland	14.2%	High	0.180	Mid	$0.98	Mid
Central Queensland, Wide Bay, Sunshine Coast	14.5%	High	0.210	Mid	$1.01	Mid
Tasmania	14.5%	High	0.273	High	$1.20	High
North Coast	15.3%	High	0.249	Mid	$1.22	High
Total	**12.5%**		**0.187**		**$0.82**	

Source: Claims payment data supplied in PPI Total Data Compilation_Copy.xls in conjunction with Phidu_data_pha_aust.xls available from http://www.phidu.torrens.edu.au/social-health-atlases/indicators-and-notes-on-the-data/social-health-atlases-of-australia-contents#population-projections (accessed 5th October, 2016)
Abbreviations: CI, Clinical Intervention

Visual examination of Table 5.4 reveals a lesser degree of consistency in the relationships at PHN area level between the prevalence of mental health issues, and CI services provided per capital and CI resources applied per capita than the prior example (Table 5.3). The heat map colouration indicate pooling for many of the PHNs with the lowest per capita CI service rate into the top half of the table but there is considerably less consistency in the bottom half of the table. 15 of 31 PHNs share the same bandings for mental health issues prevalence, and average CI service volume per capita and average CI resources (claims) per capita.

Overall, these results are insufficient to demonstrate a relationship between included population groups and the take up rates for the CI services.

It is clear that to make a more robust assessment of the impact of the CI program, more comprehensive data are required. Such data should include the characteristics of patients receiving the CI services and the types of CI services provided to enable funders and providers to be confident that the initiative is applying resources to in need populations.

Ideally the additional data collected should also include measures of interim and final clinical outcomes, as well as patient reported measures of experience with the program, to enable an assessment of clinical and cost effectiveness. It is acknowledged that this type\s of data could probably only be collected in the context of a structured trial of the CI program.

APPENDIX 1 REFERENCES

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APPENDIX 2 WORKING GROUP MEMBERS

The Department of Health established a Working Group of nominated representatives (Table A-2.**1**) to provide advice to the Department and the Assessment Group on the research questions and PICO criteria for the literature review, the literature search terms, utilisation data and analysis.

Table A-2.1 Members of the Working Group for the evaluation of the medication adherence PPI Programs

Name	Representing

APPENDIX 3 SEARCH STRATEGY

The CI search strategies for Embase, Medline, International Pharmaceutical Abstracts and Cochrane databases are outlined in Table A-3.1, Table A-3.2, Table A-3.3 and Table A-3.4, respectively, below.

Table A-3.1 Embase search strategy (20th September 2016)

#	Ovid query	Records
1	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti,kw.	53,916
2	(clinical services or intervention or care services).ti,kw.	109,901
3	(adherence or compliance or patient education).ti,kw.	73,145
4	community.ti.	124,769
5	1 and 2 and 3	167
6	1 and 2 and 4	232
7	5 or 6	375
8	(prescription review or pharmacist$ clinical services or pharmacist$ clinical intervention or ((non-dispensing or nondispensing) adj (service$ or role$))).ti,ab,kw.	121
9	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti.	50,074
10	((Randomi?ed adj3 trial$) or rct or systematic review or meta?analysis).ti.	180,309
11	9 and 10	447
12	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti.	50,074
13	exp patient education/	98,286
14	exp medication compliance/	15,500
15	12 and 13 and 14	121
16	7 or 8 or 11 or 15	987
17	editorial/ or erratum/ or letter/ or note/ or short survey/ or abstract report/ or letter/ or case study/ or (editorial or erratum or letter or note or short survey or conference abstract or abstract report or case study or case report).tw.	3,420,080
18	16 not 17	**909**

Table A-3.2 Medline search strategy (20th September 2016)

#	Ovid query	Records
1	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti,kw.	27,616
2	(clinical services or intervention or care services).ti,kw.	70,340
3	(adherence or compliance or patient education).ti,kw.	45,257
4	community.ti.	109,258
5	1 and 2 and 3	47
6	1 and 2 and 4	106
7	5 or 6	144
8	(prescription review or pharmacist$ clinical services or pharmacist$ clinical intervention or ((non-dispensing or nondispensing) adj (service$ or role$))).ti,ab,kw.	71
9	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti.	26,317
10	((Randomi?ed adj3 trial$) or rct or systematic review or meta?analysis).ti.	149,102
11	9 and 10	337

#	Ovid query	Records
12	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti.	26,317
13	exp Patient Education/	76,564
14	exp Medication Adherence/	11,884
15	12 and 13 and 14	73
17	editorial/ or erratum/ or letter/ or note/ or case study/ or (editorial or erratum or letter or note or short survey or conference abstract or abstract report or case study or case report).tw.	3,231,626
18	16 not 17	556
19	remove duplicates from 18	**537**

Table A-3.3 International Pharmaceutical Abstracts (IPA) search strategy (20th September, 2016)

#	Ovid query	Records
1	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti,kw.	35,920
2	(clinical services or intervention or care services).ti,kw.	2,362
3	(adherence or compliance or patient education).ti,kw.	3,403
4	community.ti.	5,606
5	1 and 2 and 3	22
6	1 and 2 and 4	83
7	5 or 6	101
8	(prescription review or pharmacist$ clinical services or pharmacist$ clinical intervention or ((non-dispensing or nondispensing) adj (service$ or role$))).ti,ab,kw.	68
9	(pharmacy or pharmacies or pharmacist$ or (pharmaceutical adj (care or service$))).ti.	35,920
10	((Randomi?ed adj3 trial$) or rct or systematic review or meta?analysis).ti.	8,545
11	9 and 10	119
12	7 or 8 or 11	278
13	editorial/ or erratum/ or letter/ or note/ or case study/ or (editorial or erratum or letter or note or short survey or conference abstract or abstract report or case study or case report).tw.	10,760
14	12 not 13	**269**

Table A-3.4 Cochrane Library search strategy (22nd September 2016)

#	Query	Records
1	(pharmacist$ or pharmacy or pharmacies or (pharmaceutical next (care or service$)) and (intervention$ or education or manage$ or "clinical services" or adherence or compliance) or prescription review or pharmacist$ clinical services or pharmacist$ clinical intervention or ((non-dispensing or nondispensing) next (service$ or role$))):ti,kw [in Cochrane Reviews (Reviews and Protocols), Other Reviews, Methods Studies, Technology Assessments, Economic Evaluations and Cochrane Groups]	293
2	MeSH descriptor: [Patient Education as Topic] explode all trees	7,676
3	MeSH descriptor: [Pharmaceutical Services] explode all trees	1,562
4	MeSH descriptor: [Community Pharmacy Services] explode all trees	250

#	Query	Records
5	#1 and (#2 or #3 or #4)	**172**
	Cochrane Reviews	*3*
	Other reviews	*62*
	Methods studies	*0*
	Technology assessments	*9*
	Economic evaluations	*98*
	Cochrane Groups	*0*

APPENDIX 4 SYSTEMATIC REVIEWS CHECKED FOR ELIGIBLE STUDIES

A list of systematic reviews excluded from the review are presented in Table A-4.1.

Table A-4.1 Systematic reviews excluded from Review but searched for eligible included studies

Study ID	Citation
Adunlin (2012)	Adunlin G and Mahdavian S (2012). The Effectiveness of Pharmacist Interventions on Asthma Management: A Systematic Review. Journal of Asthma and Allergy Educators 3(6):264-273.
Al-Jumah (2012)	Al-Jumah KA and Qureshi NA (2012). Impact of pharmacist interventions on patients' adherence to antidepressants and patient-reported outcomes: A systematic review. Patient Preference and Adherence 6:87-100.
Antoine (2014)	Antoine SL, Pieper D, Mathes T and Eikermann M (2014). Improving the adherence of type 2 diabetes mellitus patients with pharmacy care: A systematic review of randomized controlled trials. BMC Endocrine Disorders 14 (no pagination)(53).
Bell (2005)	Bell S, McLachlan AJ, Aslani P, Whitehead P and Chen TF (2005). Community pharmacy services to optimise the use of medications for mental illness: A systematic review. Australia and New Zealand Health Policy 2 (1) (no pagination)(29).
Bennett (2011)	Bennett MI, Bagnall AM, Raine G, Closs SJ, Blenkinsopp A, Dickman A, et al (2011). Educational interventions by pharmacists to patients with chronic pain: Systematic review and meta-analysis. Clinical Journal of Pain 27(7):623-630.
Blalock (2013)	Blalock SJ, Roberts AW, Lauffenburger JC, Thompson T and O'Connor SK (2013). The effect of community pharmacy-based interventions on patient health outcomes: A systematic review. Medical Care Research and Review 70(3):235-266.
Blenkinsopp (2005)	Blenkinsopp A and Hassey A (2005). Effectiveness and acceptability of community pharmacy-based interventions in type 2 diabetes: A critical review of intervention design, pharmacist and patient perspectives. International Journal of Pharmacy Practice 13(4):231-240.
Castelino (2009)	Castelino RL, Bajorek BV and Chen TF (2009). Targeting suboptimal prescribing in the elderly: a review of the impact of pharmacy services (Structured abstract). Annals of Pharmacotherapy(6):1096-1106.
Charrois (2012)	Charrois TL, Zolezzi M, Koshman SL, Pearson G, Makowsky M, Durec T, et al (2012). A systematic review of the evidence for pharmacist care of patients with dyslipidemia. Pharmacotherapy 32(3):222-233.
Cheema (2014)	Cheema E, Sutcliffe P and Singer DRJ (2014). The impact of interventions by pharmacists in community pharmacies on control of hypertension: A systematic review and meta-analysis of randomized controlled trials. British Journal of Clinical Pharmacology 78(6):1238-1247.
Cheng (2013)	Cheng Y, Raisch DW, Borrego ME and Gupchup GV (2013). Economic, clinical, and humanistic outcomes (ECHOs) of pharmaceutical care services for minority patients: a literature review. Res Social Adm Pharm 9(3):311-329.
Chisholm-Burns (2010)	Chisholm-Burns MA, Graff Zivin JS, Lee JK, Spivey CA, Slack M, Herrier RN, et al (2010). Economic effects of pharmacists on health outcomes in the United States: A systematic review. American Journal of Health-System Pharmacy 67(19):1624-1634.
Evans (2011)	Evans CD, Watson E, Eurich DT, Taylor JG, Yakiwchuk EM, Shevchuk YM, et al (2011). Diabetes and cardiovascular disease interventions by community pharmacists: A systematic review
Garcia-Cardenas (2016)	Garcia-Cardenas V, Armour C, Benrimoj SI, Martinez-Martinez F, Rotta I and Fernandez-Llimos F (2016). Pharmacists' interventions on clinical asthma outcomes: A systematic review. European Respiratory Journal 47(4):1134-1143.

Study ID	Citation
Jalal (2016)	Jalal ZS, Smith F, Taylor D, Patel H, Finlay K and Antoniou S (2016). Pharmacy care and adherence to primary and secondary prevention cardiovascular medication: A systematic review of studies. European Journal of Hospital Pharmacy 21(4):238-244.
Li (2010)	Li X, Mao M and Ping Q (2010). Effect of pharmaceutical care programs on glycemic control in patients with diabetes mellitus: A meta-analysis of randomized controlled trials. Journal of Pharmacy Technology 26(5):255-263.
Lindenmeyer (2006)	Lindenmeyer A, Hearnshaw H, Vermeire E, Van Royen P, Wens J and Biot Y (2006). Interventions to improve adherence to medication in people with type 2 diabetes mellitus: a review of the literature on the role of pharmacists. J Clin Pharm Ther 31(5):409-419.
Machado (2007)	Machado M, Bajcar J, Guzzo GC and Einarson TR (2007). Sensitivity of patient outcomes to pharmacist interventions. Part I: Systematic review and meta-analysis in diabetes management. Annals of Pharmacotherapy 41(10):1569-1582.
Machado (2007)	Machado M, Bajcar J, Guzzo GC and Einarson TR (2007). Sensitivity of patient outcomes to pharmacist interventions. Part II: Systematic review and meta-analysis in hypertension management. Annals of Pharmacotherapy 41(11):1770-1781.
Machado (2008)	Machado M, Nassor N, Bajcar JM, Guzzo GC and Einarson TR (2008). Sensitivity of patient outcomes to pharmacist interventions. Part III: Systematic review and meta-analysis in hyperlipidemia management. Annals of Pharmacotherapy 42(9):1195-1207.
Mohammed (2016)	Mohammed MA, Moles RJ and Chen TF (2016). Impact of Pharmaceutical Care Interventions on Health-Related Quality-of-Life Outcomes: A Systematic Review and Meta-analysis. Annals of Pharmacotherapy 50(10):862-881.
Morgado (2011)	Morgado MP, Morgado SR, Mendes LC, Pereira LJ and Castelo-Branco M (2011). Pharmacist interventions to enhance blood pressure control and adherence to antihypertensive therapy: Review and meta-analysis. Am J Health Syst Pharm 68(3):241-253.
Morrison (2001)	Morrison A and Wertheimer AI (2001). Evaluation of studies investigating the effectiveness of pharmacists' clinical services. American Journal of Health-System Pharmacy 58(7):569-577.
Nkansah (2010)	Nkansah N, Mostovetsky O, Yu C, Chheng T, Beney J, Bond CM, et al (2010). Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns. Cochrane database of systematic reviews (Online) 7:CD000336.
Omran (2012)	Omran D, Guirguis LM and Simpson SH (2012). Systematic review of pharmacist interventions to improve adherence to oral antidiabetic medications in people with type 2 diabetes. Canadian Journal of Diabetes 36(5):292-299.
Pande (2013)	Pande S, Hiller JE, Nkansah N and Bero L (2013). The effect of pharmacist-provided non-dispensing services on patient outcomes, health service utilisation and costs in low- and middle-income countries. Cochrane database of systematic reviews (Online) 2:CD010398.
Patwardhan (2014)	Patwardhan PD, Amin ME and Chewning BA (2014). Intervention research to enhance community pharmacists' cognitive services: a systematic review. Research in social & administrative pharmacy : RSAP 10(3):475-493.
Pickard (1999)	Pickard AS, Johnson JA and Farris KB (1999). The impact of pharmacist interventions on health-related quality of life (Structured abstract). Annals of Pharmacotherapy(11):1167-1172.
Pousinho (2016)	Pousinho S, Morgado M, Falcao A and Alves G (2016). Pharmacist Interventions in the Management of Type 2 Diabetes Mellitus: A Systematic Review of Randomized Controlled Trials. J Manag Care Spec Pharm 22(5):493-515.
Riordan (2016)	Riordan DO, Walsh KA, Galvin R, Sinnott C, Kearney PM and Byrne S (2016). The effect of pharmacist-led interventions in optimising prescribing in older adults in primary care: A systematic review. SAGE Open Medicine 4:2050312116652568.
Rotta (2015)	Rotta I, Salgado TM, Silva ML, Correr CJ and Fernandez-Llimos F (2015). Effectiveness of clinical pharmacy services: an overview of systematic reviews (2000-2010). International Journal of Clinical Pharmacy 37(5):687-697.

Study ID	Citation
Rubio-Valera (2011)	Rubio-Valera M, Serrano-Blanco A, Magdalena-Belio J, Fernandez A, Garcia-Campayo J, Pujol MM, et al (2011). Effectiveness of pharmacist care in the improvement of adherence to antidepressants: A systematic review and meta-analysis. Annals of Pharmacotherapy 45(1):39-48.
Ryan (2014)	Ryan R, Santesso N, Lowe D, Hill S, Grimshaw J, Prictor M, et al (2014) Interventions to improve safe and effective medicines use by consumers: an overview of systematic reviews. Cochrane Database of Systematic Reviews, DOI: 10.1002/14651858.CD007768.pub3.
Saez-Benito (2013)	Saez-Benito L, Fernandez-Llimos F, Feletto E, Gastelurrutia MA, Martinez-Martinez F and Benrimoj SI (2013). Evidence of the clinical effectiveness of cognitive pharmaceutical services for aged patients. Age & Ageing 42(4):442-449.
Salgado (2012)	Salgado TM, Moles R, Benrimoj SI and Fernandez-Llimos F (2012). Pharmacists' interventions in the management of patients with chronic kidney disease: A systematic review. Nephrology Dialysis Transplantation 27(1):276-292.
Santschi (2014)	Santschi V, Chiolero A, Colosimo AL, Platt RW, Taffe P, Burnier M, et al (2014). Improving blood pressure control through pharmacist interventions: A meta-analysis of randomized controlled trials. Journal of the American Heart Association 3 (2) (no pagination)(e000718).
Singhal (1999)	Singhal PK, Raisch DW and Gupchup GV (1999). The impact of pharmaceutical services in community and ambulatory care settings: evidence and recommendations for future research. Ann Pharmacother 33(12):1336-1355.
Thomas (2014)	Thomas R, Huntley AL, Mann M, Huws D, Elwyn G, Paranjothy S, et al (2014). Pharmacist-led interventions to reduce unplanned admissions for older people: A systematic review and meta-analysis of randomised controlled trials. Age and Ageing 43(2):174-187.
Touchette (2014)	Touchette DR, Doloresco F, Suda KJ, Perez A, Turner S, Jalundhwala Y, et al (2014). Economic evaluations of clinical pharmacy services: 2006-2010 (Provisional abstract). Database of Abstracts of Reviews of Effects(2):771-793.
Van Wijk (2005)	Van Wijk BLG, Klungel OH, Heerdink ER and De Boer A (2005). Effectiveness of interventions by community pharmacists to improve patient adherence to chronic medication: A systematic review. Annals of Pharmacotherapy 39(2):319-328.
Zhong (2014)	Zhong H, Ni XJ, Cui M and Liu XY (2014). Evaluation of pharmacist care for patients with chronic obstructive pulmonary disease: a systematic review and meta-analysis. International Journal of Clinical Pharmacy 36(6):1230-1240.