



**LITERATURE REVIEW OF THE COST-EFFECTIVENESS OF NON-DISPENSING  
PHARMACIST SERVICES INTEGRATED WITHIN PRIMARY HEALTH CARE**

**REPORT TO THE PHARMACEUTICAL SOCIETY OF AUSTRALIA  
FOR THE IPAC PROJECT**

**Final Report, February 2020.**

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## LITERATURE REVIEW OF THE COST-EFFECTIVENESS OF NON-DISPENSING PHARMACIST SERVICES INTEGRATED WITHIN PRIMARY HEALTH CARE

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### Acknowledgements:

The authors (Ms Karen Johnstone, Dr Deb Smith, and A/Prof Sophia Couzos) wish to acknowledge the Australian Government as the funding body supporting the implementation of the IPAC Project, under the Sixth Community Pharmacy Agreement (6CPA), with funding allocated for a Pharmacy Trial Program (PTP). The PTP will trial new and expanded community pharmacy programs which seek to improve clinical outcomes for consumers and/or extend the role of pharmacists in the delivery of primary healthcare services through community pharmacy. All PTP trials will be evaluated by an independent health technology assessment (HTA) body.

## **AIM**

The *Integrating Pharmacists within Aboriginal Community Controlled Health Services to improve Chronic Disease Management (IPAC)* project will investigate the impact of including a non-dispensing practice pharmacist in the primary health care team within Aboriginal Community Controlled Health Services (ACCHSs). The project employed a pragmatic, non-randomized design and will evaluate impact in terms of quality of care received by Aboriginal and Torres Strait Islander peoples. An economic evaluation to determine the cost-effectiveness of the intervention relative to usual care will be conducted. This literature review aimed to identify published literature on cost-effectiveness studies for the same or similar pharmacist interventions in the primary health care setting.

## **METHODS**

### **Bibliographic database search**

A systematic literature review of published literature available in online bibliographic databases was conducted. A senior librarian at James Cook University guided development of the initial search strategy. Medline, CINAHL and Emcare databases were searched using variations of the core terms “primary health care”, “indigenous health services”, “pharmacist” and “cost-effectiveness”. The search terms were applied in combination ((“primary health care” OR “indigenous health services”) AND “pharmacist” AND “cost-effectiveness”)) and resulting relevant articles were reviewed for any other MeSH search terms or key words that could be added to the search strategy. The amended search strategy was applied again, and the cycle was repeated until no further relevant, additional search terms were identified.

The final search (Appendix 1) was conducted and all resulting articles were downloaded to the EndNote software bibliographic management program. Duplicate titles were removed. The titles and abstracts of remaining articles were screened for relevance to the aim of the literature review and removed from the EndNote library as appropriate. The reference lists of relevant literature review articles identified from the search were checked for any citations that warranted further investigation.

Articles were excluded from further review based on the following exclusion criteria: article other than a journal article or report, study protocol, study intervention that was set within a hospital or involved specialist physicians, the intervention involved community pharmacists without specified collaboration with general practitioners (GPs), the intervention involved a team-based approach where pharmacist involvement was not explicit, the study did not include a cost-effectiveness analysis, or the full text was unavailable online or written in a language other than English. The full text of the remaining articles were reviewed for relevance resulting in a final set of articles for inclusion in the literature review. The reference lists of articles included in this review were also checked for any further relevant citations and these were included in the review as appropriate. Information about the intervention, study design, outcome measures, participants and cost analysis was extracted from articles to be included in this review.

## General internet search

A search of the internet was also conducted to identify reports on cost-effectiveness analyses on relevant interventions that had not been published in the academic literature. The search was restricted to interventions within Australia that involved integration of a clinical pharmacist into general practice. Search terms were a combination of the core terms “general practice” and “pharmacist”. Websites of relevant key health profession bodies were also searched.

## RESULTS

### Bibliographic database search

A total of 2,067 articles were retrieved and downloaded to EndNote on 5<sup>th</sup> April 2019 (Figure 1). The search was not restricted to a specific start date. A further 10 articles were identified through searches of reference lists. Duplicate articles were removed (n=287) and the remaining titles and abstracts were examined for relevance to the aim of this review. Eighty-six articles were reviewed in full.

Thirteen cost-effectiveness studies, set in primary health care and with similar interventions to the IPAC intervention, were identified for inclusion in this review (Table 1 and Table 2). Only one study was conducted in Australia with the remaining studies conducted in the United States (n=5), England (n=3), Norway (n=1), Ireland (n=1), Spain (n=1) and Brazil (n=1).

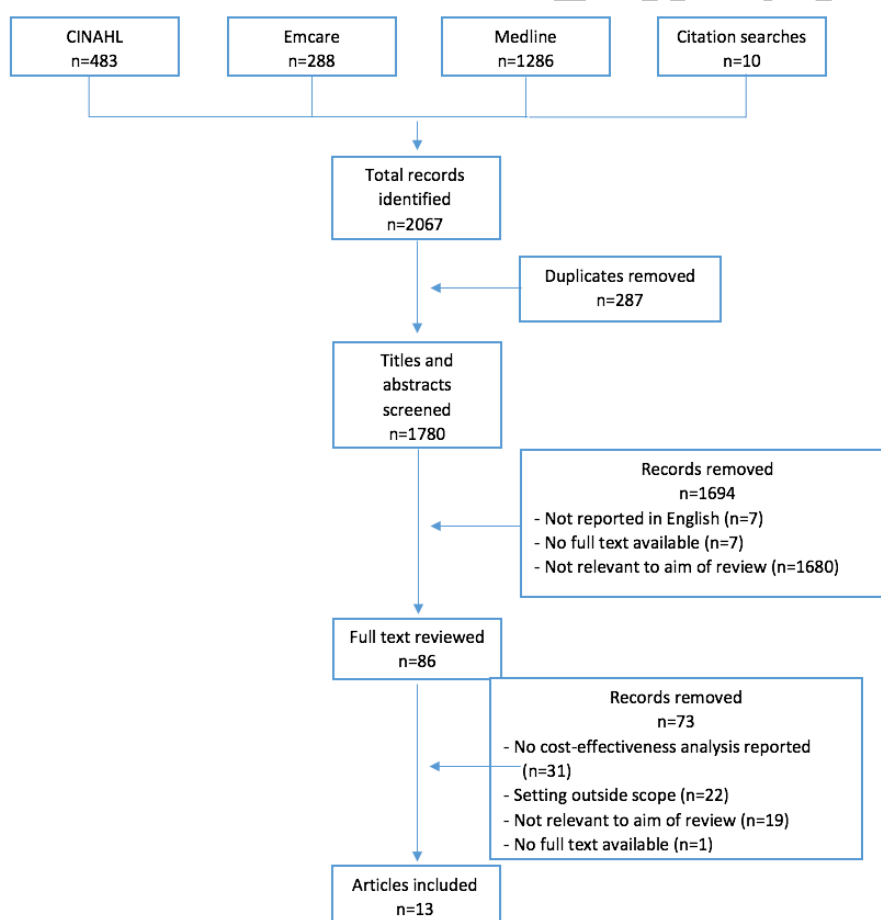


Figure 1. Flow diagram

The literature search did not reveal any cost-effectiveness studies for interventions involving a pharmacist integrated within primary health care services such as ACCHSs in Australia. Furthermore, there were no cost-effectiveness studies from any other country reporting interventions involving clinical pharmacist services to Indigenous peoples through Indigenous health services or any other type of primary health care service. Only one study, set in the United States, commented on the participation of minority populations.

Given the lack of cost-effectiveness studies that were directly relevant to the IPAC project, cost-effectiveness studies included in this review were selected to have a broader focus in general practice or other primary health care settings and involving collaborative care between a pharmacist and a general practitioner (GP).

### *Pharmacist integration*

All studies included in this review were randomised controlled trials that aimed to influence prescribing behaviour of physicians and medication use by patients through a collaborative approach to medication management involving a pharmacist. Comprehensive collaboration between pharmacists and physicians, similar to the IPAC project, was evident in most studies however some interventions did not explicitly describe patient-pharmacist collaboration. These studies appeared to involve pharmacists providing education to, and collaborating with, physicians only (Fretheim et al, 2006; Gillespie et al, 2017; Lopez-Picazo et al, 2011). For instance, Gillespie and others' (2017) study involved a research pharmacist to identify potentially inappropriate prescriptions (PIPs) and a pharmacist to provide academic detailing to a physician, with no further involvement of a pharmacist.

Only two studies explicitly mentioned co-location of the pharmacist within the primary health care facility, but it was not clear if the pharmacists were co-located solely for the purposes of the intervention or if they were existing staff at the facility (Kulchaitanaroaj et al, 2012; 2017). The remaining studies involved community pharmacists, clinical pharmacists or research pharmacists and again it was unclear if they were co-located at the primary health care facility for the intervention period.

### *Patients that were targeted*

The interventions targeted a range of patient characteristics broadly described as patients at risk of drug mismanagement, patients with certain health conditions and patients taking certain medications or a certain amount of medications.

Specifically, studies targeted patients at risk of medication error or inadequate blood monitoring (Avery et al, 2012; Elliot et al, 2014), drugs interaction (Lopez-Picazo et al, 2011) or medication misadventure (Sorensen et al, 2004). Patients with hypertension or diabetes were the focus of some studies (Kulchaitanaroaj et al, 2014; 2017; Polgreen et al, 2015; Obreli-Neto et al, 2015; Simpson et al, 2015). Other studies targeted patients with polypharmacy (Bojke et al, 2010; Cowper et al, 1998), patients with PIPs (Gillespie et al, 2017) and patients starting a specific medication for hypertension (Fretheim et al, 2006). Some studies were also focused on patients aged over 60 years (Bojke et al, 2010; Cowper et al, 1998; Gillespie et al, 2017; Obreli-Neto et al, 2015).

### *Outcomes and costs that were investigated*

Across the studies, the cost-effectiveness of interventions was demonstrated through a wide variety of outcome measures. Some studies measured change in prescribing patterns due to the intervention, as follows: cost per additional medication error avoided (Avery et al, 2012); cost per unit change in Medication Appropriateness Index (MAI; Cowper et al, 1998); cost per PIP avoided (Gillespie et al, 2017); cost per additional patient started on the drug of choice (Fretheim et al, 2006); cost to reduce mean drugs interaction by 1% (Lopez-Picazo et al, 2011); and, cost to reduce adverse drug interactions (Sorenson et al, 2004).

Other studies measured change in clinical parameters due to the intervention, as follows: cost per additional patient to achieve blood pressure control (Kulchaitanaroaj et al, 2012); cost to lower blood pressure by 1mmHg (Polgreen et al, 2015); cost to reduce annualized cardiovascular risk by 1% (Simpson et al, 2015); and, cost to improve severity of illness (Sorenson et al, 2004). Cost utility studies evaluated effectiveness of interventions in relation to quantity and quality of life, and measured cost per additional Quality Adjusted Life Year gained (QALY; Bojke et al, 2010; Elliot et al, 2014; Gillespie et al, 2017; Kulchaitanaroaj et al, 2017; Obreli-Neto et al, 2015).

The types of costs captured in the studies varied with some studies capturing costs of control and intervention groups, and others using costs related to the intervention only. The sources for costs of health providers' time were captured through a combination of methods and included logbook recordings and estimation using hourly rates, annual salary or health system billing information. The cost of medications, laboratory tests and patients' health service utilisation were commonly included in analyses and these were sourced using patient records and questionnaires. Other costs included travel, administration and materials.

### *Cost-effectiveness*

Table 2 outlines the findings of the 13 studies included in this review. Overall, the interpretation and reporting of the cost-effectiveness of interventions varied across the studies. Two interventions were considered cost-effective as the incremental cost per additional unit of health gained was within the willingness-to-pay threshold, from the perspective of the health system or society (Elliot et al., 2014; Simpson et al., 2015).

Some studies reported the probability that an intervention was cost-effective if the decision-maker's willingness-to-pay reached a certain level (Avery et al., 2012; Gillespie et al., 2017), or reported the probability that the intervention was cost-effective at a defined threshold (Bojke et al., 2010; Gillespie et al., 2017).

The remaining studies did not report a willingness-to-pay threshold, and instead compared the cost-effectiveness ratio with other studies or made general conclusions about the cost savings due to the intervention in relation to observed health outcomes (Cowper et al, 1998; Fretheim et al., 2006; Kulchaitanaroaj et al., 2017; Lopez-Picazo et al., 2011; Obreli-Neto et al., 2015; Polgreen et al., 2015; Sorensen et al., 2004).

The majority of studies noted that the sustained effects of the intervention may not have been captured within the analysis but would be important in future decisions about implementing the intervention.

### **General internet search**

The general search of the internet identified some pharmacist and general practice collaborative programs associated with the Primary Health Networks (PHN) in Australia. Western Sydney PHN (WentWest), together with University of Technology Sydney, implemented the General Practice Pharmacist Project in March 2016 (Benson, Williams & Benrimoj, 2017; PHN Western Sydney, 2018). This program involved a non-dispensing pharmacist delivering clinical and education services to patients within general practice, similar to that provided by the IPAC project intervention. The program will be evaluated with a cluster-controlled trial and an economic analysis is planned, though no further details were available.

The ACT PHN/Capital Health Network Pharmacist in General Practice pilot involves a non-dispensing pharmacist within general practice and began in 2016. This pilot involved pharmacists employed part-time within a general practice for 16 hours per week. An evaluation of the pilot program found that a clinical audit conducted by one of the pharmacists resulted in a cost saving of approximately \$125,700 over 3 years and \$183,000 over 5 years (Capital Health Network, 2018). Further details about this analysis were not found. There was some evidence of similar programs being implemented in the Brisbane area (Kidd, 2018) however details for these programs could not be found.

### **DISCUSSION**

This literature review used a comprehensive search strategy of online bibliographic databases to identify existing cost-effectiveness evaluations for interventions focused on the same population and setting as the IPAC project intervention. This literature search did not identify cost-effectiveness evaluations of pharmacist's interventions that were directly relevant to the IPAC project. This highlights the importance of the IPAC project to inform on the cost-effectiveness of pharmacist interventions relevant to the health of Indigenous Australians. The search did identify some studies that the IPAC project could draw on for the cost-effectiveness evaluation of certain health outcomes. The studies set in countries other than Australia have different health systems and therefore different management of health problems within the primary health care settings. However, these studies offered insights into ways that cost-effectiveness of the IPAC project intervention could be evaluated.

Several studies investigated the cost-effectiveness of interventions for patients with diabetes and hypertension (Kulchaitanaroaj et al, 2014; 2017; Polgreen et al, 2015; Obreli-Neto et al, 2015; Simpson et al, 2015). Obreli-Neto and others (2015) and Kulchaitanaroaj and others (2017) conducted cost-utility studies that are out of scope for the IPAC project intervention. However, the remaining studies measured effectiveness using similar biomedical outcomes as the IPAC project such as changes in blood pressure control, changes in systolic and diastolic blood pressure and change in cardiovascular risk (Kulchaitanaroaj et

al, 2014; Polgreen et al, 2015; Simpson et al, 2015). The IPAC project also investigates measures of prescribing quality such as change in the Medication Appropriateness Index (MAI). Cowper and others (1998) evaluated cost-effectiveness by measuring the change in MAI following their intervention. The use of a threshold willingness-to-pay was limited to studies reporting health gained in terms of QALYs. As the studies included in this review measured health gains in different ways, it is difficult to report the cost-effectiveness of the interventions without considering and understanding the context of each setting.

## **CONCLUSION**

Based on this literature review, the cost-effectiveness economic evaluation undertaken for the IPAC project is unique in the current academic literature. Published cost-effectiveness reports were not identified in Australia through the general internet search that was conducted, though there is work currently being done in this area through some Primary Health Networks. To our knowledge, the IPAC project intervention provides the first evaluation of the cost-effectiveness of a collaborative intervention involving pharmacists integrated within ACCHS in Australia, and indeed, the first evaluation of such an intervention for any Indigenous health service worldwide.



**Table 1. Description of cost-effectiveness studies investigating pharmacist interventions in primary health care settings. The table includes a description of the intervention and control groups, the length of the intervention and follow-up period, the clinical measures used, and the participants involved in the cost-effectiveness analysis.**

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
Avery et al, 2012  General Practice  England  Two-group pragmatic cluster randomised trial	Intervention practices were provided with simple computerised feedback for patients identified as being at risk of medication error and inadequate blood-test monitoring of medicines plus Pharmacist-led Information Technology Complex Intervention (PINCER). Then the pharmacist met with the practice team to discuss feedback and used techniques to correct medication errors including review of medical records, medication review, discussion with doctor, blood tests and improvement of local safety systems.	Simple computerised feedback for patients identified as at risk of medication error and inadequate blood-test monitoring of medicines provided to control practices plus educational materials.	Intervention: 12 weeks  Follow up: 6 months 12 months	a. History of peptic ulcer and prescribed an NSAID without co-prescription of a proton pump inhibitor b. Have asthma and prescribed a $\beta$ blocker/asthma c. Aged $\geq 75$ years receiving long term ACE inhibitors or loop diuretics without urea and electrolyte monitoring in the previous 15 months d. Methotrexate for $\geq 3$ months without full blood count in past 3 months e. Methotrexate for $\geq 3$ months without a liver function test in past 3 months f. Lithium for $\geq 3$ months without a lithium concentration measurement in past 3 months g. Amiodarone for $\geq 6$ months without a thyroid function test in the past 6 months	Patients identified with potential medication error or inadequate blood-test monitoring  No. of patients at baseline (IG;CG): a. 87/1828 (5%); 93/1970 (5%) b. 537/18906 (3%); 628/20634 (3%) c. 549/4349 (13%); 483/4722 (10%) d. 170/480 (35%); 202/483 (42%) e. 172/480 (36%); 184/483 (38%) f. 97/194 (50%); 101/224 (45%) g. 111/240 (46%); 130/253 (51%)  No. of patients at 6 months follow up (IG;CG): a. 51/1852 (3%); 86/2014 (4%) b. 499/20312 (2%); 658/22224 (3%) c. 255/4851 (5%); 436/5329 (8%) d. 122/494 (25%); 162/518 (31%) e. 121/494 (24%); 154/518 (30%) f. 67/190 (35%); 84/211 (40%) g. 81/242 (33%); 106/235 (45%)  No. of patients at 12 months follow up (IG;CG): a. 61/1852 (3%); 78/2035 (4%) b. 545/21359 (3%); 692/23520 (3%) c. 306/5242 (6%); 452/5813 (8%) d. 130/531 (24%); 194/552 (35%) e. 134/531 (25%); 186/552 (34%) f. 56/176 (32%); 88/213 (41%) g. 80/233 (34%); 92/247 (37%)

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
<p>Bojke et al, 2010</p> <p>General practice and community pharmacy</p> <p>England</p> <p>Randomised multiple interrupted time-series</p>	<p>RESPECT (Randomised Evaluation of Shared Prescribing for Elderly people in the Community over Time): the pharmacist moderated drug management in collaboration with doctor, patient and carer. The intervention included a medication review. Implemented at 2-month intervals at each primary care trust.</p>	<p>Each primary care trust, patient, general practitioner acted as their own controls.</p>	<p>Follow up: 12 months</p>	<p>-EQ-5D health status questionnaire; before pharmaceutical care, 3 months, 12 months, immediately after end of study period and 3 years post intervention.</p> <p>-‘Utility’ estimate from published preferences of 3400 members of UK population.</p> <p>-Patient age, gender, number of drugs on repeat prescription at time of recruitment</p>	<p>Patients aged 75 years and over, and taking at least five drugs on repeat prescription</p> <p>No. of patients: 599 (598 patients for utility analysis due to incomplete EQ-5D data)</p>
<p>Cowper et al, 1998</p> <p>Veteran Affairs Medical Centre</p> <p>United States</p> <p>Randomised control trial</p>	<p>The clinical pharmacist reviewed patient laboratory findings, drug lists, hospital discharge summaries, clinic notes, procedures and test results for previous 2 years to assess appropriateness of medications prescribed using the Medication Appropriateness Index (MAI). The pharmacist made written and verbal recommendations for the physician based on principles of pharmaceutical care. The pharmacist encouraged compliance with patients following drug regimen changes.</p>	<p>The clinic nurse reviewed patients’ prescription drugs before and after physician visits. No pharmacist involvement.</p>	<p>Follow up: 12 months</p>	<p>-Drug prescribing appropriateness with MAI.</p> <p>-Chronic medical conditions</p> <p>-Veteran Affairs prescribed drugs</p> <p>-Drugs for which recommendations developed</p>	<p>Patients aged 65 years and over, and evidence of polypharmacy (prescriptions of at least 5 regularly scheduled drugs)</p> <p>No. of patients at baseline (IG/CG): 105/103</p> <p>Age: 70years</p> <p>Gender: 99% male</p> <p>-MAI scores at baseline: IG/CG: 17.7/17.6</p> <p>-MAI scores at 3 months: IG/CG: 13.4/16.5</p> <p>-MAI scores at 12 months: IG/CG: 12.8/16.7</p>

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
Elliott et al, 2014  General Practice  England  Two-group pragmatic cluster randomised trial	see Avery et al, 2012	see Avery et al, 2012	Intervention: 12 weeks  Follow up: 6 months 12 months	a. History of peptic ulcer and prescribed an NSAID without co-prescription of a proton pump inhibitor b. Have asthma and prescribed a $\beta$ blocker/asthma c. Aged $\geq 75$ years receiving long term ACE inhibitors or loop diuretics without urea and electrolyte monitoring in the previous 15 months d. Methotrexate for $\geq 3$ months without full blood or liver function test in past 3 months e. Lithium for $\geq 3$ months without a lithium concentration measurement in past 3 months f. Amiodarone for $\geq 6$ months without a thyroid function test in the past 6 months	Patients identified with potential medication error or inadequate blood-test monitoring  No. of patients at 6 months follow up (IG;CG): a. 51/1852 (3%); 86/2014 (4%) b. 499/20312 (2%); 658/22224 (3%) c. 255/4851 (5%); 436/5329 (8%) d. 122/494 (25%); 162/518 (31%) e. 67/190 (35%); 84/211 (40%) f. 81/242 (33%); 106/235 (45%)
Fretheim et al, 2006  General practice  Norway  Randomised control trial	The pharmacist conducted educational outreach visits to practices to support implementation of general practice guidelines for the use of antihypertensive and cholesterol lowering drugs. Software was installed that gave audit and feedback on physicians' risk estimation, antihypertensive drugs and achievement of treatment goals installed. Computerised reminders were linked to the medical record system.	Passive dissemination of general practice guidelines – no pharmacist outreach visit.	Follow up: 12 months	a. Prescribed thiazides for hypertension for the first time b. Cardiovascular risk assessment completed c. Treatment goal achieved (recorded cholesterol level; blood pressure)	Patients starting thiazide medication for treatment of hypertension for the first time.  No. of patients at baseline (IG; CG): a. 161/2784 (5.8%); 209/2365 (8.8%) b. not reported c. 4669/15914 (29.3%); 5174/15411 (33.6%)  No of patients at follow up (IG/CG): a. 378/2184 (17.3%); 218/1968 (11.1%) b. 147/854 (17.2%); 112/768 (14.6%) c. 5502/17213 (32.0%); 6056/16593 (36.5%)  Statistically significant effect only on prescribing.

<p>Gillespie et al, 2017</p> <p>General practice</p> <p>Ireland</p> <p>Cluster randomised controlled trial</p>	<p>OPTI-SCRIPT (Optimizing Prescribing for Older People in Primary Care: academic detailing was provided by a pharmacist on how to conduct a GP-led medicine review. The medicine review was supported by Web-based pharmaceutical treatment algorithms for GPs. The algorithms provided alternative treatment options for potentially inappropriate prescription (PIP) drugs and tailored patient information leaflets.</p>	<p>Usual care and one-off simple patient-level PIP feedback.</p>	<p>Follow up: 12 months</p>	<p>Potentially Inappropriate Prescriptions defined as:</p> <ul style="list-style-type: none"> <li>-PPI for peptic ulcer disease at full therapeutic dosage for &gt;8 weeks</li> <li>-NSAID (&gt;3 months) for relief of mild joint pain in osteoarthritis</li> <li>-Long-term (i.e. &gt;1 month), long-acting benzodiazepines and benzodiazepines with long-acting metabolites</li> <li>-Any regular duplicate drug class prescription. Excludes duplicate prescribing of drugs that may be required on a PRN basis</li> <li>-Aspirin at dose &gt;150 mg/day</li> <li>-Theophylline as monotherapy for COPD/Asthma</li> <li>-Use of aspirin and warfarin in combination without histamine H2 receptor antagonist or PPI</li> <li>-Doses of short-acting benzodiazepines, doses greater than: lorazepam 3 mg; oxazepam 60 mg; alprazolam 2 mg; temazepam 15 mg; and triazolam 0.25 mg</li> <li>-Prolonged use (&gt;1 week) of first-generation antihistamines</li> <li>-Warfarin and NSAID together</li> <li>-Calcium channel blockers with chronic constipation</li> <li>-NSAID with history of peptic ulcer disease or GI bleeding, unless with concurrent histamine H2 receptor antagonist, PPI or misoprostol</li> <li>-Bladder antimuscarinic drugs with dementia</li> <li>-TCAs with constipation</li> <li>-Digoxin at a long-term dose &gt;125 µg/day (with impaired renal function)</li> <li>-Thiazide diuretic with a history of gout</li> </ul>	<p>Patients aged 70 years or over randomly selected by the practice and have specific PIPs.</p> <p>No. of patients (IG/CG): 99/97</p> <p>No. of practices (IG/CG): 11/10</p>
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Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
				<ul style="list-style-type: none"> <li>-Glibenclamide (with type 2 diabetes mellitus)</li> <li>-Aspirin with a past history of peptic ulcer disease without histamine H2 receptor antagonist or PPI</li> <li>-Prochlorperazine or metoclopramide with Parkinsonism</li> <li>-TCAs with dementia</li> <li>-TCAs with glaucoma</li> <li>-TCAs with cardiac conductive abnormalities</li> <li>-Long-term corticosteroids (&gt;3 months) as monotherapy for rheumatoid arthritis or osteoarthritis</li> <li>-Bladder antimuscarinic drugs with chronic prostatism</li> <li>NSAID with heart failure</li> <li>TCAs with prostatism or prior history of urinary retention</li> <li>-Systemic corticosteroids instead of inhaled corticosteroids for maintenance therapy in COPD/Asthma</li> <li>-Bladder antimuscarinic drugs with chronic glaucoma</li> <li>NSAID with SSRI</li> <li>-Bladder antimuscarinic drugs with chronic constipation</li> <li>-Prednisolone (or equivalent) &gt;3 months or longer without bisphosphonate</li> <li>-NSAID with ACE-inhibitor</li> <li>-NSAID with diuretic</li> </ul>	

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
<p>Kulchaitanaroaj et al, 2012</p> <p>Community-based medical offices</p> <p>United States</p> <p>Combined data from two prospective cluster-randomised controlled clinical trials</p>	<p>Pharmacists were encouraged to attend clinic visits and contact patients at baseline and at specified follow-up points. Pharmacists could also make contact at their own discretion. Specialists were involved only at discretion of the physician. Physician-pharmacist collaboration included written, 'curbside' (informal, short communications within the clinic) telephone and face-to-face communication. The pharmacists were co-located with the physicians and communicated recommendations in person around time of patient visit to physician. Pharmacists made recommendations to address suboptimal drug regimens and educated physicians as needed.</p>	<p>Physician management only.</p>	<p>Follow up: 6 months</p>	<p>Healthcare utilisation and outcomes.</p> <p>a.Achieved blood pressure control</p> <p>b.Reduction in systolic blood pressure</p> <p>c.Reduction in diastolic blood pressure</p>	<p>Patients with hypertension aged at least 21 years. Hypertension defined as high blood pressure less than 180/100mmHg.</p> <p>No. of patients (IG/CG):252/244</p> <p>At follow up: Proportion of patients who achieved blood pressure control (IG/CG): 66.0%/41.4%</p> <p>Difference in drop of mean systolic blood pressure/mean diastolic blood pressure (IG/CG): -9.08mmHg/-3.49mmHg</p>
<p>Kulchaitanaroaj et al, 2017</p> <p>Community-based medical offices</p> <p>United States</p> <p>Two prospective, cluster randomised controlled clinical trials</p>	<p>Pharmacists were encouraged to attend clinic visits and contact patients at baseline and at specified follow-up points. Pharmacists could also make contact at their own discretion. Specialists were involved only at discretion of the physician. Physician-pharmacist collaboration included written, 'curbside' (informal, short communications within the clinic) telephone and face-to-face communication. The pharmacists were co-located with the physicians and communicated recommendations in person around time of patient visit to physician. Pharmacists made recommendations to address suboptimal drug regimens and educated physicians as needed.</p>	<p>Physician management alone.</p>	<p>Follow up: 6 months</p>	<p>Predict vascular events of acute coronary syndrome, stroke, heart failure, death or none (hypertension state).</p>	<p>Patients with hypertension aged 30 years to 74 years.</p> <p>No. of patients:399 originally from intervention and usual care groups assigned to simulated intervention group and simulated usual care group.</p> <p>Mean age: 56.7 years Male: 42.6%</p>

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
<p>Lopez-Picazo et al, 2011</p> <p>Primary care teams</p> <p>Spain</p> <p>Single-blind, cluster randomised controlled trial</p>	<p>Three groups:</p> <p>Group 1 - Specialised software, PRISMAp reviewed active prescriptions checking for active ingredients for potential interactions and generated a report that was received by the physician through the mail.</p> <p>Group 2 - clinical educational sessions were presented using the interaction report.</p> <p>Group 3 - face to face interviews between physician and pharmacist occurred with the pharmacist presenting the report.</p>	No intervention	Follow up: 15 months	<p>Most important drug interactions defined as A0 using the following classification scale:</p> <p>Clinical relevance of drug interaction (decreasing levels A to D) and remedial action (0, interactions to be avoided; 1, interactions requiring surveillance; 3, interactions requiring a modification of the dosing interval.</p>	<p>Patients older than 14 years and taking more than one medication together with their treating physician</p> <p>No. of patients: 81,805</p> <p>No. of physicians: 265</p> <p>40 primary care teams stratified according to number of physicians at centres</p> <p>Baseline: Adjusted mean of 6.7 interactions/100 patients (n=5473)</p> <p>After follow-up: Adjusted mean of 5.3 interactions/100 patients (n=4353)</p> <p>Intragroup differences and relationship between intervention type and outcome (p&lt;0.001) with no improvement in control group and Group 1, and progressive improvement in other groups.</p>
<p>Obreli-Neto et al, 2015</p> <p>Primary health care unit (public health system)</p> <p>Brazil</p> <p>Randomised controlled trial</p>	<p>The pharmacist followed up individual patients for a Pharmacotherapy Workup every 6 months. Pharmacists assessed compliance, discussed medication with patients and family, suggested drug regimens to the physician, prepared special packages to provide a visual reminder that medicine was taken and developed care plans. The pharmacist also worked with other health professionals to modify diet and physical activities plans. Group education was provided by pharmacists.</p>	<p>Usual care: patients met for 3 monthly appointment with physicians and monthly appointments with nurses. No pharmaceutical care.</p>	Follow up: 36 months	<p>Mean values for intervention and control groups at baseline and follow up for:</p> <p>a.Systolic blood pressure</p> <p>b.Diastolic blood pressure</p> <p>c.Fasting blood glucose levels</p> <p>d.Haemoglobin A1c</p> <p>e.LDL cholesterol</p>	<p>Aged 60 years or over, diagnosed with diabetes or hypertension and under drug treatment</p> <p>No. of patients (IG/CG):97/97</p> <p>Proportion of patients achieving clinical outcome goals (mean reduction in clinical measures) at baseline (IG/CG):</p> <p>a.26.8%/26.8%</p> <p>b.27.9%/29.9%</p> <p>c.29.9%/30.9%</p> <p>d.3.3%/3.3%</p>

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
					<p>e.59.8%/63.9%</p> <p>Proportion of patients achieving clinical outcome goals (mean reduction in clinical measures) at follow up (IG/CG):</p> <p>a.86.6%/30.9%</p> <p>b.84.8%/27.4%</p> <p>c.70.1%/27.8%</p> <p>d.63.3%/3.3%</p> <p>e.80.4%63.9%</p> <p>No significant changes in control group between baseline and intervention.</p>
<p>Polgreen et al, 2015</p> <p>Primary care offices</p> <p>United States</p> <p>Cluster randomised controlled trial</p>	<p>Collaboration Among Pharmacist and Physicians to Improve Outcomes Now (CAPTION): Initially, a pharmacist conducted a patient medication history, patient medication knowledge assessment, and assessment of side effects and patient compliance. The pharmacist then called the patient at 2 weeks and had face to face visits with them at 1, 2, 4, 6 and 8 months, with additional visits if needed. The pharmacist developed a care plan and made recommendations to the physician to adjust therapy. This implementation trial did not require strict adherence to this protocol, but all pharmacist visits were tracked.</p>	<p>Usual care – no pharmacist involvement</p>	<p>Follow up: 9 months</p>	<p>Systolic blood pressure</p> <p>Diastolic blood pressure</p> <p>Hypertension control</p> <p>Adverse events</p>	<p>At least 18 years of age, with uncontrolled hypertension defined as BP&gt;140mmHg systolic or &gt;90mmhg diastolic. For patients with diabetes mellitus or chronic kidney disease, uncontrolled hypertension defined as BP&gt;130 mmHg and &gt;80mmHg.</p> <p>No. of patients (IG/CG): 401/224</p> <p>Mean age:61</p> <p>Male:39.7%</p> <p>Ethnicity: Blacks (38.4%)</p> <p>Hispanic or Latino (14.2%)</p> <p>At follow-up:</p> <p>Average systolic blood pressure for intervention group 6.1mmHg lower than control group</p> <p>Average diastolic blood pressure for intervention group 2.9mmHg lower than control group</p>



Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
					43% of patients with controlled hypertension in intervention group compared with 34% in control group
Simpson et al, 2015  Primary care clinic  United States  Randomised controlled trial	The pharmacist met with patients and conducted a medication history and physical examination including blood pressure measurement. The pharmacist made recommendations to the prescribing physician based on current clinical practice guidelines. The pharmacist followed up with patients to address any issues with medication management at discretion of the pharmacist, patient and physician.	Usual care – no pharmacist involvement	Follow up: 12 months	<p>Prescription drug use, changes in blood glucose, blood pressure, lipid levels</p> <p>10% or more decrease in systolic blood pressure</p> <p>Change in predicted 10 year 10-year risk of cardiovascular disease (using UKPDS Risk Engine)</p> <p>Initiation of guideline-concordant antiplatelet therapy</p> <p>Change in medication management of hypertension</p>	<p>Patients with Type 2 diabetes</p> <p>No. of patients (IG/CG):65/58 Mean age (IG/CG): 56.9/61.5 Male (IG/CG):37%/40%</p> <p>Predicted 10-year risk of cardiovascular disease at baseline (mean; IG/CG): 14.6%/14.2%</p> <p>Predicted 10-year risk of cardiovascular disease at follow up (mean; IG/CG): 12.0%/13.4%</p> <p>Annualised reduction in risk of cardiovascular event (IG.CG): 0.33%/0.06%</p>
Sorensen et al, 2004  General practice and community pharmacy  Australia (patients in Qld, NSW and WA)  Randomised controlled trial	GPs coordinated multidisciplinary teamwork which in practice saw linking up of pharmacists and GPs. Two education sessions about managing prescribing issues attended by GPs and pharmacists. A flexible intervention with the predominant process involving a home visit by the pharmacist for medication review that was initiated by a GP referral. The pharmacist made recommendations to the GP and discussed with health care team. GP developed action plan and implemented actions and followed up at 6 weeks.	Usual care	Follow up: 6 months	<p>Effectiveness assessed using the clinical value compass which is defined by health-related quality of life, patient satisfaction, clinical outcomes and costs.</p> <p>a.Functional status: Health related quality of life using SF-36 b.Adverse drug events (medication review, self-reported and physician reported through questionnaire) c.Number of GP visits d.Hospital services e.Duke's Severity of Illness Visual Analogue Scale (DUSOI-A)</p>	<p>Patients at risk of medication misadventure defined as:</p> <p>(i) on five or more regular medications; (ii) taking 12 or more doses of medication per day; (iii) suffer from three or more medical conditions; (iv) suspected by GPs to be non-adherent with their medication treatment regimen; (v) on medication(s) with a narrow therapeutic index or requiring therapeutic monitoring; (vi) had significant changes made to the medication regimen in the previous 3 months; (vii) had signs or symptoms suggestive of possible medication-induced</p>

Author, Year, Setting, Country, Study design	Intervention	Control	Intervention /Follow up duration	Clinical measures	Participants for cost-effectiveness analysis
				f. GP plans and actions implemented, and patient satisfaction	<p>problems; (viii) had an inadequate response to medication treatment; (ix) admitted to hospital in the preceding 4 weeks; or (x) at risk in managing their own medications due to language difficulties, dexterity problems or impaired sight.</p> <p>No. of patients (IG/CG):106/196 No. of GPs (IG/CG): 48/44</p> <p>Statistical significance was not demonstrated in any domain of the clinical value compass. Positive trends in ADEs and severity of illness and healthcare service costs.</p>

**Table 2. Description of cost-effectiveness studies investigating pharmacist interventions in primary health care settings. The table includes the economic measures used, the methods and the findings reported for the cost-effectiveness analysis.**

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
<p>Avery et al, 2012</p> <p>General Practice</p> <p>England</p> <p>Two-group pragmatic cluster randomised trial</p>	<p>-Direct costs of provision of the intervention: report-generation costs, pharmacist training sessions, facilitated meetings, monthly meetings, practice feedback meetings, time spent in each practice outside meetings following up errors.</p> <p>-Costs for control group: report generation costs</p>	<p>Cost per additional medication error avoided due to the intervention at 6 months and 12 months post intervention.</p> <p>Health system perspective</p> <p>Incremental cost-effectiveness analysis</p> <p>Costs and outcomes adjusted for practice characteristics. Simple probabilistic decision-analytic model to generate cost-effectiveness ratios for differences in error rates between the intervention and control groups.</p> <p><math display="block">\frac{(\text{cost PINCER} - \text{cost simple feedback})}{(\text{outcome PINCER} - \text{outcome simple feedback})}</math></p> <p>Sensitivity analysis to establish cost-effectiveness ratios when time horizon was 12 months</p>	<p>PINCER had a 95% probability of being cost effective if the decision-maker's ceiling willingness to pay reached £75 per error avoided (at 6 months) or £85 per error avoided (at 12 months). This is sustained at 12 months suggesting that the intervention could be delivered yearly and still retain equivalent cost-effectiveness.</p>
<p>Bojke et al, 2010</p> <p>General practice and community pharmacy</p> <p>England</p> <p>Randomised multiple interrupted time-series</p>	<p>-Costs of intervention to the NHS including community pharmacy costs such as time spent developing a care plan, health service utilisation over 4 years, drugs prescribed through acute and repeat prescriptions, laboratory tests, visits to general practice, home visits, telephone consultations, inpatient admission, length of stay, outpatient visits.</p>	<p>Mean incremental cost per additional QALY</p> <p>Health system perspective</p> <p>Difference-in-difference econometric model to estimate difference in mean costs and outcomes between individual experiencing usual care and same individual experiencing the intervention (comparison of costs and QALYs between pharmaceutical care and usual care)</p> <p>Incremental cost-effectiveness analysis</p> <p>Monte Carlo simulation to reflect uncertainty in estimated costs and QALYs</p>	<p>National Institute for Health and Clinical Excellence generally uses a threshold willingness to pay of £20000 and £30000 per QALY.</p> <p>Findings suggest that the pharmaceutical intervention costs £10000 per QALY gained and is therefore, on average, cost-effective. However, the uncertainty in differential costs and QALYs means that there is a 78%-81% probability that pharmaceutical care is cost-effective at a threshold between £20000 and £30000 per QALY.</p>

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
Cowper et al, 1998  Veteran Affairs Medical Centre  United States  Randomised control trial	-Costs of intervention: Fixed costs including pharmacist orientation, intervention protocol, and equipment. Variable costs related to the intervention including personnel time and supplies. Cost of health care services received by patients including clinic visits, drugs, diagnostic tests, hospitalisation and average per diem cost of inpatient care.	Cost per 1-unit change in MAI  Health system perspective  Median values of intervention and control patients compared with Wilcoxon rank sum test  Cost-effectiveness ratio $\frac{(\text{Intervention} + \text{drug cost/patient})_{\text{Intervention}} - (\text{drug cost/patient})_{\text{control}}}{\text{Change in MAI/patient}_{\text{Intervention}} - \text{change in MAI/patient}_{\text{control}}}$	Cost-effectiveness ratio for the intervention (mean change in MAI 4.0) was \$7.50 per 1-unit change in MAI. Excluding drug costs, the ratio was \$30/1 unit change in MAI.  Willingness to pay threshold not reported.  The intervention was found to be relatively low cost for improving prescribing for elderly patients.
Elliott et al, 2014  General Practice  England  Two-group pragmatic cluster randomised trial	-Direct costs of provision of the intervention as described in Avery et al, 2012. -Direct costs from health system perspective -Drew on literature-derived error-specific projected harm to generate estimates on patient outcomes and NHS costs	Cost per additional QALY Health system perspective  Economic models developed for each medication error to generate costs and QALYs for PINCER. Modelled using clinical measures at 6 months.  Involved design of Markov models, informed by published models where possible and UK sources. Models populated with probability, cost and health status data to generate outcomes and costs in a cohort with and without error present.  Incremental impact of PINCER costs and outcomes for each error estimated in practice population and used to determine total incremental impact of PINCER costs and outcomes for one practice.  Incremental cost effectiveness ratio $\frac{(\text{Cost}_{\text{PINCER}} - \text{Cost}_{\text{Simple Feedback}})}{(\text{QALY}_{\text{PINCER}} - \text{QALY}_{\text{Simple feedback}})}$ Probabilistic analysis conducted	PINCER reached 59% probability of being cost effective at a threshold ceiling willingness-to-pay for a QALY of £20000  Without ACE inhibitor errors, probability of cost-effectiveness at £20000 increased to 65%.  For the two most robust models (NSAIDs and amiodarone prescribing errors), cost-effectiveness increased to 100%.  The study found that cost-effectiveness at a threshold of £20000 was achieved by targeting specific monitoring errors with evidence of effects on patient outcomes.

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
Fretheim et al, 2006 General practice Norway Randomised control trial	-Non-recurring costs including development of software and pharmacist training. Recurring costs including printed materials, travel, salaries for pharmacist, administration, opportunity cost of physicians' time during outreach visits, number of consultations, drug costs.	Cost minimisation: if savings on drug costs were greater than intervention costs  Cost-effectiveness analysis: Incremental cost effectiveness ratio of intervention versus usual care  Health system perspective  Adjusted for baseline differences between groups.  Univariate sensitivity analyses with adjust values for variables that could impact on findings.  Used model to scale intervention to national outreach program.	Cost-minimisation analysis: Net cost of implementing the intervention in study population was US\$53,395 or US\$763 per practice.  Cost-effectiveness analysis: Cost incurred per additional patient started on a thiazide rather than another antihypertensive drug.  Study population: Cost per additional patient started on a thiazide due to the intervention was US\$454. Costs of the intervention outweighed savings in drug expenditures due to increased use of thiazides, except when intervention effects were assumed to be sustained for 2 years.  National scale up: US\$183 per additional patient started on a thiazide. The authors reported expected savings within 2 years if the intervention was implemented in a national program.  Willingness to pay threshold not reported.
Gillespie et al, 2017 General practice Ireland Cluster randomised controlled trial	-Cost of intervention: pharmacist and GP time, educational materials, consumables, travel. -Cost relating to PIPs: prescribed drugs. -Cost relating to health care service use including GP and nurse consultations, outpatient visits, hospital visits.  -Resource use through practice note searches and patient questionnaire, the EQ5D-3L, at baseline and 12 months.	Cost per Potentially Inappropriate Prescriptions avoided and cost per QALY gained  Health provider perspective  Used guidelines for health technology assessment for Ireland.  Intention to treat basis  Incremental cost effectiveness analysis Controlled for age, gender, baseline PIPs, number of GPs per practice and practice location.	The intervention was more costly and more effective in terms of PIPs avoided and QALYs gained compared with the control.  Cost effective if willing to pay €30,535 per QALY gained  Cost effective if willing to pay €1,269 per potentially inappropriate prescription avoided  84.5% probability that the intervention was cost-effective at a threshold of €2,500 per PIP avoided or higher.

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
		<p>Sensitivity analysis conducted.</p> <p>QALYs estimated from questionnaires.</p>	<p>60.2% probability that intervention cost-effective at threshold of €45,000 per QALY gained.</p>
<p>Kulchaitanaroaj et al, 2012</p> <p>Community-based medical offices</p> <p>United States</p> <p>Combined data from two prospective cluster-randomised controlled clinical trials</p>	<p>Cost of provider time, laboratory tests and antihypertensive drugs.</p>	<p>Cost for one additional patient to achieve blood pressure control</p> <p>Cost-effectiveness ratio:</p> $\frac{\text{Difference in intervention and control costs}}{\text{Difference in hypertension control rates for intervention and control groups}}$ <p>Cost to achieve an additional 1mmHg reduction</p> <p>Cost-effectiveness ratio:</p> $\frac{\text{Difference in cost}}{\text{Difference in blood pressure}}$ <p>Costs adjusted for difference in patient characteristics in intervention and control groups.</p> <p>Sensitivity analyses conducted for key assumptions of times/provider activity and costs assumed for patients who dropped out of the study</p>	<p>Cost for one additional patient to achieve blood pressure control was \$1338.05</p> <p>\$36.25 per additional 1mmHg reduction in systolic blood pressure and \$94.32 per additional 1mmHg reduction in diastolic blood pressure.</p> <p>The intervention successfully reduced systolic and diastolic blood pressure, and increased blood pressure control at increased health care costs. The authors compared their cost-effectiveness ratio with other studies and concluded that the cost-effectiveness of the intervention required further investigation.</p> <p>Willingness to pay threshold not reported.</p>
<p>Kulchaitanaroaj et al, 2017</p> <p>Community-based medical offices</p> <p>United States</p> <p>Two prospective, cluster randomised controlled clinical trials</p>	<p>Health professionals time providing direct patient care and collaborating, laboratory tests, antihypertensive medications and overheads.</p> <p>Costs of each vascular disease included cost of hospitalisation, physician fees, outpatient visits, medications, home healthcare and nursing home care.</p>	<p>Cost per QALY gained.</p> <p>Payer perspective</p> <p>Markov model cohort simulation to predict acute coronary syndrome, stroke and health failure throughout lifetime.</p> <p>6-month Markov cycles</p> <p>Incremental cost-effectiveness ratios at time horizons of 5 years, 10 years and lifetime</p> <p>Created 6 hypothetical cohorts with modified risk profiles to explore effects of intervention on</p>	<p>Lifetime horizon:</p> <p>The intervention compared with usual care increased QALYs by 0.14 per person.</p> <p>The incremental cost-effectiveness ratio of the intervention was \$26,807.83 per QALY gained.</p> <p>Horizon of 10 years:</p> <p>The incremental cost-effectiveness ratio of the intervention was \$39,084.65 per QALY gained.</p> <p>Horizon of 5 years:</p> <p>The incremental cost-effectiveness ratio of the intervention was \$78,547.07 per QALY gained.</p>

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
		individuals with high and low risk of vascular diseases for sensitivity analyses.	Willingness to pay threshold \$50000-\$100000 Intervention more cost-effective for high-risk patients
Lopez-Picazo et al, 2011  Primary care teams  Spain  Single-blind, cluster randomised controlled trial	Intervention costs: tangible costs only including administration, mailing, infrastructure to develop the PRISMAp system, training and time of pharmacist.	Incremental cost incurred to reduce the mean of potential drugs interaction per 100 patients by 1% more than the control group.  Intention to treat analysis to assess effectiveness of each intervention  Adjusted for baseline differences in patient and physician characteristics between intervention groups.  Incremental cost effectiveness analysis	Session and face to face groups - 4.2€ and 4.5€, respectively, per 1% of improvement per 100 patients beyond the control group.  The clinical educational session was the most cost-effective intervention.  Willingness to pay threshold not reported.
Obreli-Neto et al, 2015  Primary health care unit (public health system)  Brazil  Randomised controlled trial	Costs for intervention and control groups including appointments with health professionals, hospital visits, drug therapy costs.	Incremental cost-effectiveness ratio per QALY  Incremental cost-effectiveness ratio: $\frac{\text{Difference in total direct health care cost between intervention and control groups}}{\text{Difference in QALY between intervention and control groups}}$ Health utility estimated for each disease state – blindness, end-stage renal disease, lower extremity amputation, stroke, myocardial infarction, angina. Other health states set to 1.	Average pharmaceutical care costs for the intervention estimated at US\$69.60 per 36 months more than usual care but yielded greater benefits, estimated at 1.302 QALYs. Incremental cost-effectiveness ratio per QALY was estimated at \$53.50  The authors reported that the intervention had an acceptable ICER per QALY. The intervention did not significantly increase health care cost and significantly improved health outcomes. Willingness to pay threshold not reported.

Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
<p>Polgreen et al, 2015</p> <p>Primary care offices</p> <p>United States</p> <p>Cluster randomised controlled trial</p>	<p>Costs include pharmacist time spent performing activities of the intervention, physician appointments, anti-hypertensive drugs. Cost was difference between average intervention costs and control costs.</p>	<p>Cost to lower blood pressure by 1mmHg.</p> <p>Societal perspective</p> <p>Incremental cost-effectiveness ratio:</p> $\frac{\text{Additional costs of the intervention}}{\text{Change in both systolic and diastolic BP related to the intervention}}$ <p>And;</p> $\frac{\text{Additional costs of the intervention}}{\text{Percentage of subjects who achieved 'BP control' as a result of the intervention}}$ <p>Sensitivity analysis conducted</p>	<p>Cost to lower BP by 1mmHg was \$33.27 for systolic and \$69.98 for diastolic.</p> <p>Comparing rates in the intervention and control groups, the cost to increase BP control by 1 percentage point was \$22.55.</p> <p>Following sensitivity analysis that included only patients who completed the 9 month intervention (n=539):</p> <ul style="list-style-type: none"> <li>-Cost to lower BP by 1mmHg was \$38.82 for systolic and \$81.66 for diastolic.</li> <li>-Comparing rates in the intervention and control groups, the cost to increase BP control by 1 percentage point was \$26.31.</li> </ul> <p>When drug cost were deflated (n=539):</p> <ul style="list-style-type: none"> <li>-Cost to lower BP by 1mmHg was \$26.54 for systolic and \$55.82 for diastolic.</li> <li>-Comparing rates in the intervention and control groups, the cost to increase BP control by 1 percentage point was \$17.99.</li> </ul> <p>The authors concluded that the intervention demonstrated cost-effectiveness in a broader patient population than other studies of similar interventions. Willingness to pay not reported.</p>
<p>Simpson et al, 2015</p> <p>Primary care clinic</p> <p>United States</p> <p>Randomised controlled trial</p>	<p>Costs of intervention, prescription medication, health care services provided by health professionals, emergency department visits, hospitalisation; pharmacist time; drug utilisation</p> <p>Health measures: UKPDS Risk Engine</p> <p>Satisfaction measure: patient questionnaire</p>	<p>Cost to reduce annualised cardiovascular risk by 1%</p> <p>Public payer perspective</p> <p>Intention to treat analysis</p> <p>Sensitivity analysis conducted</p> <p>Incremental cost effectiveness ratio on a per patient basis:</p>	<p>95% probability that intervention is cost-effective at level of about \$4000 per 1% reduction in annualised cardiovascular risk.</p> <p>The cost-effectiveness threshold (society's willingness to pay for a reduction of 1% in cardiovascular risk) was estimated to be \$33,215.</p>



Author, Year, Setting, Country, Study design	Economic measures	Cost-effectiveness analysis method	Cost-effectiveness analysis results
		<p>Difference in overall average 1-year cost per patient between study arms</p> <p>Change from baseline in annual risk of cardiovascular event</p> <p>Estimated threshold for intervention from literature</p>	<p>The authors reported that the intervention was cost-effective in reducing cardiovascular risk in patients with Type 2 diabetes (one year time horizon).</p>
<p>Sorensen et al, 2004</p> <p>General practice and community pharmacy</p> <p>Australia (patients in Qld, NSW and WA)</p> <p>Randomised controlled trial</p>	<p>-Costs of medication and health service costs (less intervention costs) were measured pre-intervention and during the trial. GPs received payment for initial consult, discussion with pharmacist, development of action plan and consultation with patient and follow-up patient consultation, and pharmacists were paid for home visits and medication review, and discussion with GP.</p>	<p>Cost-saving per intervention patient.</p> <p>Intention to treat analysis</p> <p>Cost savings per patient deduced from differences in total sum of medication and healthcare costs between intervention and control groups.</p> <p>Marginal cost benefit per patient defined as cost savings per patient assuming no change in patient outcomes due to the intervention.</p> <p>Cost-effectiveness ratio to reduce adverse drug events</p> <p>Cost-effectiveness ratio to improve health outcomes</p>	<p>After adjusting for differences in cumulative costs vs. time (medication plus medical service costs) up to the time of patient enrolment, the cumulative cost/patient over the 8 months from enrolment was AUS\$5730 (£2234) for the control group and AUS\$5401 (£2105) for the intervention group.</p> <p>After subtracting the differences in costs for the trial between intervention and control groups [AUS\$275 (£107) per intervention patient], the net <i>cost saving</i> per intervention patient (marginal cost benefit) was AUS\$54 (~ £19) per patient relative to controls.</p> <p>Incremental cost-effectiveness ratio in reducing ADEs and in improving DUSOI-A for the groups were AUS\$69 (~ £24) and AUS\$65 (~ £23), respectively (though reduction of DUSOI-A for intervention patients was not statistically significant)</p> <p>The authors concluded that the cost-effectiveness ratio of the intervention based on cost savings, reduced adverse events and improved health outcomes was small.</p> <p>Willingness to pay not reported.</p>

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## **Appendix 1. Search strategy**

### Emcare

((“exp pharmacy/” OR “exp pharmacist/”) OR ("pharmaceutic service" OR "pharmaceutic services" OR "pharmaceutical care" OR "pharmaceutical service" OR "pharmaceutical services" OR "pharmacist\*" OR "pharmacy" OR "pharmacies")).mp.

AND

((“exp primary health care/” OR “patient care planning/” OR “exp general practice/” OR “exp indigenous health care/”) OR ("primary care" OR "primary health care" OR "primary healthcare" OR "general practice" OR "general practices" OR "family practice" OR "family practices" OR "health indigenous service" OR "health indigenous services" OR "indigenous health service" OR "indigenous health services" OR ACCHS OR "aboriginal community controlled health service" OR "aboriginal community-controlled health service" OR "aboriginal community controlled health services" OR "aboriginal community-controlled health services" OR "aboriginal medical service" OR "aboriginal medical services" OR "AMS" OR "indigenous medical service" OR "indigenous medical services" OR "medical indigenous service" OR "medical indigenous services" OR "medical aboriginal service" OR "medical aboriginal services")).mp.

AND

((“cost effectiveness analysis/” OR “exp cost benefit analysis/” OR “pharmacoeconomics/”) OR ("benefits and costs" OR "cost benefit" OR "cost effectiveness" OR "cost utility analysis" OR "cost-benefit" OR "cost-utility" OR "cost-effectiveness" OR "costs and benefits" OR "economic evaluation" OR "economic evaluations" OR "pharmaceutical economics" OR "pharmacoeconomics" OR "pharmacy economic" OR "pharmacy economics")).mp.

### CINAHL

((MH “Pharmacy and Pharmacology” OR MH “Pharmacy service” OR MH “Pharmacists”) OR ("pharmaceutic service" OR "pharmaceutic services" OR "pharmaceutical care" OR "pharmaceutical service" OR "pharmaceutical services" OR "pharmacist\*" OR "pharmacy" OR "pharmacies")).mp.

AND

((MH “Primary Health Care” OR MH “Patient Care Plans” OR MH “Patient Centred Care” OR MH “Multidisciplinary Care Team” OR MH “Family Practice” OR MH “Health Services, Indigenous”) OR ("primary care" OR "primary health care" OR "primary healthcare" OR "general practice" OR "general practices" OR "family practice" OR "family practices" OR "health indigenous service" OR "health indigenous services" OR "indigenous health service" OR "indigenous health services" OR ACCHS OR "aboriginal community controlled health service" OR "aboriginal community-controlled health service" OR "aboriginal community controlled health services" OR "aboriginal community-controlled health services" OR "aboriginal medical service" OR "aboriginal medical services" OR "AMS" OR "indigenous medical service" OR "indigenous medical services" OR "medical indigenous service" OR "medical indigenous services" OR "medical aboriginal service" OR "medical aboriginal services")).mp.

AND

((MH “Costs and Cost Analysis+” OR MH “Economics, Pharmaceutical”) OR ("benefits and costs" OR "cost benefit" OR "cost effectiveness" OR "cost utility analysis" OR "cost-benefit" OR "cost-utility" OR "cost-effectiveness" OR "costs and benefits" OR "economic evaluation" OR "economic evaluations" OR "pharmaceutical economics" OR "pharmacoeconomics" OR "pharmacy economic" OR "pharmacy economics")).mp.

Medline

((“exp Pharmacy/ or Pharmacy Research/” OR “exp Pharmacists/” OR “exp Pharmaceutical Services/”) "pharmaceutic service" OR "pharmaceutic services" OR "pharmaceutical care" OR "pharmaceutical service" OR "pharmaceutical services" OR "pharmacist\*" or "pharmacy" or "pharmacies")).mp.

AND

((“exp General Practice/ OR “exp Primary Health Care/” OR exp “Health Services, Indigenous/” OR “Health Services for the Aged/” OR “Patient Care Team/” OR “Patient Care Planning/”) OR ("primary care" or "primary health care" or "primary healthcare" or "general practice" or "general practices" or "family practice" or "family practices" or "health indigenous service" or "health indigenous services" or "indigenous health service" or "indigenous health services" or ACCHS or "aboriginal community controlled health service" or "aboriginal community-controlled health service" or "aboriginal community controlled health services" or "aboriginal community-controlled health services" or "aboriginal medical service" or "aboriginal medical services" or "AMS" or "indigenous medical service" or "indigenous medical services" or "medical indigenous service" or "medical indigenous services" or "medical aboriginal service" or "medical aboriginal services")).mp.

AND

((“Models, Economic/” OR “exp cost-benefit analysis/ or exp health care costs/ or exp economics, pharmaceutical/”) OR ("benefits and costs" OR "cost benefit" OR "cost effectiveness" OR "cost utility analysis" OR "cost-benefit" OR "cost-utility" OR "cost-effectiveness" OR "costs and benefits" OR "economic evaluation" OR "economic evaluations" OR "pharmaceutical economics" OR "pharmacoeconomics" OR "pharmacy economic" OR "pharmacy economics")).mp.