The Value of Pharmacist Professional Services in the Community Setting

A systematic review of the literature 1990-2002

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Executive Summary

This review of the value of professional pharmacist services was commissioned by the Pharmacy Guild of Australia to inform ongoing research and strategic planning for the development of professional pharmacist services in the community setting both within Australia and internationally.

This review encompasses the research effort published in the English language since 1990 supporting professional pharmacy practice in the community setting and evaluates the strength of the evidence for the effectiveness of professional pharmacist services, in terms of consumer outcomes, and where possible, the economic benefit. In reaching conclusions about the value of professional pharmacist services, we utilised the best available evidence, (i.e. studies that had employed rigorous research design) and the best available outcomes, (i.e. studies that had monitored changes in health outcomes).

It was encouraging to find a large number of trials meeting this level of methodological rigour and utilising changes in health outcomes as study endpoints. This review encompasses over 70 randomised controlled trials evaluating professional pharmacist services that have monitored patient outcomes as the end-point for the study. These studies were conducted in the community, outpatient and extended-care settings.

There is clear evidence across a number of different settings for the effectiveness of pharmaceutical care services, continuity of care services post-hospital discharge, pharmacist education services to consumers and pharmacist education services to health practitioners for improving patient outcomes or medication use.

There is more limited evidence, often limited to one or two countries, but still positive evidence for the effectiveness of pharmacist managed clinics, pharmacist review of repeat prescribing and pharmacist participation in therapeutic decision making in improving patient outcomes.

New professional services that have not yet been adequately evaluated include pharmacist administration of vaccines, pharmacist involvement in pre-admission clinics and pharmacist participation in hospital in the home services.

There were some areas of established pharmacy professional practice for which rigorous controlled studies were either not located or only a small number were located with equivocal results. More research is still required to establish best practice for medication review in aged-care facilities and medication review in the outpatient setting, as well as pharmacist participation in pharmacist-only and pharmacy-only medicines use. In addition, more research is required concerning pharmacist involvement in smoking cessation services and screening services.

Economic evaluation of the value of pharmacist professional services is limited. Nine studies meeting the review criteria assessed the impact of pharmacist professional services on drug costs, of which six showed a significant effect. Eight studies were descriptive economic studies and included comparisons of various health care

resources between the intervention and control groups, however, only 2 studies showed a reduction in health care costs. Only two full economic evaluation were located. The clinical relevance of the cost/effectiveness ratio used in one study was unclear, while the second cost-effectiveness study related to smoking cessation services in a pilot study in only 2 community services, which means the results cannot be reasonably extrapolated.

Given the scarcity of economic studies for most types of clinical pharmacist services, it is difficult to comment on their impact on drug costs, health care resource costs or cost-effectiveness. Most of the evidence comes from pharmaceutical care studies and medication review studies. There is some evidence that these interventions can reduce drug costs. Further studies would be needed to establish for how long these savings are maintained and how frequently these interventions should take place.

Common methodological limitations observed in a number of studies included the open allocation of subjects to intervention or control groups and the assessment of outcomes by reviewers who were aware of the group allocation of subjects. Methodological rigour would be improved if the pharmacists providing the intervention were unaware of the group allocation of subjects, or alternatively, if the pharmacy was used as the unit of allocation, if steps were taken to avoid cross contamination between pharmacies and subjects were unaware of pharmacy allocation. In addition, independent reviewers blinded to subject group allocation, should be utilised to monitor outcomes. One further methodological consideration is the type of end-point monitored. The variability in end-points used in the studies considered in this review often made it difficult to synthesise findings. In addition, health related quality of life measures were commonly utilised, often demonstrating no effect, which raises questions of whether this is due to the lack of effect of the service, or the lack of sensitivity of the measure. By comparison, adverse drug events were seldom utilised as an outcome measure, even where the aim of the study was to reduce medication misadventure. Where adverse drug events were monitored as an endpoint, variable methods were used and explicit criteria for assessing adverse drug events often omitted, despite their existence. Given that the focus of professional pharmacist services is to improve medication use and reduce medication misadventure adverse drug events are likely to be a more sensitive endpoint for assessing the effect than health-related quality of life measures. It would seem appropriate to give further consideration to incorporating adverse drug events, assessed by independent panels utilising explicit criteria, more commonly as an outcome measure of the services.

Overall, this review demonstrates that there is considerable high quality evidence to support the value of professional pharmacy services in the community setting. Studies evaluating the majority of professional services currently provided by community pharmacists were located and, importantly, demonstrated improvements in outcomes for patients. Improvement in economic analyses is still required. Where the evidence is sound, consideration now needs to be given to implementing these services more broadly within a country's health system.

Abbreviations

ACAT	Aged Care Assessment Team
ACE	angiotensin converting enzyme
ADE	adverse drug event
ADR	adverse drug reaction
AHRQ	Agency for Healthcare Research and Quality
BASDEC	Brief Assessment Schedule Depression Cards
BGL	blood glucose level
BMI	body mass index
BP	blood pressure
CHF	congestive heart failure
CI	confidence interval
COPD	chronic obstructive pulmonary disease
CRBRS	Crichton-Royal Behaviour Rating Scale
DDD	defined daily dose
DRP	drug-related problem
DUSC	Drug Utilization Sub-Committee
FVC	forced vital capacity
GDS	Geriatric Depression Scale
GP	general practitioner
HAART	highly active antiretroviral therapy
HbA1C	glycosylated haemoglobin
HDL	high density lipoprotein
HIC	Health Insurance Commission
HIV	human immunodeficiency virus
HMO	health maintenance organization
HRQOL	health-related quality of life
ICD-9-CM	International Classification of Diseases 9th Revision Clinical Modification
INR	international normalised ratio
KP	Kaiser Permanente
LDL	low density lipoprotein
MAI	Medication Appropriateness Index
MDI	metered dose inhaler
mmHg	millimetres of mercury
mmol	millimole
MMSE	Mini Mental State Examination
NIDDM	non-insulin dependent diabetes mellitus
NSAID	non-steroidal anti-inflammatory drug
NSW	New South Wales
OR	odds ratio
OTC	over-the-counter
PACT	Prescribing Analysis and Cost
PBS	Pharmaceutical Benefits Scheme
PEF	peak expiratory flow
PEFR	peak expiratory flow rate
QOL	quality of life
RCT	randomised controlled trial
S2	Schedule 2
S3	Schedule 3
SF-36	Short Form 36 Health Survey
SIGN	Scottish Intercollegiate Guidelines Network
TG	triglyceride
UTI	urinary tract infection

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1. Introduction

The publication "Value of Professional Pharmacist Services" (1) was originally published in 1998. It provided a compilation of published Australian and international literature from 1990 to June 1998 that was applicable to community pharmacy and that assessed pharmacist services in terms of potential cost-savings and quality of care.

This report builds on the original publication, incorporating more recent research findings and now including an evidence-based review of the literature published since 1990 concerning pharmacist professional services in the community setting. This review evaluates the strength of the evidence for the effectiveness of professional pharmacist services, in terms of patient outcomes, and where possible, the economic benefit. In reaching conclusions about the value of professional pharmacist services, we utilised the best available evidence, (i.e. that which had employed rigorous research design) and the best available outcomes, (i.e. that which had monitored changes in health outcomes). This review encompasses the research effort published in the English language supporting professional pharmacy practice.

This report was commissioned by the Pharmacy Guild of Australia to support strategic planning for the development of professional pharmacist services in Australia, as well as providing information that could support and direct the research effort in pharmacy practice within Australia. The review, however, is not limited to the Australian evidence but encompasses literature published internationally. Thus, this overview of rigorous research demonstrating the value of professional pharmacy services is able to support and inform the research effort and future development of professional pharmacy services in many countries around the world. As such it is a valuable document for all who work to further promote professional pharmacy practice.

Strategy used to identify studies of Professional Pharmacist Services

For the purpose of the review, "pharmacist services" were broadly defined to include any pharmacist activity aimed at promoting the quality use of medicines and improving patient outcomes. Inclusion criteria used for selecting research papers or reports were that they:

- were written in English;
- were published between January 1990 and 2002; or if unpublished were conducted during this time period;
- were randomised controlled studies or non-randomised controlled studies, pre-post comparisons with a control group;
- were undertaken in a community, ambulatory care, aged care or long-term care setting; or if undertaken in a hospital setting had to be relevant to community pharmacy (including outpatient clinics, services to improve continuity of care

between hospital and community settings, discharge services and drug information services).

In terms of the types of outcomes assessed, studies were included if they assessed –

- clinical outcomes including mortality, morbidity (including disease progression, symptoms, adverse events, quality of life) and adverse drug events; or
- surrogate or intermediate outcomes (including laboratory or other tests) with well-established connections to the clinical outcome(s) of interest; or
- other measurable variables with indirect or unestablished connection to the clinical outcome(s) of interest (including patient compliance/adherence with medication, knowledge of medications, use of medication devices, smoking cessation); or
- quality of prescribing or quality of medication use.

Economic outcomes were also included if they were presented for studies that assessed patient outcomes. Economic analyses for studies that had not demonstrated an improvement in patient outcomes were excluded.

Studies for which only an abstract could be obtained were not included in the review. Studies that assessed interventions that were performed by a group of health professionals in which the role of the pharmacist could not be isolated were also excluded. Studies that assessed outcomes only in terms of satisfaction, such as patient or physician satisfaction with the service were not included. Studies that monitored overall reductions in medication use as the sole outcome measure, with no potential to determine whether that change was likely to improve or worsen patient outcomes were excluded.

Studies published in the Australian and international literature that assessed the impact and value of professional pharmacist services were identified through searching the following databases –

- MEDLINE (via Ovid) (1990- October 2002)
- International Pharmaceutical Abstracts (1990- October 2002)
- Australasian Medical Index (via AUSThealth) (1990- October 2002)
- Current Contents (1998- October 2002)
- The Cochrane Library (accessed 15 October 2002).

Full details of the search terms and strategies used are presented in Appendix I of this report.

Full articles of original research reports and systematic reviews of pharmacist services were obtained. The bibliographies of these articles were checked in order to identify any further relevant studies. Systematic review articles included Beney et al. (2), Anderson et al. (3), Morrison and Wertheimer (4) and Singhal et al. (5). References included in the original Value of Professional Pharmacist Services Review (1) were reviewed to identify studies eligible for inclusion which were published before 1998.

In order to identify unpublished studies assessing pharmacist services in the Australian setting, academics in the Pharmacy Practice area of the pharmacy schools of the following Australian universities were contacted –

- Curtin University (Western Australia)
- University of Queensland
- James Cook University (Queensland)
- Monash University (Victorian College of Pharmacy)
- University of Tasmania
- University of Sydney
- Charles Sturt University (New South Wales)
- University of South Australia

Posts to AusPharmList (an internet discussion group for Australian pharmacy http://www.auspharmlist.net/) and E-drug (and international discussion group used by health care professionals, researchers and drug policy makers http://www.essentialdrugs.org/edrug/about.php) were also made in order to request copies of any unpublished studies assessing pharmacist services. The Australian Quality Use of Medicines Map (www.qummap.health.gov.au) was also searched for government-funded projects assessing pharmacist services. Websites of relevant pharmacist organisations were also accessed to identify reports or unpublished studies relating to pharmacist services including –

- Canadian Pharmacists' Association
- National Community Pharmacists Association (USA)
- American Society of Consultant Pharmacists
- Royal Pharmaceutical Society of Great Britain
- Guild of Healthcare Pharmacists (UK).

Classification of studies

Our search strategy identified numerous services provided by pharmacists. Services were referred to by a number of different titles and for the purposes of this review a classification system was developed which could be used to synthesise the results from comparable studies.

In classifying studies into types of services, we chose to use the interventions employed. Interventions usually consisted of one or more activities, including but not limited to:

- Provision of information;
- Provision of education;
- Medication chart review;
- Review of medical case notes;
- Patient interviews;
- Development of care plans;
- Liaison or collaboration with other health care professionals
- Monitoring signs and symptoms;
- Monitoring laboratory results;
- Device education or monitoring; and
- Follow-up.

For the purposes of this review we included interventions that utilised similar activities under one category, which we defined. This is important to consider when

reading this report, because the terms “pharmaceutical care”, “clinical pharmacy services”, “medication management” and “medication review” are used in the literature to describe a variety of practice. Sometimes the words are used interchangeably, while at other times they describe different types of practice. In this review studies which have been described by the authors as “pharmaceutical care” may appear in a different section in our classification. In a similar manner, studies that are described by the authors as “medication management” or “medication review” may have been included in the pharmaceutical care section of this review. The factor that determined the study’s categorisation in this review was not the authors’ classification, but the activities that were implemented as part of the intervention. For example, any intervention that included, a patient interview by the pharmacist to identify and resolve medication problems or manage diseases, plus the development of a care plan and follow-up was categorised as pharmaceutical care. In comparison, interventions that included medication chart review, without patient involvement or interview, were considered medication review.

Services were not categorised by target group. The particular activities implemented as part of the intervention were used for categorising the study. Many studies targeted patients in specific age groups, on specific medicines or numbers of medicines or with specified diseases. Despite the different target groups, the activities implemented as part of the intervention did not necessarily differ according to the population group targeted. For this reason, there are no chapters classified according to patients with specific disease groups (sometimes called disease management) or in specific age groups (e.g. pharmacist services to the elderly). Within each chapter of this report, we have defined the criteria used to allocate studies to the classification system.

Evaluation of the effectiveness of the services

In order to perform an evidence-based review, we included and synthesised the evidence from controlled trials of sound methodology with defined outcomes. Where controlled trials were not available, studies representing the next strongest level of evidence were included. The types of outcomes measured in each of the studies were also considered.

Studies were rated according to a hierarchy of study designs based on those used by the Scottish Intercollegiate Guidelines Network (SIGN) (6), (Table 1.1) and outcome measures based on those used previously by the Agency for Healthcare Research and Quality (AHRQ) (7) as outlined in Table 1.2.

Table 1.1 Hierarchy of study designs (based on SIGN 2000) (6)

1++	High quality meta analyses, systematic reviews of randomised controlled trials (RCTs), or RCTs with a very low risk of bias
1+	Well conducted meta analyses, systematic reviews of RCTs or RCTs with a low risk of bias
1-	Meta analyses, systematic reviews of RCTs, or RCTs with a high risk of bias
2*	Case-control or cohort studies.*
3	Non-analytic studies e.g. case reports, case series
4	Expert opinion

*Note: the SIGN classification differentiates level 2 studies into 2++, 2+ and 2-. Because level 1 studies were available for nearly all categories analysed in this review, and the level 2 studies we reviewed generally only appear in Appendix II, we collapsed the level 2 classification.

Table 1.2: Hierarchy of outcome measures (Adapted from AHRQ, 2001) (7)

Level 1	Clinical outcomes – morbidity, mortality, adverse events
Level 2	Surrogate outcomes – intermediate outcomes e.g. laboratory results with well-established connections to the clinical outcomes of interest
Level 3	Other measurable variables with an indirect or unestablished connection to the target outcome e.g. pre-test/post-test after educational intervention
Level 4	Other relevant variables, but not direct outcomes e.g. patient satisfaction or medical practitioner satisfaction

Economic Analysis Methodology

We have only included economic studies that were conducted for randomised controlled trials (level 1 method). For the economic review these studies were then classified into one of the three categories defined below. These categories have been adapted from a classification used for papers submitted to the British Medical Journal (8).

Level 1. Studies with minimal economic input: studies that have included medication costs as an outcome without considering any other costs.

Level 2. Descriptive economic studies: studies that have measured and compared the costs of the intervention group versus control group without attempting to assess the cost-effectiveness of the intervention.

Level 3. Full economic evaluation studies: studies in which analytical methods have been used to assess the cost-effectiveness of the intervention.

Note, this categorisation uses the opposite numbering system to the previous two, with level 3 studies being full economic evaluation (i.e best economic evidence).

Results

The subsequent chapters of this report present the findings for 19 professional pharmacist services. Over 70 randomised controlled trials (level 1 method) which met the inclusion criteria were reviewed. A summary of the categories of pharmacist services and the number of studies reviewed in each category is presented in Table 1.3.

Table 1.3 Summary of studies assessed for each professional service

Professional Service	**Number of level 1 studies**	**Number of level 2 studies**
Pharmaceutical care services	20	6
Continuity of care services	9	1
Pharmacist clinic services	2	5
Pre-admission clinics	0	1
Medication review for repeat prescriptions	2	0
Medication review in aged care facilities	3	2
Medication review in the outpatient setting	2	0
Pharmacist services providing education to patients or consumers	16	1
Education services for health care professionals	9	9
Drug information services	0	0
Pharmacist participation in therapeutic decision making	2	0
Pharmacist involvement in non-prescription medicine use	1	0
Smoking cessation services	3	0
Pharmacist advocacy for immunisation services	2	0
Pharmacist administration of vaccines	0	0
Hospital in the home	0	0
Interventions	0	0
Screening	0	0
Monitoring	2	0
Total	**73**	**25**

There were 19 of the studies with a randomised controlled trial design (level 1 method) that included economic evaluations for the pharmacist services, including 9 studies with minimal economic input. The types of economic studies on the pharmacist services are summarised in Table 1.4.

Table 1.4 Types of economic studies on the value of pharmacist professional services

Type of services/ type of studies	**Studies with minimal economic input**	**Descriptive economic studies**	**Full economic evaluation studies**	**Total**
Discharge liaison services				0
Pharmaceutical care services	3	5	1	9
Medication review services	2	1		3
Pharmacist review of repeat prescribing	2			2
Patient education		1		1
Educational services to health care professionals	2			2
Pharmacist-run clinics		1		1
Drug information services				0
Smoking cessation services			1	1
Immunisation				0
Pharmacist-only medicines and over-the-counter medicines				0
Therapeutic decision making				0
Other				0
Total	**9**	**8**	**2**	**19**

The full results of the review of the each of the professional pharmacist services are presented in the subsequent chapters of this report.

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2. Pharmaceutical care services

The Service

Pharmaceutical care has been defined as
"…the responsible provision of drug therapy for the purpose of achieving definite outcomes that improve a patient's quality of life. These outcomes are (i) cure of a disease; (ii) elimination or reduction of a patient's symptomatology;(iii) arresting or slowing of a disease process; or (iv) preventing a disease or symptomatology (1).

The patient care process in pharmaceutical care includes the following

- Establishment of a therapeutic relationship
- Assessment, including identification of medication-related problems
- Development of a care plan
- Evaluation
- Continuous follow-up (2)

Studies included

The words pharmaceutical care, clinical pharmacy services, medication management and medication review are used in the literature to describe a variety of practices. Sometimes the words are used interchangeably, while at other times they describe different types of practice. For the purposes of this review, an intervention was considered to be a pharmaceutical care intervention if it included, as a minimum, the following:

- a one-to-one consultation between a patient and a pharmacist with a focus on managing health or resolving drug-related problems,
- development of a care-plan
- follow-up.

Pharmaceutical care is considered a patient-focused service, very often for people considered at high-risk of medication-related problems. The service is also offered to people suffering from specific conditions or with specific risk factors for diseases. For the purposes of this review, studies that focused on any of these target groups could be included.

Medication review services, which involved a medication chart review but did not involve one–to-one consultation with patients, are reviewed in another section of this report.

Studies were included if conducted in any of the following settings:

- Community;
- Hospital outpatient clinics; or
- Ambulatory care clinics.

Continuity of care services, which often incorporate the intervention detailed above, but occur across the hospital to community interface and specifically aim to improve

communication about medicines between hospital and community care providers, are reviewed in another section of this report.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), changes in medication use, knowledge or compliance (level 1, 2 or 3 outcomes).

Studies only assessing level four outcomes, such as changes in satisfaction with or opinion of the service were excluded.

Study design

Twenty randomised controlled trials (level 1 method) were located that met the review inclusion criteria. Studies were conducted in North America, Europe and Australia. Nineteen of these studies compared pharmaceutical care with usual or standard care without a pharmaceutical care intervention. One study (3) compared a pharmaceutical care service with the same service plus a clinical audit conducted by a general practitioner. Six non-randomised controlled studies (4-9) (level 2 method) were also located which were conducted in North America, Europe and Japan. In keeping with the use of the highest available level studies to determine evidence, only level 1 method studies were used to assess the evidence for the effectiveness of pharmaceutical care. The nineteen studies that had assessed pharmaceutical care against usual care were used for determining the effectiveness of pharmaceutical care. Findings of level 2 studies are summarised in Table 1, Appendix II.

While all interventions met the inclusion criteria and included a one-to-one consultation between a pharmacist and the subjects in the intervention group, a focus on health management and resolving drug-related problems, development of a care-plan and follow-up, some interventions included multiple consultations with the pharmacist, whilst others were limited to a single-consultation plus follow-up.

One difference in the implementation of pharmaceutical care was the target group. Ten randomised controlled studies (level 1 method) targeted pharmaceutical care interventions in general patient populations, with or without age restrictions, considered at to be at risk of drug-related problems. Risk criteria varied in different studies, but generally included patients on multiple medications which varied from 3 or more medicines to only those on 5 or more medicines. A further seven randomised controlled studies had disease-specific target populations which included people with asthma, heart failure, diabetes or chronic obstructive pulmonary disease (COPD). Four randomised controlled studies assessed pharmaceutical care for the management of risk-factors including hypercholesterolaemia and hypertension. One of these studies included both a COPD and hypertension arm (10, 11).

The other major difference in implementation was single site versus multi-site trials. In general the single site trials employed trained clinical pharmacists to implement the intervention. By comparison multi-site trials usually included training sessions to up-skill community practitioners to implement the service.

The unit of randomisation in the controlled trial designs was either the pharmacy or the subject. Studies were judged to have more rigorous methods (level 1+ method) where randomisation occurred by subject independent or blinded researchers were employed to undertake baseline and follow-up outcome measures and the pharmacists implementing the intervention did not have contact with the control group. Studies were judged to have significant potential for bias, where randomisation occurred by subject and no measures were reported of how bias from the pharmacist delivering the intervention was minimised (level 1- method). In some other studies the unit of randomisation was the pharmacy to overcome cross contamination within pharmacies. One study matched pharmacies and allocated the pharmacies to intervention and control group, with subsequent selection of patients through a randomisation process. Although randomisation was generally achieved through valid randomisation procedures such as computer generated random number tables, one study employed a "coin-toss". Randomisation procedures such as a "coin-toss" may introduce more potential for bias, however, the randomisation procedure was not used to determine the level of bias in this review (that is, whether a study method was 1+ or 1-) because a number of articles did not describe the randomisation procedure that had been used. Multi-site studies that reported difficulties in implementation across sites, were judged as having potential for bias (level 1- method).

Follow-up periods in the randomised controlled trials (level 1 method) varied from a minimum of 3 months, through to 18 months, which had the potential to impact on the likelihood of detecting a difference for outcome measures, where the outcome measures utilised may have required longer time frames to demonstrate an effect.

Sample sizes in some studies were small. Unfortunately, power calculations were not always reported. Thus for some studies it was not possible to determine if the non-significant result, particularly where trends were observed, was a real result or due to lack of sufficient numbers of participants.

Study outcomes

Outcome measures employed in the studies varied, but included:

- Health-related Quality of Life as measured by the SF-36, Health Status Questionnaire or Nottingham Health Profile instrument (level 1 outcome)
- Disease specific quality of life, as measured by specialised survey instruments (level 1)
- Combined all-cause mortality and non-fatal disease specific events (level 1)
- Adverse drug events including side effects (level 1)
- Disease symptom severity (level 1)
- Hospital admissions (level 1)
- Emergency department attendances (disease-related attendances judged to be level 1)
- Surrogate endpoints, for example glycosylated haemoglobin, blood pressure (BP), lipid levels, peak expiratory flow rate (PEFR) (level 2)
- Medication appropriateness, measured by the Medication Appropriateness Index (MAI) (level 3)
- Medication or disease-state knowledge (level 3)

- Medication compliance (level 3)
- Medication device use (level 3)
- "Improvement in the process of cholesterol risk management", a composite endpoint of lipid profile measurement, prescribing of lipid-lowering medication, and increased dosage of lipid-lowering medication (level 3)
- Medication use (level 3).

Evidence for effectiveness of practice

When viewed collectively, the evidence (level 1) suggests pharmaceutical care is effective in improving patient outcomes. Trials focusing on patients with asthma (level 1+ and 1- for method with level 1 outcomes) and heart failure (level 1+ for method and level 1 outcomes) provide the strongest evidence for the effectiveness of the service. The asthma trials found pharmaceutical care improved signs and symptoms for people with asthma, with the trial for heart failure finding an improvement in combined all-cause mortality and non-fatal heart failure-related events.

Other studies (level 1- for method) have shown a reduction in adverse drug events (level 1 outcome), an improvement in medication appropriateness (level 1+ for method, level 3 outcome), a reduction in medication problems (level 1- for method, level 3 for outcomes), improvements for surrogate end-points such as blood pressure, glycosylated haemoglobin and cholesterol levels in some studies (level 2 for outcomes) and measures of improved management of cholesterol risk (level 3 outcome).

Future work needs to focus on how to maximise service delivery, including uptake by pharmacists and targeted delivery to those in need and for whom outcomes can be improved.

Australian studies support the efficacy of the practice in the Australian health-care setting.

The practice does not appear to have an impact on quality of life measures, with nine of the thirteen studies utilising this outcome reporting no effect and the others only finding small effect, but as discussed in more detail further in this chapter, this may be due to the lack of sensitivity of the measure, rather than a failure of the service.

Given the focus of pharmaceutical care is on identifying and resolving medication-related problems, more consideration should be given to utilising adverse drug events or medication incidents at an outcome measure.

No full economic evaluation on the cost-effectiveness of the care services was located. The strongest economic evidence comes from an Australian study which showed reduced drug costs, however, this was a head to head trial comparing the delivery of pharmaceutical care services against pharmaceutical care services plus an audit. All other trials assessed pharmaceutical care services against usual care, which, if economic evaluations were undertaken, the most appropriate comparison groups for determining cost effectiveness. Further studies are needed to establish the sustainability of any cost savings and how frequently pharmaceutical care interventions should take place.

Evidence for efficacy of changes in morbidity and mortality (Level 1 outcomes)

Quality of life

Thirteen of the 19 randomised controlled trials comparing pharmaceutical care with usual or standard care used quality of life as an outcome measure and the majority of these reported no significant differences between intervention and control groups on overall quality of life scores (Table 2.1). Quality of life was used as an outcome measure in both arms (COPD and hypertension) of the study by Gourley et al. (11). Not all studies reported power calculations to determine whether sample sizes were large enough to detect effect.

Six studies comparing pharmaceutical care with standard care that targeted a general patient population used quality of life as an outcome measure. One of these studies, using the SF-36, reported statistically significant difference between the control and intervention groups on quality of life scores, however, overall scores in both groups declined and the difference between groups was judged not clinically significant (12). Another of these studies (13) (level 1- for method) reported a statistically significant difference in favour of the intervention group for two of the eight domains of the SF-36 (role emotional and mental health). Quality adjusted life years were calculated, which equated the improvement as an extra 1.5 days per year of perfect health for the intervention group patients. The four other studies targeting a general patient population reported no significant differences. At least two of these studies did not include sample sizes large enough to demonstrate effect, with only one of these showing a slight trend towards effect (14, 15).

Six studies targeting specific disease-states (2 diabetes, 3 asthma, 1 COPD) used quality of life as an outcome measure. Two trials focusing on asthma utilised general and asthma-specific quality of life measures. One trial used only an asthma-specific measure (16). One trial (level 1- method) focussing on patients with asthma reported significant improvements in general and asthma specific quality of life (17), while one other asthma study reported a significant difference in favour of intervention group for the vitality domain of the SF-36 (18) (level 1+ for method). A study targeting children and adolescents with asthma found no significant effects using disease-specific quality of life measures (16). In the study targeting patients with COPD (11) it was reported that the intervention group improved for all 8 attributes of the Health Status Questionnaire while 3 of the 8 attributes worsened for the control group. The statistical significance of the difference was not reported, however. Both studies targeting diabetes found no significant differences for quality life scores.

Two randomised controlled trials targeted at patients with hypertension measured quality of life. One of these studies while demonstrating no difference in overall quality of life measures, reported significant improvements in one domain of the measure, energy (19) (level 1- for method). The other study reported no significant differences between the intervention and control groups (11)(level 1- method).

A randomised control trial comparing pharmaceutical care alone versus pharmaceutical care plus a clinical audit by a general practitioner in a general patient population judged to be “likely to benefit from clinical audit or medication review”

(3) used quality of life as an outcome measure. There were no significant differences between the groups for patient rating of quality of life at the end of the study.

Table 2.1 HRQOL

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect	Comment
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems							
Nissen and Tett, 2002 (13)	1-	Multi-centre Community setting Rural Australia	≥ 1 chronic condition & ≥5 medications	50 intervention versus 49 control patients 6 month follow-up	SF – 36	Significant difference for two domains; emotional and mental health	Overall effect is small (QALY= 1.5 extra days per year)
Bernsten et al., 2001 (14)	1-	Multi-centre Community pharmacies Europe	≥ 65 years & ≥4 medications	704 intervention and 636 control patients 18 months follow-up	SF - 36	No effect	
Volume et al., 2001 (15)	1+	Multi-centre Community pharmacies Canada	≥ 65 years & ≥3 medications	159 intervention and 204 control patients 12 to 13 months follow-up	SF – 36	No effect	
Krska et al., 2001 (20)	1-	Multi-centre General medical practices Scotland	≥ 65 years & ≥2 chronic conditions & ≥4 medications	168 intervention and 164 control patients 3 month follow-up	SF – 36	No effect	
Hanlon et al., 1996 (21);	1+	Single centre Outpatient clinic USA	≥ 65 years & ≥5 medications	88 intervention and 84 control 1 year follow-up	SF – 36	No effect	
Carter et al., 2001 (22) Ellis et al., 2000 (23); Ellis et al., 2001 (24)	1+	Multi-centre Ambulatory care clinic USA	High risk patients	523 intervention and 531 control 12 month follow-up	SF – 36	Statistically significant difference between groups	Not considered likely to be clinically significant

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect	Comment
Pharmaceutical care for diabetes							
Clifford et al., 2002 (25)	1+	Single centre Outpatient clinic Australia	> 18 years with diabetes & high risk of complications	48 intervention and 25 control 6 months follow-up	Diabetes specific quality of life instrument	No effect	Follow-up of six months, may be too short to show effect
Jaber et al., 1996 (26)	1+	Single centre Outpatient clinic; USA	African-Americans with NIDDM	17 intervention and 22 control 4 month follow-up	Health Status Questionnaire 2.0	No effect	Follow-up of four months, may be too short to show effect
Pharmaceutical care for asthma							
Herborg et al., 2001 (17, 27)	1-	Multi-centre Community pharmacies Denmark	16 to 60 years with moderate to severe asthma	209 intervention and 204 control 12 month follow-up	Nottingham health profile Living with Asthma	Significant improvements in HRQOL and asthma specific QOL	
Cordina et al., 2001 (18)	1+	Multi-centre Community pharmacies Malta	14 years or older with asthma	64 intervention versus 55 control Follow-up 12 months	SF-36 Living with Asthma Questionnaire	Vitality dimension of SF-36 significantly different No effect for Asthma Questionnaire	
Stergachis et al., 2002 (16)	1+	Multi-centre Community pharmacies USA	Paediatric and adolescent patients with asthma	153 intervention and 177 control Follow-up 12 months	Disease specific instruments	No effect	
Pharmaceutical care for COPD							
Solomon et al., 1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	40 years and older with COPD	43 intervention and 55 control Follow-up 6 months	Health Status Questionnaire 2.0	Trend to improvement but not statistically significant	Small sample size and relatively short follow-up period
Pharmaceutical care for preventative care - hypertension management							
Park et al., 1996 (19)	1-	Two centres Community Pharmacies USA	Hypertension, on medication and BP ≥ 140/90 mmHg	23 intervention versus 26 control 4 months follow-up	Health Status Questionnaire 2.0	Energy/fatigue score improved significantly compared to control	
Solomon et al., 1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	≥ 18 receiving dihydropyridine ± diuretic therapy	63 intervention and 70 control Follow-up 6 months	Hypertension/ Lipid Form 5.1	No effect	

Adverse drug events

Three studies, all of which targeted general patient populations, utilised adverse drug events as an outcome measure (level 1 outcome) (Table 2.2). One (level 1+ method) utilised a validated adverse drug event questionnaire as the measure and deemed a 2 point decrease over time as a clinically important improvement. Pre-and post-intervention measures revealed 54% of patients in the intervention group and 38% in the control group had a clinically important improvement in scores (p=0.024) (28). In an earlier study by the same authors (29) (level 1- for method) using patient self-report of medication side effects and problems as an outcome measure there were no significant difference in composite scores between the groups. Another study utilised patient self-report of adverse effects with independent assessment by a clinical pharmacist blinded to patient group (level 1+ for method) and found a trend towards improvement with 30% of patients in the intervention group compared to 40% in the control group reporting adverse drug events (p=0.19) (21).

Combined all-cause mortality and non-fatal disease specific events

One study (30) (level 1+ for method) which targeted patients with heart failure utilised combined all-cause mortality and non-fatal heart failure events as a primary outcome measure. Clinical events were assessed by a blinded physician committee. The combined measure was significantly lower in the intervention group (4 events) compared to the control (16 events) over the 6-month study (p=0.005). The effect was predominantly due to a difference in the number of heart-failure-related hospitalisations or emergency visits as the numbers of deaths were small (three deaths in the intervention versus five in the control group, p=0.48).

Disease symptom severity, days of illness

Four of the studies focusing on patients with a specific disease-state utilised disease symptom severity as an outcome measure (Table 2.3). Two of the three randomised trials that targeted patient groups with asthma reported improvements in symptom scores (18) (level 1+), (17) (level 1-). The study targeting children and adolescents with asthma used a asthma severity instrument and reported no significant effects (16) (level 1+ method). One study which focused on patients with asthma utilised days of illness as an outcome measure and found reduced days of illness in the intervention group compared with the control (17). By comparison, two other trials focusing on asthma used days absent from work or school as the outcome measure and reported no significant differences in intervention and control groups (16, 18). In the COPD arm of a multicentre study (10, 11) symptom interference with daily activities and breathlessness was assessed. There was no statistically significant difference between the groups.

A European multi-centre trial targeting general patient group reported signs and symptoms was an outcome measure. The paper did not provide enough detail as to how this was measured, nor were results reported, so no conclusions can be drawn (14).

Table 2.2. Adverse drug events

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect	Comment
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems							
Jameson and VanNoord, 2001 (28)	1+	4 centres Physician practices USA	≥5 medications	179 intervention and 161 control patients 6 month follow-up	Adverse drug effects	"Clinically important improvement" in adverse drug effects scores (defined as a decrease in score of 2 points or more from baseline) was seen for 58 patients (38%) in the control group and 67 patients (54%) in the intervention group (p=0.024).	Internal validity of measure assessed, but not external validity
Jameson et al. 1995 (29)	1-	Single-centre Health Centre USA	At risk of medication-related problems	27 intervention versus 29 control patients 6 month follow-up	Side effects and problems	Composite scores for side effects improved for both groups over the 6-month study period, there was no significant difference between the groups.	Measure not validated
Hanlon et al., 1996 (21)	1+	Single centre Outpatient clinic USA	≥ 65 years & ≥5 medications	88 intervention and 84 control 1 year follow-up	Adverse drug events	Trend towards less side effects in intervention (30%) compared with control (40%), but not statistically significant.	

Table 2.3 Symptoms

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Pharmaceutical care for asthma						
Herborg et al., 2001 (17, 27)	1-	Multi-centre Community pharmacies Denmark	16 to 60 years with moderate to severe asthma	209 intervention and 204 control 12 month follow-up	Days of illness	Less days of illness in the intervention group (3.81 per patient) compared to the control (6.57 per patient), p value between groups not reported.
Cordina et al., 2001 (18)	1+	Multi-centre Community pharmacies Malta	14 years or older with asthma	64 intervention versus 55 control Follow-up 12 months	Days absent from work/ school Asthma symptoms	No effect on number of days absent from work/school. Higher proportion of patients in the intervention group (80%) than in the control group (64%) that reported 'no wheezing' or 'only nighttime wheezing' (p=0.051). A smaller proportion of the intervention group (20%) than the control group (36%) reported nighttime wheezing all or most of the time at the final assessment, stated to be significant, no p value reported.
Stergachis et al., 2002 (16)	1+	Multi-centre Community pharmacies USA	Paediatric and adolescent patients with asthma	153 intervention and 177 control Follow-up 12 months	School days absent due to asthma	Mean school days absent due to asthma were 1.1 for the intervention and 1.7 for the controls (p=0.094).
Pharmaceutical care for COPD						
Solomon et al., 1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	40 years and older with COPD	43 intervention and 55 control Follow-up 6 months	Breathlessness (Borg scale) Symptom global assessment scale	Trend for improvement in patient-rated scores of symptom interference with daily activities and breathlessness

Health resource use: Hospitalisation and emergency admissions

The results of studies using health resource use (hospitalisation and emergency admissions) as an outcome measure are summarised in Table 2.4. One study targeting a general patient population (14) (level 1+ method) assessed number of hospital admissions as an outcome measure. The study was conducted in seven European countries, however data from only four countries was available for this outcome. Although there was a lower proportion of patients in the intervention group reporting one or more hospitalisations (36% intervention versus 40% control) the difference was not statistically significant. One other study targeting a general patient population assessed emergency admissions and found no significant differences between groups (20) (level 1- method). Power calculations for the sample size required to detect a difference in admissions were not reported.

The three studies targeting patients with asthma utilised hospitalisations as an outcome measure (18) (level 1+), (17) (level 1-) (16) (level 1+), however, only one study (18) reported a statistically significant reduction in hospitalisations. One study targeting patients taking lipid-lowering medications who were discharged from hospital (31) assessed hospital readmission rates as an outcome measure. Hospital readmission rates during the 6-month study were low and there was no significant difference between the groups.

Table 2.4 Health resource use

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems						
Bernsten et al., 2001 (14)	1-	Multi-centre Community pharmacies Europe	≥ 65 years & ≥4 medications	704 intervention and 636 control patients 18 months follow-up	Hospitalisation GP visits	No effect on hospitalisations, GP visits
Krska et al., 2001 (20)	1-	Multi-centre General medical practices Scotland	≥ 65 years & ≥2 chronic conditions & ≥4 medications	168 intervention and 164 control patients 3 month follow-up	Health resource use Emergency admissions	No effect
Pharmaceutical care for asthma						
Herborg et al., 2001 (17, 27)	1-	Multi-centre Community pharmacies Denmark	16 to 60 years with moderate to severe asthma	209 intervention and 204 control 12 month follow-up	Use of health care resources	Increased visits to the GP in the early months of the study by the intervention group compared to control ($p<0.05$). Intervention group patients used fewer hospital, emergency department and clinic visits compared to controls, but the differences were not statistically significant.
Cordina et al., 2001 (18)	1+	Multi-centre Community pharmacies Malta	14 years or older with asthma	64 intervention versus 55 control Follow-up 12 months	Hospitalisation	Less hospitalisations (0 versus 8, $p<0.05$)
Stergachis et al., 2002 (16)	1	Multi-centre Community pharmacies USA	Paediatric and adolescent patients with asthma	153 intervention and 177 control Follow-up 12 months	Hospitalisation Healthcare utilisation	No effect.
Pharmaceutical care for COPD						
Solomon et al., 1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	40 years and older with COPD	43 intervention and 55 control Follow-up 6 months	Health resource use	In the four weeks prior to the final visit there was a significantly lower number of visits to other health care providers in the intervention group compared to the control ($p=0.038$).

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Pharmaceutical care for Cholesterol risk management						
Peterson et al., 2002 (31)	1-	Single-centre Community setting Australia	On lipid-lowering therapy, cardiovascular disease recently discharged for cardiovascular/ cerebrovascular admission	39 intervention and 42 control Follow-up 6 months	Hospital readmissions	No effect on hospital readmissions. Sample size may be too small to expect an effect on hospital admissions (power calculations not reported)
Hypertension management						
Solomon et al., 1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	≥18 years & receiving dihydropyridine ± diuretic therapy	63 intervention and 70 control Follow-up 6 months	Health resource use	In the four weeks prior to the final visit there was a lower number of hospitalisations and visits to other health care providers in the intervention group compared to the control ($p<0.05$).

Evidence for efficacy, as measured by surrogate endpoints (Level 2 outcomes)

Surrogate endpoints including changes in blood pressure, glycosylated haemoglobin, lipids, and peak expiratory flow rates were utilised in eight of the randomised controlled trials (including hypertension arm of the study by Solomon et al (10), with variable findings. One study targeting a general patient population (10, 24) reported diseases-specific level 2 outcomes for patients with selected diagnoses that were included in the study. The results of studies using surrogate endpoints are summarised in Table 2.5.

The two studies targeting patients with diabetes reported surrogate (level 2) outcomes. One study reported an improvement in glycosylated haemoglobin and fasting blood glucose (26), while the other found no statistically significant difference between intervention and control groups on glycosylated haemoglobin (25). In a study targeting a general patient population (22), glycosylated haemoglobin levels were measured for a subgroup of patients with type 2 diabetes and no significant differences between control and intervention group patients was found. Both these latter two studies had patient groups with baseline glycosylated haemoglobin levels between 8 and 9 (marginally above the target value of below 8). Larger patient groups are likely to be required to observe significant differences where only small improvements are likely to be observed, especially where time frames were 6 months or less (25). Two studies focusing on patients with hypertension reported improvements in blood pressure measurements (19) (10) (hypertension arm of study). The studies focusing on patients with asthma reported no changes in peak expiratory flow rates (16-18). Three studies utilised lipid levels as an outcome measure. One study targeting a general patient population reported a significant difference in favour of the intervention group for changes in total and LDL cholesterol levels over the course of the study for a subgroup of patients with hyperlipidaemia (24). In another study focusing on a diabetic population, all subjects were within normal limits over the study period (26). In a study focusing on patients being treated with lipid-lowering medications (31) there were no significant differences between groups for median total cholesterol levels at the end of the study. The within group improvement (compared to baseline) in total cholesterol for the intervention group was statistically significant, while it was not for the control group.

Table 2.5 Surrogate end-points

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems						
Carter et al., 2001 (22); Ellis et al., 2000 (23); Malone et al., 2001 (12); Ellis et al., 2001 (24)	1+	Multi-centre Ambulatory care clinic USA	High risk patients	523 intervention and 531 control 12 month follow-up	HbA1C Total and LDL cholesterol	For patients with a diagnosis of dyslipidaemia (208 intervention, 229 control) absolute mean changes in total cholesterol levels decreased by 17.7 mg/dL in intervention versus 7.4 mg/dL in the control, p=0.028. Changes in LDL levels decreased by 23.4 mg/dL in the intervention versus 12.8 mg/dL in the control p=0.042. No differences between groups in the number of patients achieving goal lipid values (p=0.97). For patients with a diagnosis of type 2 diabetes (177 intervention, 158 control) there was no significant reductions in HbA1C levels between group, nor in the number of patients achieving a level below 8%.
Pharmaceutical care for diabetes						
Clifford et al., 2002 (25)	1+	Single centre Outpatient clinic Australia	> 18 years with type 1 or 2 diabetes and considered at high risk of complications	48 intervention and 25 control 6 months follow-up	HbA1C	No effect Baseline measures were close to desired range, which may have made improvement difficult within timeframe
Jaber et al., 1996 (26)	1+	Single centre Outpatient clinic USA	African-Americans with NIDDM	17 intervention and 22 control 4 month follow-up	Fasting plasma glucose HbA1C	Significant improvement in HbA1C in the intervention group compared to baseline (11.5 ± 2.9% baseline, 9.2 ± 2.1% final), with no significant improvement in the control group (12.2 ± 3.5% baseline, 12.1 ± 3.7% final). Significant decrease in fasting plasma glucose for the intervention group (11.1 ± 4.0 mmol/L baseline, 8.5 ± 2.3 mmol/L final) but not for the control group (12.7 ± 4.7 mmol/L baseline, 11.0 ± 3.9 mmol/L final). Difference between the groups was significant for both measures (p<0.05).

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Studies assessing interventions for asthma						
Herborg et al., 2001 (17, 27)	1-	Multi-centre Community pharmacies Denmark	16 to 60 years with moderate to severe asthma	209 intervention and 204 control 12 month follow-up	PEFR	No effect on PEFR
Cordina et al., 2001 (18)	1+	Multi-centre Community pharmacies Malta	14 years or older with asthma	64 intervention versus 55 control Follow-up 12 months	PEFR	No effect on PEFR although trend towards better rates
Stergachis et al., 2002 (16)	1+	Multi-centre Community pharmacies USA	Paediatric and adolescent patients with asthma	153 intervention and 177 control Follow-up 12 months	PEF	No effect on PEF
Pharmaceutical care for cholesterol risk management						
Peterson et al., 2002 (31)	1-	Single-centre Community setting Australia	On lipid-lowering therapy, cardiovascular disease & recently discharged for cardiovascular/ cerebrovascular admission	39 intervention and 42 control Follow-up 6 months	Total cholesterol level	Within group improvement in cholesterol levels in the intervention group compared to baseline was significant ($p< 0.005$), while it was not within the control group ($p=0.26$). However, no difference was observed between groups.

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect
Pharmaceutical care for hypertension management						
Park et al., 1996 (19)	1-	Two centres Community Pharmacies USA	Patients with hypertension on medication and BP ≥ 140/90 mmHg	23 intervention versus 26 control 4 months follow-up	BP	Reduction in the mean systolic BP (from 165.5 ± 21.1 mmHg at baseline to 149 ±18.9 mmHg and 143.2 mmHg at visits 3 and 4, respectively) ($p<0.05$) for intervention group. Significant reduction in mean diastolic BP at visits 3 and 4 (from 87.8 ± 9.9 mmHg at baseline to 84.1 ± 9.5 mmHg and 83.2 ± 8.0 mmHg at visits 3 and 4, respectively). The number of patients achieving "controlled" BP was also significantly different between baseline and visit 4 for the intervention group. There were no significant changes in BP or number of patients with controlled BP between baseline and visit 4 for the control group. The control group, however, did have a lower mean systolic BP (147.9 ± 19.6 mmHg) and diastolic BP (83.3 ± 8.5mmHg) at baseline than the intervention group, and a greater number of patients with "controlled" BP at baseline. No between group statistical analyses were presented.
Solomon et al.,1998 (10) Gourley et al., 1998 (11)	1-	Multi-centre Clinics USA	18 years and over receiving dihydropyridine ± diuretic therapy	63 intervention and 70 control Follow-up 6 months	BP, Pulse	The intervention group had significant reduction in systolic BP compared with the control group at the final visit ($p< 0.05$). The baseline systolic BP was 146.7 mmHg at baseline and 138.5 mmHg at the final assessment for the intervention group. For the control group the systolic BP was 146.2 mmHg at baseline and 144.9 mmHg at the final assessment. There were no significant differences in diastolic BP or pulse.

Evidence for efficacy on changes in medication use, risk factor management, knowledge or compliance (Level 3 outcomes)

Four of the five studies that employed changes in medication use (Table 2.6) as an outcome measure reported significant improvements in medication use (27, 29, 33). These results are further supported by rigorous evidence from one RCT (level 1+) demonstrating improvements in the appropriateness of medication use, as measured by the medication appropriateness index (21) (Table 2.6). The Medication Appropriateness Index is a validated measure (34), however, only one study employed this measure.

One study (Table 2.6) utilised the number of pharmaceutical care issues, using a previously published classification system, as the outcome measure. The study (level 1-) found significant reduction in pharmaceutical care issues in the intervention group compared with control group patients. This study, however, had a high chance of bias, with pharmacists delivering the intervention and assessing the numbers of pharmaceutical care issues aware of the control and intervention status of the subjects (20).

The other outcome measures utilised were changes in changes in compliance and changes in knowledge. Four studies assessed changes in knowledge (14, 17, 21, 35) with two reporting an improvement compared to the control group, one study found no difference, but baseline knowledge rates were very high, while the third study found no improvements at 18 months. It is unclear how this time frame related to the pharmaceutical care intervention.

Eight studies assessed changes in compliance (10, 14, 15, 18, 19, 21, 31, 35). One found improved compliance rates in those utilising hypertension medications (10), and a second found improved compliance in the elderly considered at risk of medication-related problems (35), another reported that there was no overall improvement in compliance rates, but a greater proportion of subjects in the intervention group who were non-compliant at baseline had improved medication adherence at 18 months (14). Five studies reported no change in compliance, however, all had high baseline compliance rates (15, 18, 19, 21, 31). One study (29) measured a score for “understanding and compliance”, which was not significantly different between the groups at the end of the study.

Two studies that focused on patients with asthma reported improvements in inhaler technique as a result of the pharmaceutical care intervention (18, 27). One study targeting cholesterol level management for patients at high risk of cardiovascular events used a composite primary outcome measure of “improvement in the process of cholesterol risk management” (level 3 outcome) (33). This composite measure included measurement of a fasting cholesterol panel by a physician, new prescription for a cholesterol-lowering medication and increasing the dose of an existing cholesterol medication, with only the first event counted. The primary endpoint was attained for a significantly higher proportion of the intervention group than the control group (57% of the intervention group versus 31% of the control group, $p<0.001$).

Table 2.6 Medication use

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect Comment
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems						
Jameson et al., 1995 (29)	1-	Single-centre Health Centre USA	At risk of medication-related problems	27 intervention versus 29 control 6 month follow-up	Medication use	Patients in the intervention group had significantly fewer regular prescribed medications than the control (difference 1.1 drugs, p=0.004) and fewer daily doses than controls (difference 2.15 doses, p=0.007)
Krska et al., 2001 (20)	1-	Multi-centre General medical practices Scotland	≥ 65 years & ≥2 chronic conditions & ≥4 medications	168 intervention and 164 control patients 3 month follow-up	Resolution of pharmaceutical care issues	Significantly more pharmaceutical care issues of nearly all types (such as potential/suspected ADRs, ineffective therapy, monitoring issues, requirement for education, inappropriate dose) were resolved in the intervention group compared to the control group
Hanlon et al., 1996 (21);	1+	Single centre Outpatient clinic USA	≥ 65 years & ≥5 medications	88 intervention and 84 control 1 year follow-up	Medication appropriateness index (MAI)	Covariate-adjusted MAI improved by 24% for intervention group at 3 months compared to baseline, and a 6% improvement for control group (p=0.0006). Differences maintained at 12 months (28% and 5% improvement for intervention and control, respectively, p=0.0002).
Bernsten et al., 2001 (14)	1-	Multi-centre Community pharmacies Europe	≥ 65 years & ≥4 medications	704 intervention and 636 control patients 18 month follow-up	Medication use	No effect
Pharmaceutical care for heart failure						
Gattis et al., 1999 (30)	1+	Single centre Outpatient clinic USA	Patients with heart failure	90 intervention and 91 control 24 weeks follow-up	Medication use	Overall ACE inhibitor use not significantly different between groups. Patients in the intervention group were closer to target ACE inhibitor doses at the 6-month follow-up compared to the control group p<0.001). Patients in the intervention group who were not on an ACE inhibitor were more likely to receive an alternative vasodilator (75%) compared to the control group (26%) (p=0.02)
Pharmaceutical care for asthma						
Herborg et al., 2001 (27)	1-	Multi-centre Community pharmacies Denmark	16 to 60 years with moderate to severe asthma	209 intervention and 204 control 12 month follow-up	Medication use	Greater reduction in the use of β_2−agonist medication and increase in the use of inhaled corticosteroids by the intervention group than the control group,

Reference	Level of evidence	Setting	Target population	Evaluable sample & follow-up	Measure	Effect Comment
Pharmaceutical care for cholesterol risk management						
Tsuyuki et al., 2002 (33), Simpson et al., 2001 (36)	1+	Multi-centre Community Pharmacies Canada	Patients with high risk of cardiovascular events	344 intervention versus 331 control 16 weeks follow-up	Medication use	34 (10%) intervention patients and 14 (4%) controls received a new prescription for cholesterol lowering medication (OR 2.5, 95% CI 1.3-4.6, $p<0.003$). Dose increase of cholesterol-lowering medication occurred in 12 (3%) intervention and 4 (1%) controls (OR 3.0, 95% CI 0.99 to 8.8, $p=0.07$)

Australian research

The provision of pharmaceutical care in the community setting in Australia has been tested, with one randomised controlled study in a hospital outpatient clinic (level 1+), one randomised controlled study in rural and remote communities (level 1-), one randomised controlled trial in the metropolitan community setting (level 1-) and one randomised trial comparing pharmaceutical care service with pharmaceutical care service plus clinical audit (level 1-) undertaken in the community setting. Other studies undertaken with the ambulatory population living in the community using uncontrolled designs (level 3) have also been undertaken.

A randomised controlled trial (level 1+) of pharmaceutical care programs provided through an outpatient department for patients with diabetes was undertaken in Western Australia (25). Outcomes measured included health related quality of life (level 1) and glycosylated haemoglobin (level 2) and patient satisfaction (level 4). The intervention included consultation with a clinical pharmacist, development of a care plan and follow-up and was carried out with the co-operation of the diabetes health care team. The diabetes health care team cared for control patients. The diabetes team was aware of the group allocation status of patients. Forty-eight patients were recruited to the intervention group and 25 to the control. Follow-up was for a six-month period. The outcome measures failed to demonstrate any significant differences. This may be accounted for by the relatively small sample size, which may not have been sufficient to detect differences in the quality of life measure, and the baseline glycosylated haemoglobin levels, which were only slightly above target ranges of below 8% (8.4% and 8.5% for intervention and control groups respectively).

A randomised controlled trial (level 1- method) of pharmaceutical care services for people living in rural and remote communities considered to be at high risk of medication-related problems was undertaken in Queensland (13). Risk criteria included the use of at least 5 regular medications and one or more chronic health conditions requiring close medical attention. Additionally people who were experiencing events that their GP considered would be improved by care coordination were also included. The patient was the unit of randomisation for the study. Ninety-nine patients were randomised, 50 to the intervention and 49 to the control group. The pharmaceutical care intervention involved collaboration between the community pharmacist and the patient's GP. The pharmacist interviewed the patient, conducted a medication review, developed a care plan in collaboration with the GP, initiated the action plan and carried out follow-up. Given the setting of the study, there was potential for cross-contamination between the groups, particularly in the small rural townships. The study was conducted over a period of 6 months. The outcome measures for the study were health related quality of life (measured using the SF-36) (level 1 outcome), patient assessment of health care (level 4 outcome) and economic measures (see economic assessment). At the end of the study there were statistically significant differences in favour of the intervention group in scores for two of the 8 domains of the SF-36, role emotional and mental health. The mental component score of the SF-36 was significantly different between the groups, however there was no significant difference in the physical component score. To quantify the clinical relevance of this difference quality adjusted life years were calculated, via a Quality of Well Being Index, as a gain of 0.004 for the intervention group over the 6-month period. This equated to an extra 1.5 days/year of perfect health for the intervention group. There were no significant changes in ratings of health care by patients after the study period.

A study conducted in the community setting in Hobart, Tasmania assessed the impact of a pharmaceutical care intervention for patients taking lipid lowering medication who were discharged from hospital after an acute cerebrovascular or cardiovascular admission (31) (level 1- method). Patients were randomised at discharge. Six weeks after discharge, the study pharmacist conducted a home visit for all patients at which total serum cholesterol was measured. Patients in the intervention group were also assessed for current medications, compliance and drug-related problems and provided with education. Summary findings were sent to the patient's GP. Follow-up for intervention patients was conducted monthly for 6 months. The study pharmacist conducted patient assessment for both groups at the end of the study period. Eighty-one of the 94 patients recruited completed the study. Outcome measures included hospital re-admissions (level 1 outcome), total cholesterol levels (level 2 outcome) and patient-reported compliance (level 3 outcome). Hospital admission rates were low for both groups during the study and no significant difference was detected. Total cholesterol levels were not significantly different between the groups at baseline or at the end of the study. Within group improvement in total cholesterol levels (compared to baseline) were significant for the intervention group ($p<0.005$), but not for the control group ($p=0.26$). Patient reported compliance did not change significantly in either group.

A randomised comparative study of two collaborative models for the provision of pharmaceutical care services was undertaken in NSW (level 1- method) (3). Patients were referred into the study by their general practitioner, with the general practice as the unit of randomisation. The two arms of the intervention were delivery of pharmaceutical care services compared to the delivery of pharmaceutical care services with a GP clinical audit to identify patients appropriate for referral. In this study, general practitioners identified patients at risk of medication related problems and referred them to their preferred pharmacy for a medication review, the majority of which took place in the person's own home. Subsequent meetings were held between the general practitioners and pharmacists to discuss the review's findings and recommendations. The general practitioner undertook follow-up and reassessment at three months. The comparative model was similar with the addition of a clinical audit undertaken by the general practitioner prior to the referral to the pharmacist. There were 382 patients recruited by 38 GPs, of which 362 completed the study. The main outcome measures were quality of life (level 1 outcome - using an instrument that measured overall health, pain level and quality of life), number of medications used (level 3 outcome) and medication costs (economic). At the end of the study a majority of patients in both groups rated their overall health as worse than at baseline (90.5% of pharmaceutical care-only patients, 94.6% of pharmaceutical care plus clinical audit group patients). There were no significant differences in the proportion of patients reporting improved quality of life (38.2% pharmaceutical care-only group versus 32.6% pharmaceutical care plus clinical audit group, $p=0.266$). A greater proportion of the pharmaceutical care-only group (42.7%) showed improved rating of pain compared to the pharmaceutical care plus audit group (33.2%) ($p=0.06$ between groups). Assessment of medication use revealed an overall mean reduction in medication costs of 9.1% as a result of implementing the service, with both models contributing to a reduction in medication costs (see economic evaluation).

An uncontrolled South Australian implementation trial (level 3) (37) of pharmaceutical care services included 119 general practitioners and 64 pharmacists who provided services to 1,000 patients. The service included a medication review with the patient undertaken by the pharmacist usually at the patient's home, a subsequent meeting between the general practitioner and pharmacist to discuss findings and recommendations, and a follow-up visit to the patient to implement the recommendations. Case notes were kept for all service delivery,

which included an assessment written by the pharmacist based on their initial home-visit, a subsequent plan which had been negotiated with the doctor as well as outcomes found at follow-up. Independent researchers coded the case notes to determine the nature of medication-related problems, actions taken and outcomes. Results indicated 90% of people who received the service had one or more medication-related problems, with 2,764 problems identified. Follow-up data were available for 978 problems, with 61% reported as resolved or well managed and a further 20% considered to be improving. Cost savings have been estimated as a result of this study, but the lack of a comparison group limits any conclusions that can be made on the basis of these results.

Pharmaceutical care services were also trialed in five community pharmacies in an uncontrolled study in South Australia (level 3) (38). Two hundred and five patients were enrolled. The service consisted of a comprehensive review undertaken by the pharmacist, usually within the pharmacy, with appropriate follow-up consultations where necessary. Case notes were kept for all service delivery. Upon completion of the project, independent researchers coded the case notes to identify medication-related problems, actions taken and outcomes. At baseline, 179 patients were considered to have at least one medication-related problem, with 526 medication-related problems identified in total. Over the 11 months of the study, 678 consultations were implemented. At follow-up, outcomes as recorded by the participating pharmacists were available for 432 problems. Overall, 75% of problems were recorded as being well managed or resolved at follow-up; improving in 12% and unchanged in the remaining 13%. Cost savings have been estimated as a result of this study (39), but the lack of a comparison group limits any conclusions that can be made on the basis of these results.

A study conducted in the community setting in Sydney (40) (level 3 method) involved two stages. Stage 1 of the study was the developmental phase for the project and stage 2 the extension phase. Trained community pharmacists conducted medication reviews for patients referred by a GP using a standard protocol. Subsequently the pharmacist met with the GP to discuss findings and recommendations. Follow-up was undertaken three months later. A clinical panel comprising of a clinical pharmacist, general practitioner, clinical pharmacologist and physician reviewed the case notes from the service and independently rated the clinical significance of the findings, recommendations and changes implemented using established criteria. Outcomes measured included the number of medications per patient (level 3 outcome), the clinical significance of medication regimen review changes (as assessed by the panel) and cost savings (economic). Overall, 105 patients received a service in stage 1 and 179 patients in stage 2. There was a significant decrease in the mean number of medications per patient after the study compared to baseline with a mean reduction of 1 medication per patient. Cost savings were estimated as a result of this, but the lack of a comparison group limits any conclusions that can be made. Only reviews conducted in stage 2 were evaluated for clinical significance. The agreement of significance amongst panel members was poor, however, all four panel members judged at least 20% of changes to result in a significant positive effect, while three panel members judged at least 40% of changes to be significant.

An uncontrolled study undertaken in the general practice setting in Western Australia (41) (level 3 method) assessed a pharmaceutical care intervention for elderly patients. Patients were referred to the pharmacist by their GP. The pharmacist interviewed the patient in the GP surgery, prepared a report for the patient's doctor and conducted follow-up home visits. Reports were prepared for 60 patients. There were 199 suggestions regarding drug selection

or dose changes that were made to prescribers, however, only 73 (37%) were acted upon. There were no changes in outcome measurements (level 3 outcomes) of number of surgery visits, numbers of regular medications taken, change of dose time and doses taken daily. Patients' self-rated compliance, drug knowledge and "wellness" improved for the majority of the 49 patients that completed baseline and final questionnaires, however statistical significance was not reported.

Economic assessment

Nine pharmaceutical care studies utilizing a randomised controlled design included an economic component.

Three controlled trials compared the medication costs in the intervention group with the control group.

In the first study in 332 patients, there was no significant difference in the average monthly costs of prescribed medication per patient between groups, either at initial interview or after intervention (20). In the second study in 56 patients, the 6-month cost of drugs decreased in the intervention group that received a pharmacotherapy consultation and increased in the control group ($p = 0.008$) (29).

A study in 362 patients compared medication costs in two models for the provision of domiciliary based medication reviews in Australia (3). There was a 9.1% reduction in overall mean medication costs that represented an annual drug cost saving of approximately $79,450.00 when data were extrapolated to one year. The reduction in total mean medication costs was significantly greater in the model 1 (with medication review only) than in the model 2 (with clinical audit and medication review ($p <0.05$). The monthly medication cost per patient decreased by $27.51 in the model 1 and by $10.77 in the model 2.

Five studies were descriptive economic studies and compared cost of various health care resources between groups.

A randomised controlled trial in 1053 patients measured resource use in terms of clinic visits including pharmacist interventions, drugs, hospitalisations and laboratory tests. Mean annual costs increased in both groups during the study but there was no significant difference between the intervention and the control group (32).

A randomised controlled trial assessed the health care-related resource usage in 6 of the 7 countries participating to the study (14). There was very little information on how and which costs were measured. Between-group analysis indicated there were no significant differences between the total cost for control and intervention patients in any country.

A randomised controlled trial in 675 patients assessed community pharmacist intervention in cholesterol risk management (33, 36). Compared to the control group incremental costs in the intervention group to a government payer and community pharmacy manager were $6.40/patient and $21.76/patient respectively during the 4-month follow-up period. There was no indication that these costs were associated with improved clinical outcomes.

A randomised controlled trial in 99 patients assessed the efficacy of pharmaceutical care services in rural and remote areas of Australia (13). Pharmaceutical Benefits Scheme and

Medicare Benefits Scheme costs increased for both intervention and control groups. However, the total increase was less important in the intervention group (no statistical comparison) with yearly net cost savings of $87.21 per patient.

A randomised controlled trial in 268 patients assessed the efficacy of a pharmacotherapy consultation (28). Medical and drug costs were measured for the 6-month periods before and after the consultation. There were no significant differences between the intervention and the control groups.

One study performed a full economic evaluation of the cost-effectiveness of a pharmacist intervention in 208 patients (21, 42). It found that health services use and costs were comparable between groups. The benefit was estimated as the improvement in drug prescribing appropriateness assessed with the Medication Appropriateness Index (MAI). Intervention costs ranged from $7.50-30 per patient and per unit change in drug appropriateness. The clinical relevance of this cost-effectiveness ratio is difficult to appreciate, as the MAI is not commonly used.

In conclusion, 2 studies showed a decrease in drug costs associated with the intervention and one study did not show this effect. Four studies compared a variable range of health care costs and 3 did not show any effect (no statistical results for the fourth one). There is only one study that included a full economic evaluation but its results are difficult to interpret. The two studies done in Australia showed a decrease in medication costs (3), a lower increase in health care costs (no statistical result) (13) associated with pharmaceutical care compared to control groups. Neither of these 2 studies showed an association between reduction in drug costs and improvement of clinical outcomes.

Taken as a whole, there is limited evidence that pharmaceutical care services can decrease drug costs. The strongest evidence comes from an Australian study (3), however, this was a head to head trial comparing delivery of pharmaceutical care services against pharmaceutical care services plus an clinical audit. . Further studies would be needed to establish for how long the cost savings are maintained and how frequently pharmaceutical care interventions should take place. The only cost-effectiveness study located used a cost-effectiveness ratio for which the clinical relevance was difficult to assess.

Comment

A number of rigorous studies evaluating pharmaceutical services have now been undertaken. The trials focusing on patients with asthma (level 1+ and 1- for method with level 1 outcomes) and heart failure (level 1+ for method and level 1 outcomes) provide the strongest evidence for the effectiveness of the service. Collectively, the studies provide evidence for the effectiveness of pharmaceutical care, although the variability in outcome measures utilised make aggregation of study results difficult. Consideration needs to be given to the outcome measures employed. The majority of studies utilised the quality of life measure as an outcome, with or without surrogate endpoints. There was little evidence for any impact on quality of life measures. This raises the question as to whether this is a result of service delivery or if the measures utilised thus far are simply not sensitive enough or appropriate as an outcome measure of the service. Interestingly most studies employed quality of life as the outcome measure, with few utilising adverse drug events, drug-related problems or medication appropriateness as an outcome. This is surprising given that the focus of pharmaceutical care services is on resolving drug related problems and that rigorous

methodologies, including explicit criteria are available for assessing drug-related problems and are commonly used in the assessment of drug-related problems as a cause of hospital admission (43).

The limitations of work done to date have been the lack of comparative endpoints across studies other than the quality of life measures, the latter for which its sensitivity for this service is unclear. While a number of trials have been undertaken, the variability in the application of end-points utilised means the evidence for effectiveness of single endpoints apart from quality of life is limited to one or two controlled trial results. Stronger evidence could only be obtained through more consistent application of end-points that were relevant to the patient groups included. The difficulty in selecting end-points arises where criteria for inclusion are based on the numbers of medicines that people take, rather than a disease specific focus. It would appear that where inclusion criteria are based on numbers of medicines or doses people take, that the most appropriate outcome measure would be drug-related problems or adverse drug events, defined by explicit criteria and assessed by independent researchers, blinded to patient allocation.

Taken as a whole and considering the variable end-points employed, the results suggest that pharmaceutical care services are effective in improving patient outcomes. Studies (level 1- for method) have shown a reduction in adverse drug events (level 1 outcome), an improvement in medication appropriateness (level 1+ for method, level 3 outcome), a reduction in medication problems (level 1- for method, level 3 for outcomes), improvements in signs, symptoms for people with asthma (level 1+ and level 1- for method, level 1 for outcomes), an improvement in combined all-cause mortality and non-fatal heart-failure related events in patients heart failure (level 1+ method, level 1 outcome), improvements for surrogate end-points such as blood pressure, glycosylated haemoglobin and cholesterol levels in some studies (level 2 for outcomes) and measures of improved management of cholesterol risk (level 3 outcome). The variability observed in study results across studies, particularly with multi-centre trials suggests future work needs to focus on how to maximise service delivery, including uptake by pharmacists and targeted delivery to those in need and for whom outcomes can be improved.

Studies assessing the provision of structures to support pharmaceutical care interventions

The other types of controlled studies that are reported in the literature and described as an assessment of pharmaceutical care, for the purposes of this review, were considered to be an assessment of the provision of structures to support the wide-scale implementation of pharmaceutical care.

Three controlled trials (level 1 and level 2 method) were located that assessed patient outcomes when pharmacists were provided with support structures and encouragement to facilitate the delivery of a “pharmaceutical care” intervention (44-49). While these studies may have implications for the wider implementation of pharmaceutical care services in the community, the results were not used to assess the effectiveness of pharmaceutical care as such because some patients in the intervention group may not have actually received the service.

A randomised controlled trial (48, 49) (level 1+ method) conducted in 36 community pharmacies in the USA assessed an intervention for adult patients with COPD or asthma. In

pharmacies randomised to the intervention group pharmacists were provided with training, recent patient-specific clinical data (including peak expiratory flow rates [PEFRs], hospitalisations, compliance), educational materials and resources as support strategies to facilitate "pharmaceutical care". A computer alert system was provided which identified study patients when they filled any prescription. Patients of pharmacies in one control group received instruction on peak-flow monitoring a peak-flow meter and monthly follow-up calls, but information and support strategies to facilitate pharmaceutical care were not given to the pharmacy. Pharmacies in a second control group provided usual care. There were 1113 patients enrolled in the study of which 947 (85.1%) and 893 (80.7%) completed interviews to assess outcomes at 6 and 12 months, respectively. Outcomes assessed included quality of life, breathing-related hospital admissions (level 1 outcomes), PEFRs (level 2 outcome) and compliance (level 3 outcome). There were no significant benefits found for the intervention compared to the two control groups. Patients in the intervention group actually had significantly higher PEFRs at 12 months compared to control group 2 (usual care). Asthma patients in the intervention group had a significantly greater number of breathing-related emergency department or hospital visits than control group 2 (usual care). In intervention pharmacies there was a low rate of use of the data provided to support and facilitate pharmaceutical care (pharmacists accessed patient-specific data only about 50% of the time) indicating a possible lack of enthusiasm for providing the expanded service.

The Kaiser Permanente/USC Patient Consultation Study (44, 45, 47) was conducted in an HMO in the USA. The study involved 2 concurrent prospective studies, one of which was randomised (level 1 method). The study compared three models of pharmacist patient consultation a) counselling when deemed necessary by a pharmacist; b) the California state model – a mandatory requirement that all patients receiving a new or changed prescription receive pharmacist counselling; c) the Kaiser Permanente (KP) model – a targeted, structured consultation to high risk patients. In pharmacies allocated to the KP model, pharmacists used patient-specific clinical/physician information to conduct a drug regimen review (with further information obtained from the patient if required), drug monitoring, physician consultation (where necessary), patient education and follow-up. A template was used to identify eligible patients and guidelines for actions to follow were available for KP model pharmacists. The study ran for 23 months. Although the KP and state models were associated with some changes in HRQOL the overall effect was judged by the investigators to be "not consistent and not clinically important". In the random-assignment study the KP model was associated with a lower likelihood of a patient being hospitalised during the 23-month study period compared to the control (overall a 3.3% lower likelihood of at least one admission per new prescription filled for the KP model, for urgent or emergency admission there was a 4.0% lower likelihood for the KP model). Based on a mean number of prescriptions filled of 12 per 2 years it was estimated that a reduction of 10-20% could be expected.

Excluded studies

The following pharmaceutical care studies were reviewed but excluded due to the lack of a control group (level 3 for method)
Berringer et al. 1999 (50)
Bluml et al., 2000 (51)
Shibley and Pugh, 1997 (52)
Hsia Der et al, 1997 (53)

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3. Continuity of Care Services

The Service

Continuity of care services aim to improve medication management for people as they move from hospital back to the community or between different institutions. The service can include activities such as provision of discharge and medication summaries to the patient and their local doctors and pharmacists, the development and co-ordination of care plans to assist medication management, education for the patient about their medicines and where necessary, home visits after discharge from hospital. The services may be provided by either hospital or community pharmacists.

Studies included

For the purposes of this review we included studies that had aimed to provide continuity of care services through facilitating information provision between care providers based in the hospital and those based in the community setting, with or without home visits to the patient post-discharge.

Studies had to include liaison with at least one community practitioner. Studies that did not include liaison that facilitated provision of information about management between care providers in different settings (across the continuity of care) were excluded from this review.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions or re-admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), knowledge or compliance (level 1, 2 or 3 outcomes).

Studies only assessing level four outcomes, such as changes in satisfaction with or opinion of the service were excluded.

Study design

The studies assessed within this section focused on the provision of continuity of care services, however, they differed in the implementation of that service. A total of nine randomised controlled trials (level 1 method) were located which met the inclusion criteria. Additionally one non-randomised controlled trial (level 2 method) was located (1), this study is summarised in Appendix II Table 2.

Five randomised controlled trials included home visits as part of the continuity of care service (Table 3.1). One trial, however, provided the visit to both intervention and control patients, thus not providing a design that enables an assessment of what difference the home visit makes (2). All trials had to include liaison with at least one community practitioner. The liaison varied between studies, with two studies providing discharge or care plans directly to the patients' nominated general practitioner and community pharmacist as part of the intervention (3, 4), one study providing the care plan as part of the intervention to the community pharmacist only (5), one study providing the care plan which was developed at

the home visit, only to the general practitioner via the patient and via telephone (6), and one further study providing the care plan to the patient to provide to their community practitioners (2). All studies targeted high-risk patients, with the patient as the unit of randomisation. Four of the studies were located in a single institution, with the remaining study being across four institutions (4).

Four randomised controlled trials did not include home visits (Table 3.2). One of these studies used telephone follow-up within two days of discharge as the intervention (7, 8), while another used telephone follow-up three and seven days after discharge in addition to pharmacist involvement in the discharge process and corrective actions for potential risks for re-hospitalisation (9). Two studies used in-hospital assessment and education, development of a discharge plan or pharmaceutical care assessment and communication of that plan to the community health providers (10, 11). It should be noted that in two of these studies (8, 9) the liaison with community practitioners was part of standard care and the studies were assessing standard care versus standard care plus telephone follow-up (8) or standard care plus pharmacist involvement and telephone follow-up (9).

Studies were judged to have significant potential for bias (level 1- method), where the pharmacist who undertook the intervention was aware of the group allocation of patients and also responsible for measuring the outcomes, particularly where the primary outcome was number of medication related problems, medication knowledge and adherence. Follow-up periods varied between 10 days and 12 months.

Study outcomes

Study outcomes varied across studies but included level 1 outcomes such as hospital re-admissions, deaths and quality of life. All other outcomes were level 3 outcomes, including medication knowledge, adherence, changes to the medication regimen and medication-related problems. Three studies assessed the number of medication related problems. This was considered to be a level 3 outcome, as while adverse drug events (a level 1 outcome) was included, drug related problems also include issues such as compliance and unnecessary therapy (level 3 outcomes), which may not necessarily equate to an adverse event.

Evidence for effectiveness of practice

There is sound evidence (level 1-) that pharmacist implemented continuity of care services post hospital discharge that include active patient follow-up and are targeted to high-risk patients improve patient outcomes including reducing hospital re-admissions (level 1 outcomes), numbers of medication-related problems, as well as improving medication knowledge and adherence (level 3 outcomes).

There were three level 1+ studies that did not demonstrate as positive effect, however, one did not include any active patient follow-up, nor target high-risk patients, one was a multi-centre study, and third did not target high risk patients.

Continuity of care services post hospital discharge have been demonstrated to be effective in the Australian setting.

All studies that have demonstrated an effect have been undertaken within single institutions. Future research needs to evaluate the implementation of these services across a wider scale in order to facilitate national implementation.

Further rigour needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation.

Medication-related problems and adverse drug events should be standardised for use as an outcome measure to facilitate comparisons between studies.

Robust cost-effectiveness studies are lacking, both within Australia and internationally.

Evidence for efficacy of changes in morbidity and mortality (Level 1 outcomes)

Three of the five studies employing continuity of care services with active follow-up with the patient through a home visit used hospital re-admissions as a outcome measure (4-6). One study (level 1- method) showed significant reductions in hospital re-admission rates (6), while another study (level 1-method) showed a trend for a reduced proportion of the intervention group to be re-readmitted, but the difference did not reach statistical significance (5). A third study, which was a multi-centre trial (4) (level 1+ method) failed to demonstrate any effect on hospital re-admission rates.

Three of the four studies that did not include home visits used level 1 outcome measures. One of these studies (level 1- method) assessing the impact of pharmacist involvement in the discharge process plus telephone follow-up found significant improvements in hospital re-admissions and a combined measurement of death or hospital re-admission (9). The difference between the groups was mainly due to the lower number of heart failure-related hospital admissions in the intervention group. The randomised controlled trial (level 1+) assessing standard care plus telephone follow up showed a trend towards improving patient outcomes as measured by reduction in hospital re-admissions (7, 8). This effect did not reach statistical significance, however, but may have resulted from an insufficient sample size. One study not utilising any sort of active patient follow up, either telephone or home visit, failed to show a significant difference in unplanned re-admissions, mortality or functional health status between intervention and control groups (11). The study design, however, may have

contributed to the lack of observable effect, as it included all patients including surgical and medical patients rather than targeting high-risk patients.

Evidence for efficacy measured with level 3 outcomes

Studies employing continuity of care services with active follow-up (3, 5, 6) provide evidence (level 1-) that the service improves level 3 outcomes including numbers of medication related problems, medication knowledge and adherence. The study results showing reduction in medication-related problems, and improvements in compliance and adherence are possibly subject to bias as it does not appear that the pharmacists assessing these outcomes were blinded to the group allocation of patients. The multi-centre study (4) (level 1+ method) failed to demonstrate any effect on level 3 outcomes including knowledge and adherence to medicines or hoarding of medicines.

Among the four studies that did not include home visits three assessed level 3 outcomes. The study which included telephone follow-up for the intervention group after discharge from hospital (7, 8) (level 1+ method) found significantly fewer patients in the intervention group attending the emergency department after discharge compared to the control group. One study not utilising active patient follow-up by telephone (10) (level 1- method) found a trend towards higher compliance scores for patients in the intervention group compared to the control group, however, the difference did not reach statistical significance. Due to the small number of evaluable patients this may be a sample size effect, rather than representing no real difference between groups. Another study not utilising any sort of active patient follow-up after discharge (11) (level 1+ method) found significantly lower mean numbers of visits to health care professionals (including planned and unplanned visits) for the intervention group compared to the control, but no differences in the number of medication changes after discharge.

Further supporting evidence

One other randomised controlled trial was located (12) (level 1+ method), which while similar did not meet the inclusion criteria for this review as liaison with community care providers was undertaken as required, rather than routinely. This study, however, provides further support for the involvement of the pharmacist across the continuity of care in improving level 3 (knowledge and compliance) outcomes for patients. The study targeted high-risk geriatric patients with follow-up sessions undertaken either in the patient's home, over the telephone or in the pharmacist's office, the majority (85%) of which took place by telephone. The follow-up visits were conducted 1week, 2 to 4 weeks, 2 months and 3 months post-discharge. The pharmacist intervention also included assessment of drug-related problems and education for patients upon discharge from the hospital. The study found no impact from the service on hospital readmission rates. The intervention was found to improve patient compliance and knowledge of medication (level 3 outcome) as assessed by blinded independent researchers.

Economic assessment

None of the studies included in the review presented economic outcomes.

Australian research

Three randomised controlled studies assessing pharmacist-led continuity of care services in Australia were located. One randomised controlled study (level 1-) undertaken in Adelaide assessed the impact of discharge medication management services implemented by pharmacists. This study provides evidence that the service is effective in reducing medication related problems (level 3 outcomes) and improving knowledge (3). A community pharmacist provided the intervention. Eligible patients were aged 65 years and over, at risk of undesirable medication events and discharged from an acute care hospital. A control group received the standard discharge service from the hospital, while the intervention group received in hospital assessment and education, discharge summaries forwarded to the patient's general practitioner and pharmacist and home visits within one week of discharge that included development of a care plan which was also communicated with the patient's community health providers. Follow-up occurred at 6 weeks. The group receiving the medication liaison service had significantly fewer medication-related problems six weeks after discharge from hospital, as well as improved medication knowledge and compliance. There is a chance of bias in these study results, with the pharmacist delivering the intervention, also measuring the outcomes and aware of the group allocation of patients.

Another study (level 1- method) undertaken in a single hospital in Tasmania assessed a service provided to patients admitted to medical wards who were 60 years or older, had at least two chronic medical conditions and were taking four or more regular medications (6). There were 136 participants (65 intervention and 71 control). Both groups received usual care in hospital with the intervention group receiving a home-visit by a clinical pharmacist five days post discharge. Follow-up for both groups occurred at 90 days and was conducted by a clinical pharmacist to assess unplanned re-admissions, out of hospital deaths, number of drug-related problems, number of medications and level of compliance. Twenty-eight percent of patients in the intervention group had an unplanned re-admission compared to 45% in the control group ($p=0.05$). There were no significant differences in the number of deaths between the two groups. There was a significantly lower proportion of patients in the intervention group (65%) that had at least one drug related issue at 90 days than the control group (86%) ($p<0.01$). The intervention group also reported significantly higher rates of compliance with medications. Again, the chance for bias exists with the pharmacist assessing the outcomes not blinded to patient allocation.

The other randomised controlled trial undertaken in Australia (level 1+) (11) did not include a home visit, but assessed the effectiveness of discharge planning from within the hospital. The study found no effect. However, the study design may have contributed to the lack of observable effect, as it included all patients rather than high risk patients, including surgical and medical patients.

Further support for the effectiveness of continuity of care services in the Australian setting is provided by other randomised controlled studies, that were not included in this review because the intervention was delivered by a multidisciplinary team consisting of a pharmacist and clinical nurse. The studies conducted in South Australia evaluated the impact of continuity of care services on the outcomes for patients discharged from an acute care hospital (13, 14). This intervention involved counselling before discharge from hospital, followed by a pharmacist and nurse visiting a patient's home a week after discharge from hospital to optimise the management of the patient's medication, identify any early deterioration in the patient's condition and facilitate medical follow-up if required. The

outcomes measured included the frequency of unplanned re-admissions to hospital and death within 6 months of discharge from hospital (level 1 outcomes). The intervention was associated with a reduced frequency of "hospital readmission and death" for patients with congestive heart failure (13) and patients discharged from medical and surgical wards (14). The intervention demonstrated no effect on quality of life scores.

Comment

There is good evidence from level 1- method studies for the effectiveness of continuity of care services when targeted to patients at risk of medication related problems and when the service includes patient follow-up post-discharge. All studies that have demonstrated an effect, however, have been undertaken within single institutions. One multi-centre study, with rigorous methodology (level 1+ method) failed to demonstrate any effect. Future research needs to evaluate the implementation of these services across a wider scale in order to facilitate national implementation.

The main methodological limitation of the studies reviewed was the lack of blinded assessment of patient outcomes. In a number of cases the pharmacist delivering the service was aware of patient group allocation and also monitored patient outcomes, which introduces a significant level of bias. Further rigour needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation.

Medication-related (or drug-related) problems have been used as an outcome measure in some studies, however there are differences in the definition and classification of medication-related problems between studies. There is a need to standardise this outcome measure to facilitate comparison between studies. Explicit criteria are available for assessing medication-related problems and are commonly used in the assessment of medication-related problems as a cause of hospital admission (15). It would seem appropriate to employ similar criteria to improve the rigour of outcomes assessment in continuity of care studies.

Table 3.1 Randomised controlled studies of continuity of care services including a home visit to the patient

Reference	Level	Setting	Subjects	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Nazareth et al., 2001 (4)	1+	4 hospitals UK	Patients included were over 75 years, taking four or more medicines at discharge and discharged to areas within hospital catchment.	Within hospital assessment. Discharge plans written and distributed to patient, and patient's chosen general practitioner and community pharmacist. Home visit between 7 and 14 days post discharge.	181 intervention and 181 in control. Follow-up period was 6 months	Level 1 Readmission to hospital, deaths, general well being Level 3 Knowledge and adherence to medicines, hoarding	Hospital readmission rates at 3 months were 39% and 39.2% in intervention and control groups respectively. No significant difference observed. No significant differences in secondary endpoints were observed either, nor where there trends towards significance. Sample size of 195 in each group was calculated to be the amount required to show reduction in hospitalisations from 40% to 25%.
Naunton and Peterson, 2002 (6)	1-	Single hospital Tasmania, Australia	Medical ward admissions, 60 years or older, at least two chronic medical conditions and taking four or more regular medications.	Usual care in hospital, followed by intervention group receiving a home-visit by a clinical pharmacist five days post discharge, which included liaison with community-based health services.	65 intervention and 71 control. Follow up for both groups occurred at 90 days	Level 1 Unplanned re-admissions within 90 days, out of hospital deaths Level 3 Drug-related problems medications, compliance, medication use	28% of patients in the intervention group had an unplanned readmission compared to 45% in the control group ($p=0.05$). No statistical significance for mortality (5 in the intervention group compared with 8 in the control group). 65% of patients in the intervention group had at least one drug related issues at 90 days compared with 86% in the control group ($p<0.01$). The intervention group reported higher rates of compliance (87% self reported never miss, compared with 42%; $p<0.0001$)

Reference	Level	Setting	Subjects	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Spurling, 2002 (3)	1-	Single hospital South Australia	Patients 65 years and over and considered at high risk of medication related problems as determined by risk criteria.	Within hospital assessment & education, communication with community health providers within 24 hours of discharge, a home visit within one week, development of a care plan, which was communicated to GP and community pharmacist.	51 in the intervention group and 58 in the control group Follow-up at 6 weeks.	Level 3 Number of medication-related problems Knowledge and adherence Use of resources	Statistically significant improvement in knowledge scores between intervention and control groups at 6 weeks ($p<0.001$). Seven people (14%) in the intervention group were considered to have poor compliance at 6 weeks, compared with 23 (50%) in the control group ($p<0.001$). The number of medication-related problems was significantly different at 6 weeks with 124 problems identified in the control group compared with only 49 in the intervention group.
Shaw et al., 2000 (5)	1-	Psychiatric hospital Scotland	Patients included were from the adult or care of the elderly acute admission wards.	Within hospital assessment and within hospital intervention. Discharge plan sent to community pharmacist. Subsequent home visits at one, four and 12 weeks for all patients.	51 patients in the intervention group and 46 in the control group.	Level 1 Hospitalisations Level 3 Medication related problems, but no definition of this and how it was assessed were provided Medication knowledge	Ten percent of the intervention group and 26% of the control group were readmitted with 3 months. This difference did not reach statistical significance. (This may be a sample size effect, rather than representing no real difference between groups). The intervention group was found to have less medication related problems than the control group at 12 weeks (1.4 versus 2.4), although no information is provided on how this was assessed. Changes in knowledge about medications were observed to improve in both groups over time

Reference	Level	Setting	Subjects	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Smith et al., 1997 (2)	1-	Single hospital UK	65 years and over considered at risk of medication-related problems	All patients received usual care within hospital. Intervention patients also received extra counselling plus a written care plan to be provided to their community practitioners and were also provided with a telephone helpline during their first seven days post discharge. All patients received a home-visit 7 to 10 days post-discharge	28 in the study group and 25 in the control. Follow-up 7 to 10 days post discharge.	Level 3 Medication use and compliance Changes to medication regimen	Compliance rates were considered better in the study group compared with controls ($p<0.01$). Unintentional changes to the medication regimen occurred at a similar rate in both groups.

Table 3.2 Randomised controlled studies of continuity of care services that did not include a home visit to the patient

Reference	Level	Setting	Subjects	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Stowasser et al., 2002 (11)	1+	Two hospitals Australia	Patients discharged from medical and surgical wards to the community	Intervention group received within hospital assessment on admission and discharge. Discharge medication plans developed and communicated to patient's chosen GP and community pharmacist.	113 patients in the intervention group and 127 in the control group. Follow-up in 30 days.	Level 1 Mortality Re-admissions within 30 days functional health status (SF-36) Level 3 Post discharge resource utilisation Changes to medication regimen	Unplanned re-admissions were not significantly different (8% versus 9.4%). There were no significant differences observed in SF-36 scores between control and intervention groups. The mean number of visits to health-carers after discharge was significantly lower for the intervention group (7.54 per patient) compared to controls (9.94 per patient), $p<0.05$. There were no significant differences in the number of medication changes after discharge ($p>0.05$).
Cannon and Hughes, 1999 (10)	1-	Single hospital, UK	Over 65 years and considered at risk of medication related problems	Intervention group received within hospital pharmaceutical care assessment which was communicated to the patient's community pharmacist.	19 patients in the intervention group and 17 in the control group. Follow-up by telephone in 30 days	Level 3 Compliance Changes to medication regimen	There was a trend towards higher compliance scores (assessed with 5-point questionnaire) for the intervention group compared to the control, however, the difference was not significant ($p>0.05$). A greater proportion of the control group (82%) had changes to discharge medication than the intervention group (44%) at follow-up (statistical significance was not reported). No power analysis was performed.
Dudas et al., 2001 (7, 8)	1+	Single hospital USA	Patients discharged on medications	Telephone call from the pharmacy within two days of discharge compared to pharmacy facilitated discharge alone. Pharmacy facilitated discharge included patient counselling (verbal and written) & telephoning discharge prescriptions to the patients' community pharmacy.	79 intervention 111 control. Follow-up at 6 weeks	Level 1 Hospital re-admissions within 30 days Level 3 Emergency department visits	Hospital re-admissions were reported as 15% in the intervention group compared with 25% in the control group. This did not reach significance ($p=0.07$), but may be due to a sample size effect. Eleven patients in the intervention group compared to 27 patients in the control group attending the emergency department within 30 days (10% phone call versus 24% no phone call, $p=0.005$).

Reference	Level	Setting	Subjects	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Rainville 1999 (9)	1-	Medical Center, Vermont , USA	Patients ≥50 years with heart failure	Control group received routine discharge, which included written prescriptions, physician discharge instructions and a nurse review of diet, treatment plan and medication. The intervention group received routine care plus pharmacist review of medication, education and corrective action for potential risks for re-hospitalisation. A follow-up telephone call to patients 3 and 7 days after discharge.	17 intervention, 17 control patients. Followed up by the pharmacist 30 and 90 days and 12 months	Level 1 Mortality; Hospital re-admissions within 12 months for heart failure (patient reported)	During the 12 months of post-discharge monitoring 10 patients in the control group (59%) were readmitted to hospital for heart failure compared with 4 (24%) in the intervention group ($p<0.05$). The total number of re-admissions was 26 in the control group and 20 in the intervention group; in each group there were 16 re-admissions for reasons other than heart failure. Either death or readmission in the post-discharge period occurred for 14 patients in the control group (82%) and for 5 intervention patients (29%) ($p<0.01$).

Excluded studies

Studies considered but excluded from this review because they were either not controlled or actual patient outcomes were not measured included:

Brookes et al., 2000 (16)
Cattell et al., 2001 (17)
Choo and Cook, 1997 (18)
Cromarty et al., 1998 (19)
Cromdos and Allen, 1992 (20)
Duggan et al., 1998 (21)
Dvorak et al., 1998 (22)

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4. Pharmacist clinic services

The service

Pharmacist-managed or pharmacist-run clinics described in the international literature provide care to patients with chronic conditions including diabetes mellitus, hypertension, hyperlipidaemia, coronary artery disease, asthma and epilepsy and to those receiving anticoagulant therapy. Pharmacist services provided in these clinics include monitoring drug therapy outcomes, ordering and interpreting laboratory tests, making recommendations to physicians, providing education to patients, providing a point of contact for patients for queries or concerns and providing follow-up. In some clinics pharmacists have prescribing rights or, using approved protocols, make drug therapy selections and adjustments to drug therapy including dosage changes.

Pharmacists may also provide services in clinics to patients prior to their admission to hospital (pre-admission clinics). These services include medication history taking, prescription transcription and provision of information and advice to patients and health care professionals. These are considered separately from pharmacist-managed clinics in this chapter.

Pharmacist-managed clinics

Studies included

Studies were included if they assessed a service described as a pharmacist-managed, pharmacist-operated or pharmacist-run clinic. The service was provided to outpatients or ambulatory care patients or was located in a community setting. Clinics for hospital inpatients were excluded. Studies assessing only satisfaction with or opinion of a service were excluded.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), knowledge or compliance (level 1, 2 or 3 outcomes).

Studies only assessing level four outcomes, such as changes in satisfaction with or opinion of the service were excluded.

Study designs

Two randomised controlled trials (level 1- method) were located which assessed a pharmacist-managed clinic (Table 4.1). Both of these studies assessed hypertension clinics and were conducted in the USA. There were also five non-randomised studies with a control or comparison group located (level 2 method). The level 2 studies assessed pharmacist-managed or operated clinics for patients receiving anticoagulant therapy (1-3), a lipid clinic for patients with a diagnosis of coronary artery disease (4) and a drug therapy monitoring

clinic for patients with a variety of chronic conditions (5). All five level 2 studies were conducted in the USA. These studies are summarised in Appendix II Table 3.

The clinics assessed in both the randomised controlled studies (level 1- method) provided care for adult patients with essential hypertension. The study by Okamoto and Nakahiro (6), conducted in a single managed care facility, assessed the service for patients taking one of a series of targeted antihypertensive medications. The study by Vivian (7), conducted in a single Veterans' Affairs Medical Centre, assessed a service for patients taking any antihypertensive medication.

The pharmacist service provided in the managed care setting (6) involved the clinical pharmacist managing the patient's drug treatment with the aim of minimising the number of medications taken by the patient and making necessary changes to ensure the most appropriate therapy was used. The pharmacist determined the most appropriate therapy, ordered laboratory testing as required and counselled the patient. The patient's physician was contacted to approve any therapeutic changes. For the clinic in the Veterans' Affairs medical clinic (7), the pharmacist also provided counselling as well as compliance assessment and adjustment of antihypertensive therapy. In this study the clinical pharmacist had prescribing rights for antihypertensive medications and was able to change the drug selection and dosage in accordance with National guidelines.

Both randomised controlled trials were conducted over a six-month period, in one study the number of visits during the study period was at the discretion of the clinical pharmacist (6), while in the other study patients attended the clinic on a monthly basis for six months (7).

In both studies the patient was the unit of randomisation. The studies were both rated as level 1- for method as there was no mention of blinded or independent assessment of the patient outcomes.

Study outcomes

Both randomised controlled studies assessed patient health outcomes and surrogate health outcome measures. Outcome measures included:

- Health-related quality of life (measured with the SF-36 instrument) (level 1 outcome)
- Emergency room visits related to blood pressure (level 1)
- Hospitalisations (level 1)
- Surrogate health outcomes (systolic and diastolic BP, proportion of patients achieving goal BP levels) (level 2)
- Patient compliance (level 3)
- Number of prescriptions (level 3)

Evidence for effectiveness of practice

Two randomised controlled trials (level 1- method) provide evidence for the effectiveness of pharmacist-managed hypertension clinics for improving blood pressure measurements (level 2 outcomes) in adult patients with essential hypertension in the USA health setting.

Level 2 evidence suggests pharmacist managed clinics can improve HbA1C levels for patients with diabetes, improve lipid levels for those with coronary artery disease, and reduce major haemorrhagic events for those on anticoagulant therapy.

There is a lack of research in the Australian setting assessing pharmacist-managed clinics.

Further studies of rigorous methodology (level 1 method) are required to evaluate pharmacist-managed clinics for chronic conditions within Australia and internationally

Further rigour needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation.

Only one study included an economic assessment, however, no firm conclusions can be drawn due to methodological limitations. Further economic evaluations are required.

Evidence for efficacy for changes in morbidity (Level 1 outcomes)

Quality of life

Both level 1 studies used quality of life as an outcome and both used the SF-36 measure. The only significant difference was in one of the 8 domains of the SF-36 (role-physical), which was significantly higher in the intervention group in the study by Okamoto and Nakahiro (6) (level 1- method). There were no significant differences in any domains of the measure in the other study (7) (level 1- method). This study had a small number of patients (26 intervention and 27 control patients completed the study), and the authors stated that there was insufficient power to detect a difference in health perceptions. It should also be noted that the target group for both clinics was patients with hypertension. Given that treatment of hypertension often aims to prevent long term complications, it may be that a six month follow-up is insufficient for detecting changes to quality of life. Improvement in hypertension management is unlikely to translate into improvement in quality of life for many patients.

Hospitalisations and emergency room visits

Only one study assessed hospitalisations and emergency room visits related to blood pressure (6). During the six-month study period there were no hospital admissions in either group. There were four blood pressure-related emergency room visits in the control group compared to none in the intervention group. Due to the small number of these events an assessment of the impact of the intervention on this outcome measure cannot be made. Assessments of whether or not the emergency room visits were blood pressure-related were made by investigators who were not blinded to subject group allocation.

Evidence for efficacy, as measured by surrogate endpoints (Level 2 outcomes)

Change in blood pressure was used as an endpoint in both of the randomised controlled trials. Both studies found significantly greater decreases in diastolic and systolic blood pressure over a six-month period for patients managed by the pharmacist clinic compared to those receiving usual physician care. In the study conducted in a managed care facility (6) the mean reduction in systolic BP was 9.1 mm Hg for the intervention and 1.3 mm Hg for the control group ($p<0.001$). The mean reduction for diastolic BP was 5.2 mm Hg for the intervention group and 1.5 mm Hg for the control group ($p<0.001$). In the study conducted in the Veterans' Affairs medical centre (7) the mean reduction in systolic BP from baseline was 18.4 mm Hg for the intervention group and 3.98 mmHg for the control group ($p=0.01$). Mean changes in diastolic BP were reduction of 12.4 mm Hg for the intervention group and an increase of 2.5 mm Hg for the control group ($p=0.001$). Mean diastolic BP, however, was significantly higher for the intervention group than the control group at baseline. In this study the proportion of patients achieving goal BP levels (according to National guidelines) was also used as an outcome measure. The proportion of patients in the intervention group achieving goal levels (81%) was significantly higher than in the control group (30%) ($p=0.001$).

Evidence for efficacy on changes in medication use or compliance (Level 3 outcomes)

One of the randomised controlled trials (6) assessed the number of prescription medications per patient. At the end of the six-month study period there were no significant differences in the mean number of antihypertensive medications per patient between the groups or compared with baseline values.

Compliance was used as an outcome measure in the study by Vivian (7). There were no significant differences in the compliance between the intervention and control groups.

Further supporting evidence

Further supporting evidence for the effectiveness of pharmacist-run clinics for other disease states or conditions is provided by non-randomised controlled trials (level 2 method). These studies suggest pharmacist managed clinics can improve HbA1C levels for patients with diabetes (5) and improve lipid levels for those with coronary artery disease (4). Level 2 evidence evaluating pharmacist managed anticoagulant clinics also suggests the clinics can reduce major haemorrhagic events (3), unplanned clinic visits, emergency room visits and unplanned hospitalisations (1, 3) (see Appendix II Table 3).

Economic assessment

One randomised controlled trial compared hypertension care provided by pharmacist-run clinics with physician-run clinics (6). Total costs and costs of antihypertensive drugs per patient were not different between the groups. The total cost of clinic visits per patient was significantly higher in the pharmacist-run clinics due to a higher number of visits per patient in this group. A cost-effectiveness analysis concluded that the cost/effectiveness ratios expressed in terms of costs of decreasing diastolic or systolic blood pressure by 1 mm Hg were lower in the pharmacist-run clinics than in the physician-run clinics. However, very few

details were available on the methodology that was used to perform the cost-effectiveness analysis. It seems there were shortcomings in the identification of all relevant costs. (6)

Australian research

All controlled studies that were located assessed pharmacist-managed clinics conducted in the USA. No studies assessing the impact of a pharmacist-managed or pharmacist-run clinic on patient outcomes in the Australian setting were located.

Comment

Two randomised controlled trials (level 1- method) provide evidence for the effectiveness of services provided in a pharmacist-managed hypertension clinic for reducing blood pressure measurements in adult patients with essential hypertension. Both of these studies were conducted in single centres in the USA which limits the generalisability of the findings. Future research needs to evaluate the wider implementation of these services.

Both studies utilised quality of life (measure with the SF-36 instrument) as an outcome. There was little evidence for any impact of quality of life measures, although one study had insufficient sample size to detect a difference and follow-up periods were relatively short. It is not clear whether the lack of impact on quality of life measures is the result of service delivery, insufficient follow-up or if the measures utilised thus far are simply not sensitive enough or appropriate as an outcome measure of the service. One study used hospitalisations and blood pressure-related emergency visits as an outcome measure. The low numbers of these events limited the ability to assess the impact of the service on these outcome measures. Larger studies conducted over a longer time frame are required to assess the impact of this service on hospital admission rates.

Evidence from non-randomised studies (level 2 method) suggests pharmacist managed clinics can improve HbA1C levels for patients with diabetes (5) and improve lipid levels for those with coronary artery disease (4). Level 2 evidence evaluating pharmacist managed anticoagulant clinics also suggests the clinics can reduce major haemorrhagic events (3), unplanned clinic visits, emergency room visits and unplanned hospitalisations (1, 3).

Further studies of rigorous methodology (level 1 method) are required to evaluate pharmacist-managed clinics for other chronic conditions and for the management of anticoagulant therapy. Further rigor needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation.

Studies excluded

The following studies assessing pharmacist-managed clinics were reviewed but excluded due to lack of a control group:
Pauley, Magee et al., 1995 (8)
Tadros, Ledger-Scott et al., 2002 (9)
Cording, Engelbrecht-Zadomy et al 2002 (10)
Radley, Hall et al., 1994, Radley and Hall, 1994 (11, 12)
Farnsworth, Kim et al., 2001 (13)
Spalek and Gong, 1999 (14)
O'Donnell, Chen et al., 2001 (15)
Chiquette et al., 1998 (16) (outcomes of the comparison group were not compared over the same period of time)

Pre-admission clinics

Studies included

Pre-admission clinics are utilised to facilitate the hospital admission process. Studies assessing a pharmacist service in a pre-admission clinic were included if they described the involvement of a pharmacist in patient assessment prior to hospital admission in a pre-admission clinic.

Study designs

One non-randomised controlled trial (level 2 method) (17) conducted in a single hospital in the UK was located. This study assessed a pharmacist pre-admission service for patients undergoing elective general surgery. Other studies located lacked a control or comparison group (18-20) (level 3 method).

In the controlled study (17) (level 2 method) the first 50 patients on a consultant's elective surgery admission list were allocated to the intervention group, with 50 patients from another consultant's list allocated to the control group. The pharmacist intervention involved taking a written medication history from the patient, writing the patient's regular medications on their hospital medication chart, writing discharge medication requirements on a discharge advice note, providing advice to clinicians and the patient. The control group received a standard post-admission ward visit from the same pharmacist.

It appears from this study that pharmacist interventions could have occurred for the pre-admission clinic group, either at the time of the pre-admission clinic or during hospital stay, while the control group interventions occurred during hospital stay. The overall intervention rate was one of the outcome measures. Unfortunately, it cannot be determined from the study report, when the interventions occurred for the pre-admission clinic participants. This is a major limitation of the study design, as differences in the pharmacist intervention rate during hospital stay is probably a more relevant endpoint for determining the effectiveness of the pharmacist participation in the pre-admission clinic.

Study outcomes

The study outcomes assessed in the controlled trial (level 2 method) were:

- Number of pharmacist interventions required for prescribing errors or omissions (level 3 outcomes)
- Number, classification and clinical significance of pharmacist interventions (graded by 2 independent panels) (level 3)

Evidence for effectiveness of practice

Pharmacist involvement in pre-admission clinics appears to be a relatively new service and consequently little research has been undertaken in this area.

Level 2 evidence from one UK study suggests pharmacist involvement in pre-admission clinics may reduce error rates, but poor methodology limits any conclusions that can be drawn.

No Australian studies were located.

Admission to hospital is a point where continuity of care can break down. Future research in this area should not necessarily limit the service to patient assessment prior to admission, but also include liaison services with community care providers, which is co-ordinated with the post-discharge continuity of care service to support the entire continuum of care for the patient.

Further rigorous research, including economic evaluation is required.

The results of the study by Hick et al. (17) found prescription writing was more accurate for the intervention group than the control. There were 10 pharmacist interventions for prescribing omissions and 3 interventions for "wrong drug prescribed" in the control group. For the intervention group there were no pharmacist interventions required for omissions or wrong drug.

Overall the clinical significance of the pharmacist interventions for the intervention group was rated more highly by the assessment panels using the rating two scales than that for the control group. Overall pharmacist intervention numbers for the 2 groups were similar, 76 (124 component parts) in the intervention group and 79 (111 component parts) in the control. These results should be interpreted with care, however, as the report of study outcomes does not enable an assessment of differences in the pharmacist intervention rate during hospital stay, which would have been the better outcome measure. This currently limits the conclusions that can be made about the effectiveness of the service.

Economic assessment

No economic evaluations were presented in the included study

Australian research

No published studies were located assessing pharmacist involvement in pre-admission clinics in the Australian setting.

Comment

There have been insufficient studies undertaken at this time to determine the effectiveness of pharmacist involvement in pre-admission clinics. Early research provides insight into methodology, although the limitations in existing methodologies need to be overcome. Future research needs to consider differentiating activities and outcomes associated with the pre-admission clinics from those relating to hospital stay to determine whether the pre-admission clinics make any difference to patient outcomes during hospital stay.

It is interesting to note the lack of research in this area, particularly in comparison to the more comprehensive assessment of pharmacist involvement in continuity of care services post discharge. (See continuity of care services on discharge from hospital in Chapter 3). Studies indicate that continuity of care is also an important issue on admission to hospital (21, 22). One Australian study which examined problems with medication histories on admission found that, on average, one medicine was omitted from the medication history for every two patients admitted (21). Error rates of this level have the potential to lead to a significant number of adverse drug events and potentially patient harm. It would seem this area of research deserves considerably more attention. Future research in this area should not necessarily limit the service to patient assessment prior to admission, but also include liaison services with community care providers, which is co-ordinated with the post-discharge continuity of care service to support the entire continuum of care for the patient.

Table 4.1 Table of randomised controlled trials evaluating pharmacist-managed clinics

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Educational visits to physicians following use of pharmacy records to identify patients						
Okamoto and Nakahiro, 2001 (6)	1-	Managed care facility, California, USA (Single centre)	18 years or older, had a diagnosis of essential hypertension, and were taking one of the targeted anti-hypertensive medications (nifedipine, verapamil, captopril, diltiazem, clonidine, terazosin, propranolol, lisinopril). In the pharmacist-managed clinic the clinical pharmacist managed the patients' treatment but contacted the physician to obtain consent for any therapeutic changes. The pharmacist determined the most appropriate medication regimen for the patients, ordered any necessary laboratory tests and educated the patient. The number of appointments was at the discretion of the pharmacist. The control group received usual care from the physician	164 intervention, 166 control Follow-up at 6 months	Level 1 HRQOL (SF-36); Emergency room visits primarily related to BP, and hospitalisations Level 2 Systolic and diastolic BP Level 3 Scheduled clinic visits, number of prescriptions per patient	The only significant difference in HRQOL scores between the groups at 6 months was in the "role-physical" domain that was significantly higher in the intervention group ($p=0.03$). There were no hospital admissions in either group during the study period. There were four BP-related emergency room visits in the control group compared to none in the intervention group. The mean reduction in systolic BP was 9.1 mm Hg for the intervention and 1.3 mm Hg for the control group ($p<0.001$). The mean reduction for diastolic BP was 5.2 mm Hg for the intervention group and 1.5 mm Hg for the control group ($p<0.001$). The number of scheduled clinic visits during the study was significantly higher for the intervention group (mean 5.2) compared to the control group (mean 1.4) ($p<0.001$). There were no significant differences in the average number of anti-hypertensive medications per patient between the groups or compared with baseline.

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Vivian, 2002 (7)	1-	Clinic at a Veterans Affairs Medical Center Philadelphia, USA	Patients with essential hypertension and aged 18 years or older. Intervention patients attended the pharmacist-managed clinic once a month over 6-months. The clinical pharmacist had prescribing authority and made appropriate anti-hypertensive drug therapy changes in accordance with Joint National Committee on the Detection, Evaluation and Treatment of High Blood Pressure guidelines, but did not change other medications. The intervention group also received medication and lifestyle counselling and compliance assessment at each visit. Control patients received normal care from primary care providers	26 intervention, 27 control Follow-up at 6 months	Level 1 HRQOL (SF-36) Level 2 Systolic and diastolic BP; Number of patients achieving goal BP below 140/90 mmHg Level 3 Compliance	HRQOL: There were no significant differences in SF-36 scores within or between groups (p>0.2). BP: Number of patients achieving the goal BP was significantly greater in the intervention compared to control group (intervention 21/26 (81%) versus control 8/27 (30%), p=0.001). Mean changes in systolic BP from baseline were –18.4 mmHg (95% CI –26.3 to –10.5) for the intervention group and –3.98 mmHg (95% CI –11.8 to 3.8) for the controls (p=0.01). Mean changes in diastolic BP were –12.4 mm Hg (95% CI –16.5 to –8.28) for the intervention group and +2.54 (95% CI –1.49 to 6.57) for the control group (p=0.001). Mean diastolic BP was significantly higher for the intervention group than the control group at baseline. Compliance: no significant differences

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5. Medication review for repeat prescriptions

The Service

Repeat prescribing allows a patient to obtain a repeated supply of medication without the need for a doctor's consultation. Studies have been undertaken to assess whether a service involving the review of repeat prescriptions by a pharmacist achieves similar or improved patient outcomes compared to usual care, where review is undertaken by another health professional.

Studies included

Studies were included if they involved the pharmacist as the identified person responsible for review of the repeat prescription and actively assessed the continuing need for the medication.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), knowledge or compliance (level 1, 2 or 3 outcomes). Studies only assessing level four outcomes, such as changes in satisfaction with or opinion of the service were excluded.

Study design

Two randomised controlled trials (level 1- method) assessing review of repeat prescribing by pharmacists were located (Table 5.1). These studies were both undertaken in the community setting in the UK. Both studies involved a patient interview by the pharmacist to determine continued need for therapy.

The manner in which the service was implemented varied between the two studies. One study conducted in Scotland (1) (level 1- method) assessed a new repeat prescribing service in which community pharmacists monitored and authorised repeat prescribing and dispensing. General medical practices were the unit of randomisation. Eligible patients seen in the practices were aged 16 years or older on repeat medications that did not require a review by their doctor in less than 3 months. Control group practices continued to issue repeat prescriptions according to standard practice while in intervention practices patients were issued with 3-month prescriptions to last them until the next time the GP considered the patient needed to be reviewed (3, 6 or 12 months). The prescriptions were kept by a trained community pharmacist of the patient's choice who authorised and dispensed the prescription at monthly intervals. At the time of dispensing the pharmacist reviewed the medication and interviewed the patient using a standard protocol (to assess issues such as compliance, adverse effects, interactions, and whether there was a continued need for the medication).

Another study conducted in England (2, 3) (level 1- method) assessed a "clinical medication review" service which was conducted by a study pharmacist in an office located in the general practice or in the patient's home. Eligible patients were aged 65 years or over and taking at least one repeat prescription medication. The clinical medication review service was

described as a "process where a health professional reviews the patient, the illness, and the drug treatment during a consultation". The review was undertaken to assess whether medication required continuation, whether changes were necessary and whether referral for medical assessment was required. Issues assessed through the review included the therapeutic efficacy of each drug, the progress of the patient's conditions, compliance, actual or potential adverse effects, drug interactions and the patient's understanding of their treatment. The unit of randomisation for the study was the patient. Intervention patients received the clinical medication review service while those in the control group received usual care and review of treatment by their GP when required.

The studies were rated level 1- for method due to the lack of blinded assessment of outcome measures.

Study outcomes

Outcome measures used in the two randomised controlled trials were varied and included:

- Acute hospital admissions (level 1 outcome)
- Mortality (level 1)
- Number of repeat medicines (level 3)
- Number of changes to repeat prescriptions (level 3)
- Dose frequency (level 3)
- Identification of adverse reactions/side effects, drug interactions or compliance problems (level 3)

Evidence for effectiveness of practice

Two studies (level 1- method) demonstrated that patient outcomes were no different to usual care, when pharmacists reviewed the continuing need for repeat prescriptions which were usually provided by a physician. The applicability of these findings across different disease states is not yet known, however.

Studies have only been undertaken in the UK which limits the generalisability of the results to other countries, where health systems may differ considerably

Future studies need to be undertaken in other health systems and include blinded assessment of patient outcomes to provide further evidence of the effectiveness of this pharmacist service.

Economic studies are still required. No full economic evaluations were located. There is only limited evidence from one randomised controlled trial that medication review of repeat prescribing can decrease drug costs. There is currently no evidence that review of repeat prescribing by pharmacists is more cost-effective than usual care.

Evidence for efficacy of changes in morbidity and mortality (Level 1 outcomes)

The two studies reporting mortality as an outcome measure found no significant differences between the groups. In the study assessing review of repeat prescribing in the community pharmacy setting (1) death rate in the intervention group was 3.6% and in the control group was 3.8%. In the study assessing a clinical medication review service conducted by a study pharmacist in a general practice office (3) the death rate during the study period was 2.5% for the intervention group and 4.5% for the control group, which was not a significant difference (OR = 0.56, 95% CI 0.29 to 1.1).

There were also no significant differences in hospitalisation rates reported in these two studies. In the study in the community pharmacy setting (1) the proportion of patients admitted to hospital was 6% for the intervention group and 6% for the control group. In the clinical medication review study (3) the proportion of patients with one acute hospital admissions was 13% in the intervention group and 10% in the control group (p=0.61), while the proportion of patients admitted more than once was 6% for the intervention group and 7% for the control group.

Evidence for efficacy for level 3 outcome measures

In the study by Zermansky et al (3) assessing a clinical medication review service the number of repeat medications and the mean number of dose times per day was compared before and after the study. There was an increase in the mean number of repeat medications for both groups compared with baseline, however the mean increase in the intervention group (0.2 repeat medications per patient) was significantly lower than the control group (0.4 repeat medications per patient) (p=0.01). The mean number of dose times per day was not significantly different between the groups. In the study conducted in the community pharmacy setting (1) the median number of medications prescribed was reported as significantly lower in the intervention group compared to the control (p=0.003).

The number of changes to repeat medications (such as drug started or stopped, dose changed, drug switched) was also assessed in the study by Zermansky et al (3). There was a mean of 2.2 changes per intervention patient and 1.9 per control patient during the study, which was significantly different (p=0.02).

Further supporting evidence

One other study, which was not directly comparable to the two reported above, provides further support for pharmacist involvement in repeat prescribing. The study, also conducted in England (4) (level 1- method) assessed the quality of repeat prescribing following review of repeat prescriptions by a pharmacist. A community pharmacist reviewed medical notes and all repeat prescriptions with three or more items on the day they were written to identify drug-related problems (DRPs). Drug-related problems were defined broadly as “any problem with the prescribed medication that the community pharmacist considered was not good prescribing practice”. The review was conducted in a single GP surgery and took place before routine review and signing of the prescription by the GPs. Prescriptions were then randomised to intervention or control after DRPs were identified. Discussions of suggested prescription interventions for DRPs were then held between the pharmacist and GP at a meeting (once or twice a week). Intervention group prescriptions were discussed at the first meeting following the identification of the DRP, while control prescriptions were discussed

after a minimum of one consecutive issue of the prescription. The number of DRPs resolved by pharmacist-GP collaboration and by the GP alone was compared. A total of 511 repeat prescriptions were reviewed (248 assigned to the intervention and 252 to the control) with 11 not assigned to a group because the DRP was deemed to require immediate attention. The outcome measure was the number of drug related problems resolved. Ninety repeat prescriptions (36%) in the intervention group and 86 (34.1%) prescriptions in the control group were identified as having DRPs. For the intervention prescriptions 77 (85.6%) of the interventions suggested were accepted by the GP and acted on, while for the control prescriptions 11 (12.8%) were resolved through routine monitoring by the GP ($p<0.001$). The outcome measurement appears to have been undertaken by the study pharmacist, which has potential to bias the results. A review of a sample of the prescriptions was carried out by independent GPs to assess clinical significance. It was estimated that an intervention resulting in or potentially resulting in improved patient care occurred for every 19 prescriptions reviewed by the community pharmacist.

Economic assessment

In the randomised controlled trial which assessed the efficacy of a pharmacist reviewing repeat prescriptions through consultations with elderly patients in general practice in UK (3), monthly drug costs rose in both groups over the one-year study period but the rise was significantly less in the intervention group ($p = 0.0001$). The average reduction in net cost of drugs per patient per 28 days was £4.72 (£2.41 to £7.04). There were no changes in the use of health services (general practice consultations, hospital admissions).

In the randomised controlled trial which assessed the role for community pharmacists in controlling and monitoring repeat prescriptions (1), 66% of patients in the intervention group did not require their full quota of prescribed drugs, representing 18% of the total prescribed costs (estimated annual drug cost avoidance of £43 per patient). No data were presented for the control group.

Collectively, these studies provide very limited economic evidence. No full economic evaluations were located. Further studies are required.

Australian research

Controlled trials assessing pharmacist review of repeat prescribing in the Australian health care setting were not located.

Comment

Randomised controlled trials (level 1-) assessing the capacity for pharmacists to review the continuing need for repeat prescribing have demonstrated that patient outcomes when the pharmacist provides the service are no different to usual care, usually provided by the physician. Currently, however, it is not known if these results are applicable across different disease states. Both studies were undertaken in the UK which limits the generalisability of the results to other countries, where differences in the health system may impact on the results. Both studies had methodological limitations, with assessment of outcomes by reviewers who were not blinded to group allocation. Future studies need to be undertaken in other health systems and include blinded assessment of patient outcomes to provide further evidence of the effectiveness of this pharmacist service.

Table 5.1 Randomised controlled trials (Level 1) assessing pharmacist review of repeat prescribing

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Zermansky et al., 2001(3) Petty et al., 2002 (2)	1-	General practices, Leeds Health Authority, UK	Eligible patients were community-dwelling, aged 65 or older and were receiving at least one medication on repeat prescription. The pharmacist interviewed the patient, reviewed their medical conditions and treatment, assessed continuing need, suboptimal treatment, side effects, drug interactions, contraindications and medication costs. The pharmacists made recommendations/referrals to the general practitioner and implemented minor changes, including changes the GP considered did not require a consultation.	581 intervention, 550 control 12-month study period	Level 1 Acute admissions Mortality Level 3 Number of repeat medicines, dose frequency; Number of changes to repeat prescriptions; GP visits, hospital outpatient attendances	15 (2.5%) deaths in the intervention group and 25 (4.5%) in the control group (OR = 0.56, 95% CI 0.29 to 1.1). Seventy-eight (13%) intervention patients had one acute hospital admission compared to 55 (10%) control (p=0.61). Mean of 2.2 changes to repeat prescriptions per intervention patient and 1.9 changes per control (p=0.02). Repeat medications increased in both groups. The mean increase was significantly less in the intervention group (0.2 repeat medicines) compared to control (0.4 repeat medicines). (p=0.01). No significant differences in the number of doses per day between groups (p=0.17). No significant effects on use of health care resources.
Bond et al., 2000 (1)	1-	General medical practices and community pharmacies Grampian, Scotland Multi-centre	Eligible patients were aged 16 years or older on repeat medications that did not require review by their doctor in less than 3 months. Intervention patients were issued with 3-month prescriptions to last them until the next time the GP needed to reviewed them (3, 6 or 12 months). The pharmacist then authorised and dispensed the prescription at monthly intervals. At this time, the pharmacist reviewed the patient and the medication according to a standard protocol (including compliance, adverse effects, interactions, need for medication). The pharmacist recorded the information at each visit.	905 intervention group 1405 for the control 12 month study period.	Level 1 Deaths Hospital admissions Level 3 Number of medications; Adverse reactions Drug interactions Compliance problems identified;	Death rate for the intervention group (3.6%) was the same as the control group (3.8%). Number of patients admitted to hospital was 54 (6.0%) in the intervention group and 80 (5.7%) in the control (p=0.856). A higher median number of drugs prescribed for the control group compared to the intervention group (p=0.003). There were significantly more compliance problems identified in the intervention group compared to the control group (p=0.0001)

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6. Medication Review in Aged Care Facilities

The Service

The elderly living in long-term care facilities are considered to be at particular risk of medication-related problems, including adverse drug reactions. Medication review services have been implemented in aged care facilities to address this problem. Pharmacist–conducted medication review (also known as drug regimen review) involves a review of the medication record and medical case notes with an assessment of all factors likely to influence therapeutic outcomes. This involves collection of information about a patient's medications, their relevant medical history and laboratory test results. This information is used to identify and resolve medication-related problems.

Studies included

Medication review services were considered to be those that were primarily medication chart and medical case note review, without active consultation with the patient. Studies were included if they assessed medication review services conducted by a pharmacist for residents of an aged care facility. Studies including medication review as part of a pharmaceutical care intervention were not included in this section but are reviewed in the other relevant section of this report.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), knowledge or compliance (level 1, 2 or 3 outcomes). Studies only assessing level four outcomes, such as changes in satisfaction with or opinion of the service were excluded.

Study design

Three randomised controlled studies (level 1- method) assessing pharmacist conducted medication review services for residents of aged care facilities were located (Table 6.1). These studies were conducted in Australia and the UK. There were two non-randomised controlled studies (level 2 method) located which met the inclusion criteria. The two studies were conducted in Australia (Appendix II, Table 4).

The intervention differed between studies. While all the studies included medication review in the aged-care setting, the study by Roberts et al. (1, 2) was undertaken within the context of establishing cultural change as medication review services had not been offered in nursing homes in Australia before. This study, in addition to the medication review, included supportive activities such as focus groups and researcher support by telephone and face-to-face to facilitate the intervention. Nursing staff also received problem based education by the pharmacists and wall charts and bulletins were produced. By comparison the UK study (3) was primarily a medication review, but did include liaison with nursing home staff to ascertain problems they had identified. One study was undertaken in the aged-care hostel setting in Australia (4), which caters for residents with lower level care needs, and so who are

often healthier, than residents in nursing homes. This study used a similar approach to the Australian nursing home study (1, 2).

The studies were well designed, although it appears that the reviewers undertaking outcome assessments were not blinded to group allocation, which has the potential to bias study results. Despite this limitation, design strengths included the use of validated instruments for outcome assessment, such as the Resident Classification Instrument (1, 2), the Mini Mental State Examination, Geriatric Depression Scale, Brief Assessment Schedule Depression Cards, and Crichton-Royal Behaviour Rating Scale (3) or data collected from independent data sets, such as prescription dispensing data (1, 2).

Study outcomes

Outcome measures used in the randomised controlled trials included:

- Mortality (level 1 outcome);
- HRQOL (SF-36) (level 1);
- Cognitive function, behavioural disturbance and depression (measured using Mini Mental State Examination (MMSE), Geriatric Depression Scale (GDS), Brief Assessment Schedule Depression Cards (BASDEC), Crichton-Royal Behaviour Rating Scale (CRBRS)) (level 1)
- Disability (measured using disability indices including the Resident Classification Instrument) (level 1);
- Adverse events (level 1);
- Hospitalisations (level 1);
- Number of accidents or falls (level 1);
- Medication use (level 3);
- Medication incidents (level 3)

Evidence for effectiveness of practice

There are only a limited number of studies conducted world-wide assessing medication reviews in nursing homes.

Best practice is not yet clear with studies reporting mixed results. One study (level 1-) reported finding a decrease in mortality, however, this was not supported by changes in other morbidity outcomes. A second study (level 1-) found no effect, although insufficient sample sizes and the lack of sufficient follow-up may have contributed to this finding. Given the significant potential for problems and ultimately harm to patients in aged-care facilities, from inappropriate medication use, it seems apparent that there is great need for further rigorous research in this area to establish best-practice.

In general, no significant difference was seen in other morbidity measures, although one study reported improvement in some domains of the SF-36 quality of life measure.

Two of the three studies reported significant changes in medication use. One found an overall reduction in medication use, the second found a decrease or increase in medication use dependent on the culture of the organisation. The third study found a reduction in medication use in both groups, however, no significant differences between groups was observed.

Consideration needs to be given to further study using outcome measures that are suitable for the setting. Adverse drug events may be a more suitable outcome measure. Non-specific morbidity outcome measures may not be suitable in this instance. Assessment of outcomes by reviewers blinded to group allocation is also required.

No full economic evaluation on the cost/effectiveness of the medication review services was located. There is some evidence from randomised controlled trials that medication review services in nursing homes can decrease drug costs. However, none of the studies showed an association between reduction in drug costs and improvement of clinical outcomes.

Further studies are needed to establish how long savings are maintained and how frequently medication review should take place.

Evidence for efficacy of changes in morbidity and mortality (Level 1 outcomes)

Only one of the two studies utilising mortality as an endpoint reported a reduction in mortality in the intervention group (3). Fourteen deaths occurred during the intervention phase in the control homes compared to 4 deaths in the intervention homes ($p=0.028$). This finding was not supported changes in any other morbidity outcomes, however.

The only study to report an effect on morbidity measures, was that undertaken in aged-care hostels (4), which found a reduction in adverse events in the intervention group (30%) compared to the control group (40%) reported by patients when they were asked about specific types of events. The statistical significance of this was not reported, however, and the link to adverse drug events was not clear. This study also found some significant improvements in some of the quality of life domains, but not in overall quality of life scores (4). The UK study (3) reported that the number of accidents or falls did not differ significantly between the groups. No changes were observed in MMSE scores or depression

scores. An increase in behavioural disturbance, measured by CRBRS scores, was observed in the intervention group at the end of the study compared to the control. However, this was not thought to be due to the intervention, as an increase in CRBRS scores occurred before the implementation of medication reviews (3). The Australian nursing home study (2) found frequency of hospitalisation, annual mortality rate, number of residents for which adverse events were reported and changes in measures of disability for residents were not significantly different between the intervention and control groups.

Evidence for efficacy for level 3 outcome measures

Two studies reported significant changes in medication use. The clinical pharmacy intervention undertaken in Australian nursing homes was found to reduce overall medication use by 11% to 15% and improve the quality of medication use in the nursing homes. A significant reduction in the use of benzodiazepine hypnotics, laxatives, non-steroidal anti-inflammatory drugs and antacids was associated with the intervention (1, 2). The study undertaken in Australian hostels found increases or decreases in medication use, which appeared to be dependent on the culture of the hostel (4). In hostels having an organisational structure (staffing, documentation procedures) that facilitated change there was an average reduction in overall drug use of 13.8% with the intervention. A significantly greater proportion of residents in the intervention group ceased cardiovascular drugs, benzodiazepine hypnotics, antidepressants and antipsychotic medications, while a greater proportion started osmotic and stool-softening laxatives, artificial tears and selective serotonin reuptake inhibitors (4). The UK study showed reduced medication use in both groups compared to baseline. The reduction was greater for the intervention group (0.9 drugs per patient) than the control (0.5 drugs per patient), however, this difference between groups was not statistically significant (3).

Economic assessment

The randomised controlled trial conducted in the UK assessed the impact of pharmacist medication review in nursing homes on the use of health care resources recorded over two 4-month periods, before and after the intervention (3, 5). Residents who had their medication reviewed had a significant reduction in total costs associated with primary and secondary resource use of £178 per resident over the 4-month period compared to the control group ($p=0.028$). This included a saving of approximately £22 in the medicine budget even accounting for the pharmacist's time.

The randomised trial which assessed a clinical pharmacy intervention in 52 nursing homes in Australia (1, 2) found a 14.8% reduction in drug use in the intervention group relative to the control group (non-significant). This was associated with a decrease in PBS drug costs of $64 per resident over one year. As the cost of delivering the pharmacist intervention was estimated at $48 per resident per year, this resulted in a net cost saving of $16 per resident per year. The HIC database used for calculating PBS drug costs had some limitations: records were only available for drug items with a schedule price above the co-payment, no drug data could be retrieved for 15.5% of residents and data from more than one person could be attributed to one person. The study did not look at other medical and laboratory costs and did not include a sensitivity analysis.

In conclusion, there is some evidence from randomized controlled trials that medication review services in nursing homes can decrease drug costs. However, none of the studies

showed an association between reduction in drug costs and improvement of clinical outcomes. Further studies would be needed to establish how long these savings are maintained and how frequently medication review should take place. We have not located any full economic evaluation on the cost/effectiveness of the medication review services.

Australian research

Level 1 Australian research has been included in the section above. There have been two other controlled (level 2) Australian studies undertaken (6, 7) which provide only limited further support for the effectiveness of medication reviews in nursing homes. Both reported no overall changes in medication use, although one (6) found that medication use was significantly reduced in residents whose general practitioner reported having an effective professional relationship with the pharmacist undertaking the review. One of these studies used the Sickness Impact Profile as an outcome measure, finding significant improvements in the psychological measure, but not the physical measure, for the intervention group compared to baseline, but failed to report statistical tests between groups (7). The level 2 studies are summarised in Appendix II, Table 4.

Comment

There are only a limited number of randomised controlled studies assessing medication reviews in nursing homes. Best practice is not yet clear with studies reporting mixed results. Only one study (level 1-) reported finding a decrease in mortality, with a second (level 1-) finding no effect. The decrease in mortality reported in the one study was not supported by changes in morbidity outcomes.

Only one study used adverse events as an outcome, showing a reduction in specific adverse events, although the validity of the measure is unclear and it was not clear whether these were adverse drug events. No effect was observed for other morbidity measures used. Two studies reporting changes in medication use, one finding an overall reduction in medication use, the second finding a decrease or increase in medication use dependent on the culture of the organisation and a third finding no effect.

Consideration needs to be given to the types of outcome measures that are being utilised in these studies. The measures employed in the studies reviewed here were general measures such as the Sickness Impact Profile and Disability, Behaviour and Mental State scales. This needs to be compared with the types of medication that were found inappropriate, including analgesics, laxatives, antacids, and psychoactive agents. It may be that measures more specific to symptom changes that would be expected from changes to these medications are more suitable. As mentioned previously, health-related quality of life appears to be an insensitive measure. Adverse drug events may be a more suitable measure, but were not commonly utilised in these studies.

Aged-care facilities are recognised as an area where there are significant problems with medication use (9). In some countries, pharmacist involvement in aged-care facilities is mandated (e.g. USA) or required as part of best-practice or accreditation standards (eg, Australia). Given the significant potential for problems and ultimately harm to patients, from inappropriate medication use in aged-care facilities, it seems apparent that there is great need for further rigorous research in this area to establish best-practice.

Table 6.1 Randomised controlled trials of pharmacist medication review services in aged care facilities

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Furniss et al., 2000 (3) Burns et al., 2000 (5)	1-	Nursing homes in South Manchester, UK Multi-centre	The study pharmacist conducted medication reviews for all residents in the intervention group nursing homes that gave consent. The pharmacist collected information on current medications, medical history and current problems. The homes were revisited by the pharmacist 3 weeks after the review, to monitor medication changes.	330 residents in the 14 nursing homes agreed to participate (158 intervention, 172 control). 4-month observation phase followed by a 4-month intervention phase.	Level 1 Mortality; Number of accidents or falls; Cognitive function, behavioural disturbance, Depression Crichton-Royal Behaviour Rating Scale (CRBRS)) Level 3 Number of prescribed medications	There were 14 deaths during the intervention phase in the control homes compared to 4 deaths in the intervention homes (difference between groups p=0.028). The number of accidents or falls did not differ significantly between the groups. Mini Mental State Examination (MMSE) scores and the number of residents with MMSE scores less than 23 did not change significantly over the course of the study in either group. Depression scores did not change significantly. Crichton-Royal Behaviour Rating Scale (CRBRS) scores were significantly higher in the intervention group at the end of the study compared to the control (i.e. an increase in behavioral disturbance). This decline was not thought to be due to the intervention, however, as an increase in CRBRS scores occurred before implementation of medication reviews. There was a reduction in the mean number of drugs prescribed for residents in both groups during the intervention phase. The reduction was greater for the intervention group (0.9 drugs per patient) than the control (0.5 drugs per patient), however, this difference was not statistically significant.
Roberts et al., 2001 (2) Departments of Medicine Pharmacy and Social and Preventive Medicine, 1995 (1)	1-	Nursing homes in Queensland and New South Wales, Australia Multi-centre	Year-long clinical pharmacy service involving individualised medication reviews, education for nursing home staff. The intervention was supported with activities to develop professional relationships between the nursing home staff and the pharmacist. Medication reviews were documented and placed in the resident's medical record, made available to the resident's GP and discussed with staff.	The study involved 3230 residents (905 in intervention homes, 2325 in control homes). Outcomes assessed at end of intervention period.	Level 1 Mortality; Hospitalisation rates; Disability Level 3 Medication use; Medication incidents;	Frequency of hospitalisation, annual mortality rate, number of residents for which adverse events were reported and changes in measures of disability for residents were not significantly different between the intervention and control groups. The clinical pharmacy intervention was, however, found to reduce overall medication use by 11% to 15% and improve the quality of medication use in the nursing homes. A significant reduction in the use of benzodiazepine hypnotics, laxatives, non-steroidal anti-inflammatory drugs and antacids was seen in the intervention

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Quality of Medication Care Group (4)	1-	Aged-care hostels in Queensland, Australia Multi-centre	This study assessed whether a service model similar to that described above for nursing homes (2) would be beneficial to residents of aged-care hostels. The medication review process, however, differed in the way information was collected. Due to less complete written records, medication information was supplemented from oral histories from the staff or resident, in some hostels information was collected by the pharmacist while in others the information was collected by a registered nurse. Pharmacist recommendations from the review reports were discussed with or mailed directly to the prescriber, with copies given to the hostel. The intervention period was 7 months. .	In total 1982 residents (983 intervention, 999 control group) from 38 hostels were involved Outcomes assessed at end of intervention period	Level 1 Mortality; HRQOL (SF-36); Hospitalisations Disability (using disability indices) Adverse effects ("mishaps"); Level 3 Medication use;	No statistically significant differences were found in overall mortality, hospitalisations, HRQOL or overall disability indices between the groups. There were was a significant improvement in the role-physical scale of SF-36 ($p<0.05$) for the intervention group relative to control. The disability index scores showed significantly improved "sociability", "mobility" and less "confusion", however there was significant deterioration in scores of "motivation" and "verbal disruption and/or physical aggression". Post-intervention adverse events were reported by 30% of the intervention and 40% of the control group when asked about specific types of "mishaps". The intervention resulted in both decreases and increases in medication use. The effect on overall medication use depended on the "organisational culture" of the hostel. In hostels having an organisational structure (staffing, documentation procedures, good communication) that facilitated change there was an average reduction in overall drug use of 13.8% with the intervention relative to controls. A significantly greater proportion of residents in the intervention group ceased cardiovascular drugs, benzodiazepine hypnotics, antidepressants and antipsychotic medications, while a greater proportion started osmotic and stool-softening laxatives, paracetamol, artificial tears and selective serotonin reuptake inhibitors.

Excluded studies

Level 3 study Elliott and Thomson 1999 (8)

References

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9. Roughead EE, Semple SJ, Gilbert AL. Quality Use of Medicines in Aged-Care Facilities in Australia. Drugs and Aging 2003; in press.

7. Medication review in the outpatient setting

The service

Pharmacist–conducted medication review (also known as drug regimen review) involves a review of the medication record and medical case notes with an assessment of all factors likely to influence therapeutic outcomes. This involves collection of information about a patient's medications, their relevant medical history and laboratory test results. This information is used to identify and resolve medication-related problems.

Studies included

Studies were included in this section if they were undertaken in the outpatient setting, involved a review of medical records and case notes to identify and resolve medication-related problems without also including a pharmacist interview with the patient for this purpose. Studies involving medication review as part of a pharmaceutical care intervention are reviewed in another section of this report. Unlike the pharmaceutical care studies, the medication review studies did not mention a patient interview conducted by the pharmacist. In addition, studies had to include patient outcomes or changes in medication use as a study end-point.

Study design

Two randomised controlled trials assessing medication review services in the outpatient setting were located (level 1 method) (1, 2). The studies are summarised in Table 7.1. Study designs varied between the two studies, although both studies assessed patients at risk of medication misadventure. In one study the clinical pharmacist reviewed computerised medication profiles and medical records of intervention patients a day prior to the patient's clinic visit for potential and actual drug-related problems (1). A medication review form was completed and attached to the medical records for the patient's physician and the pharmacist was also available to discuss the review with the physician. Control patients received usual care. The second study was slightly different, with a patient interview prior to the pharmacist medication review (2). The patient interview was not undertaken by the pharmacist but by trained staff or volunteers. This study was therefore categorised as medication review by a pharmacist, rather than pharmaceutical care, in which a pharmacist undertakes the interview. The pharmacist subsequently reviewed all the information collected at the interview with issues arising being addressed with the patient and/or their physician and followed-up where appropriate. Recommendations to physicians were made via a letter. Patients in the control group where referred to their usual pharmacist. It should be noted that both studies relied on written communication to physicians as the main method to communicate the review recommendations.

One study used independent assessors and administrative databases to assess the outcomes (2) limiting potential for bias (level 1+ method). In addition the pharmacist delivering the intervention had no contact with the control group. The second study had more potential for bias with the clinical pharmacist responsible for the intervention, and thus aware of patient group allocation, monitoring the outcomes of patients in both groups (level 1- method) (1).

Study outcomes

The outcomes monitored in the studies included:

- Symptoms (level 1)
- Number of prescriptions (level 3)
- Number of drug-related issues identified and resolved (level 3)
- Patient knowledge (level 3)
- Patient adherence (level 3)

Evidence for the effectiveness of the service

Currently, evidence for the effectiveness of medication review (review of medication charts and case notes) is lacking. Only two randomised controlled trials were located, and neither provides evidence for the effectiveness of the service. .

Both studies relied on written communication to physicians as the main method to communicate the review recommendations. This is a passive method of engagement and may have contributed to the lack of effect observed in the study outcomes.

Future study of medication review in the outpatient setting should examine whether a more active process of engagement with physicians has any effect.

Neither study provides evidence for the effectiveness of the service. The more robust study (2) found a significant difference in the mean number of non-prescription medications discontinued in the intervention group. However, no significant differences between the intervention and control groups were reported for any other outcome measures, including number and costs of prescribed medications, overall number of non-prescribed medications, symptoms reported, knowledge of drug therapy or adherence to drug therapy. The level 1-study (1) reported a decrease in the average number of medications per patient, which decreased by 0.21 in the intervention group while increasing by 0.48 in the control group. The significance of the difference between groups, however, was not reported.

Economic analysis

One randomised controlled trial assessed the impact of a medication review performed by a clinical pharmacist in a general medicine clinic (1). The net result of a single medication review was a decrease of 0.69 prescription per patient for a monthly medication cost savings of $3.91.

There are not yet enough trials of this service to draw firm conclusions about its cost-effectiveness.

Australian research

No controlled trials undertaken in the Australian setting and assessing patient outcomes were located.

Comment

Currently, evidence for the effectiveness of medication review (review of medication charts and case notes) is lacking. Only two randomised controlled trials were located, and neither provides evidence for the effectiveness of the service. It is interesting to note that both studies relied on written communication to physicians as the main method to communicate the review recommendations. This is a passive method of engagement and may have contributed to the lack of effect observed in the study outcomes. Hospital-based drug utilisation evaluation studies (3), and medication review of repeat prescribing (4), which have involved active engagement with physicians concerning the reviews findings, suggest medication review can be effective. Future study of medication review in the out-patient setting should examine whether a more active process of engagement with physicians has any effect.

Table 7.1 Medication review services to outpatients

Reference	Level	Setting	Subjects, intervention	Evaluable sample	Study outcomes	Results
Britton and Lurvey, 1991 (1)	1-	Outpatient clinic, Veterans' Affairs Medical Center Oklahoma, USA	Patients receiving 5 or more medications were eligible. Computerised medication profiles and medical records of intervention patients were reviewed by a clinical pharmacist one day prior to their clinic visit for potential and actual drug-related problems. A medication review form was completed an attached to the medical records for the patient's physician and the pharmacist was also available to discuss the review with the physician. Control patients received usual care.	315 intervention and 257 control Immediate follow-up	Level 3 Number of prescriptions	The average number of medications per patient decreased by 0.21 in the intervention group while increasing by 0.48 in the control group (p value not reported).
Grymonpre et al., 2001 (2)	1+	Community-based health clinic in Winnipeg, Canada, single-centre	Patients, 65 years or older, taking two or more medications. All participants received a home interview about medicines conducted by trained staff or volunteers (not necessarily a pharmacist) The intervention group received a pharmacist-conducted review of information collected at interview with issues arising being addressed with the patient and/or their physician and followed-up where appropriate. Recommendations to physicians were made via a letter. Patients in the control group where referred to their usual pharmacist.	56 intervention, 58 control 6 and 12 month follow-up	Level 1 Symptoms Level 3 Number of drug-related issues identified and resolved, number of medications, patient knowledge and adherence.	After the intervention there were no significant differences between the intervention and control groups for number and costs of prescribed medications, overall number of non-prescribed medications, symptoms reported, knowledge of drug therapy or adherence to drug therapy. There were a greater mean number of non-prescription medications discontinued in the intervention group.

References

1. Britton ML, Lurvey PL. Impact of medication profile review on prescribing in a general medicine clinic. American Journal of Hospital Pharmacy 1991;48:265-270.
2. Grymonpre RE, Williamson DA, Montgomery PR. Impact of a pharmaceutical care model for non-institutionalised elderly: results of a randomised controlled trial. International Journal of Pharmacy Practice 2001;9:235-241.
3. Dartnell JGA. Understanding, influencing and evaluating drug use. Melbourne: Therapeutic Guidelines Limited; 2001
4. Granas AG, Bates I. The effect of pharmaceutical review of repeat prescriptions in general practice. International Journal of Pharmacy Practice 1999;7:264-275

8. Pharmacist services providing education to patients or consumers

The Service

Pharmacist education or counselling services include the provision of verbal and/or written information and advice for patients or consumers. Verbal education may be provided individually (one-to-one) or to small groups. Education services are generally provided through face-to-face interactions between the pharmacist and patient but may also be conducted by telephone or using video technology. Education services may be single or multiple session services.

Studies included

Studies were included in this section of the review if they assessed a pharmacist intervention described as counselling, education or verbal information provision to patients or consumers, with or without the provision of written information, compliance aids or self-monitoring. Pharmacist interventions described as adherence or compliance programs where also included if education, counselling or the provision of information was a major component of the program.

Studies including patient education as part of a pharmaceutical care intervention, a drug information service, discharge liaison, smoking cessation or immunisation services were not included in this section but are reviewed in the other relevant sections of this report.

Studies were included if they were conducted in the community setting, in ambulatory care or outpatient clinics. Studies in conducted in hospitals were included only if they assessed discharge education or counselling services.

Studies must have included at least one patient outcome, which could have included quality of life, symptoms of disease, adverse events, hospital admissions or emergency visits, surrogate health endpoints (laboratory or other tests such as BP, pulmonary function tests, breath tests for *Helicobacter pylori*), patient knowledge, compliance/adherence with medication or technique in the use of medication devices. Studies that only included patient satisfaction with or opinion of the service (level 4 outcomes) as an endpoint were excluded.

Studies that employed educational strategies at discharge or at outpatient clinics were included in this review, but studies that conducted within hospital education were excluded.

Study design

Sixteen randomised controlled trials (level 1 method) were located that met the review inclusion criteria. Fifteen studies assessed one-to-one education interventions and one study compared one-to-one education, and small group education with a control group. Studies were conducted in Europe and the United States. One non-randomised controlled, study (1) was also located (level 2 method, Appendix II Table 5). In keeping with the use of the highest available level studies to determine evidence, only level 1 method studies were used to assess the evidence for the effectiveness of pharmacist education services.

In the 15 randomised controlled studies (level 1 method) that assessed a one-to-one education intervention 13 studies involved at least one face-to-face interaction between the pharmacist and patients in the intervention group. These interactions took place in varied settings including the patients' home, community pharmacies, primary care clinics and hospital settings including outpatient clinics. The length of time taken for the education varied but was not mentioned for a number of the studies. The number of education sessions also differed across studies: some studies involved a single face-to-face interaction between the pharmacist and the patient (2-6), while others included multiple sessions (7-12). A number of studies used follow-up telephone calls or telephone support when needed in addition to the face-to-face-consultation (2, 4, 5, 10, 11).

One of the 15 randomised controlled trials assessing one-to-one education involved a service described as "telepharmacy" counselling (13). This service involved the use of two-way interactive video technology to provide counselling on metered dose inhaler technique to adolescents living in a rural area of the United States. One other randomised controlled trial assessed a telephone counselling service for patients taking lipid-lowering medications who predominantly lived in distant rural locations (14).

Thirteen of the 15 studies assessing one-to-one education used a single intervention and control group design. One study (7) which assessed the impact of domiciliary pharmacy visits to an elderly population compared three groups: one receiving counselling during home visits, a second receiving home visits but no counselling and a third control group receiving no visits from the pharmacist. Another study targeting asthma patients (15) compared 4 groups (education alone, monitoring alone, education plus monitoring, and a control receiving no intervention).

The patient group targeted in the studies varied. Of the 15 studies (level 1 method) assessing one-to-one education, one study targeted a general patient population discharged from hospital and two targeted an elderly patient population at risk of medication related problems. The remaining 12 studies targeted patients with a specific condition or disease state (2 targeted patients with heart failure, 3 *Helicobacter pylori* infection, 1 HIV infection receiving HAART, 1 dyspepsia, 2 asthma, 1 hypertension, 1 renal transplant and 1 post cardiac surgery (receiving lipid-lowering medication). The randomised controlled trial assessing group and one-to-one education targeted patients with diabetes. The follow-up period varied considerably between the different studies from one week (3) to 2 years (14).

The study by Blenkinsopp et al. (8) which assessed an extended adherence support program for patients with hypertension, used a patient-centred approach in the delivery of the pharmacist intervention. The advice, information and referral (if necessary) provided by the pharmacist were based on the patient's responses to a questionnaire. The questionnaire was developed to assess the individual patient's information needs and medication-related problems.

Another difference in the implementation of the studies was the use of other materials to complement the verbal education provided by the pharmacist. Printed educational information was also provided to patients in five of the studies assessing one-to-one education (2, 4, 9, 11, 12), with three further studies providing written information when required (7, 8, 16) and in one an educational video (15). Other materials provided by the pharmacist to aid patient compliance with medications were medication calendars, diaries and small (pocket-sized) dose administration aids.

The unit of randomisation used in most of the studies was the patient. For two studies involving community pharmacists the pharmacy was the unit of randomisation (3, 8). Use of the pharmacy as the unit of randomisation avoided the pharmacist having to vary practice with the different patient groups. Most studies used valid randomisation procedures including random number tables and computer generated randomisation schemes. Studies were judged to have more rigorous methods with less chance for bias (level 1+ method) if they used independent researchers, blinded to group allocation to assess baseline and follow-up outcome measures. Most studies were rated as level 1- for method due to the potential for bias in the outcome assessment process. In many studies it appeared that the pharmacist involved in delivering the intervention was also involved in the outcome assessment process. Some studies also involved contact between the pharmacist delivering the intervention and the patients in the control group during the course of the study.

Some studies had only small sample sizes. Unfortunately power calculations were not always reported. Thus, in some studies it is not possible to tell if the lack of effect was a real observation or due to inadequate population numbers.

Study outcomes

Outcome measures employed in the studies varied, but most studies included patient compliance or adherence with medication as an outcome measure (level 3 outcome). In most studies compliance was assessed by patient self-report, a tablet count or a combination of both. The majority of the randomised controlled studies (10 studies) measured at least one health outcome (level 1 outcome) or surrogate health outcome (level 2 outcome).

Outcomes measured included:

- Health-related Quality of Life as measured by the SF-36, “Quality-of -Wellbeing” Scale, Nottingham Health Profile (level 1 outcome)
- Disease specific quality of life, as measured by specialised survey instruments (level 1)
- Disease symptom severity (level 1)
- Hospital admissions (level 1)
- Emergency department attendances (disease-related attendances judged to be level 1)
- Surrogate endpoints, for example BP, lipid levels, exercise tests, pulmonary function tests, HIV viral load suppression, breath test for *Helicobacter pylori* infection (level 2)
- Knowledge of medication or monitoring of condition (level 3)
- Medication compliance or adherence (level 3)
- Medication device use (level 3)
- A “risk assessment profile” of medication use and behaviour (level 3)

Evidence for effectiveness of practice

For the purposes of this review, studies were assessed in the following categories:

- Single session counselling at the point of dispensing for limited duration therapy
- Single session counselling for long-term therapy
- Multiple session education
- Multiple session education plus active self-monitoring.

The results of studies assessing one-to-one educational interventions suggest both single session and multiple session education are effective, with stronger evidence and better outcomes for effectiveness of multiple session education. There is currently a lack of published controlled studies assessing the impact of small group education delivered by pharmacists for patients or consumers.

Single session counselling delivered by telepharmacy has been shown to be effective (level 1- method) in the short-term for improving metered dose inhaler technique.

Single session extended counselling was found to be more effective in the short term than standard counselling for improving quality of life measures for patients presenting to community pharmacies with symptoms of dyspepsia. The efficacy of extended counselling over standard counselling for patients on *Helicobacter* eradication therapy was unclear, with one study finding improved adherence and the second finding no effect on adherence, dyspepsia symptoms or *H. pylori* status.

There is level 1+ evidence for the efficacy of multiple session education for improving blood pressure and compliance in patients with hypertension and compliance in renal transplant patients.

Multiple session education was also found to be effective (level 1-) in improving compliance in the elderly, and those on lipid-lowering therapy, therapy for chronic heart failure and anti-retroviral therapy. Multiple session education also was found to be effective (level 1-) for improving the symptoms of heart failure and for improving lipid profiles in those with existing heart disease. Multiple session education plus active self-monitoring was found to be effective (level 1-) for reducing hospitalisation, improving quality of life and improving compliance in patients with heart failure.

No controlled studies assessing education by pharmacists to patients in the community setting in Australia were located.

Rigorous evaluation of group education by pharmacists for consumers is lacking in both the Australian and international setting.

Most studies assessing the effect of education utilised changes in compliance and knowledge as an outcome and did not include changes in health outcomes. Where compliance is measured, consideration should also be given to including level 1 or 2 outcome measures, such as changes to health status or surrogate end-points.

Currently, there is a lack of economic studies in this area, which limits any conclusions that can be drawn about the cost-effectiveness of patient education by pharmacists.

Single session counselling at the point of dispensing

Single session counselling at the point of dispensing for limited duration therapy

Three studies assessed single session counselling at the point of dispensing for limited duration therapy compared to usual care (Table 8.1). All of these studies focused on use of *Helicobacter pylori* eradication therapy or treatment of dyspepsia. Two of the studies were for prescribed medicines, while the third was for pharmacy only medicines. The intervention was either counselling alone, counselling plus printed material and compliance aids or counselling plus telephone follow-up. Follow-up periods varied from one week to three months.

One further study (2) compared single session counselling at the point of dispensing with a referral letter to the patient's GP (see comment below).

HRQOL
One study (3) (level 1- method) assessing the effect of community pharmacist counselling for customers presenting with dyspepsia found a statistically significant improvement for the intervention group using a specific gastrointestinal quality of life instrument. The study follow-up period, however, was only for one week with no further measurements to assess whether the effect was sustained. Additionally the community pharmacists carrying out the intervention recruited the patients which had the potential to introduce bias if patients more likely to respond were selected.

Symptoms and surrogate end-points
One study assessed the impact of pharmacist medication counselling plus telephone follow-up on gastrointestinal symptoms in symptomatic patients receiving combination therapy following positive *H. pylori* breath tests (5) (level 1- for method), with no differences observed between control and intervention groups at the 3 month follow-up. No differences were also reported for *H. pylori* eradication rates.

Compliance
One of the two studies targeting patients taking combination therapy for *H. pylori* infection showed improved compliance in the intervention group (4), with the second study reporting no differences with high compliance rates in both groups (5).

Single session counselling for long-term therapy

Compliance and knowledge; device use
Two studies assessed single session counselling for long-term therapy (Table 8.2). One study reported a trend to improved compliance scores for single session counselling by elderly patients on discharge from hospital (6). Subgroup analysis revealed elderly patients discharged from the acute care hospital had significant improvements in medication knowledge and compliance scores, with no effect observed in those discharged from the rehabilitation unit (6). The numbers involved in this study make generalization of the results difficult. The second study assessed telepharmacy counselling about metered dose inhalers for adolescents with asthma, finding this to be effective in improving their metered dose inhaler technique (13).

Comment

This review only encompassed trials published since 1990. As counselling has been considered part of professional pharmacist services for a considerable period of time, it may be that there are trials published pre-1990 that do not appear here. There were five studies published since 1990 assessing one-to-one single session counselling, all of which had significant potential for bias (level 1-). Taken collectively, the studies do provide evidence of the effectiveness of single session counselling in the short term. Improvement in metered dose inhaler technique was observed after telepharmacy counselling (13). Single session extended counselling was found to be more effective than standard counselling for improving quality of life measures for patients presenting to community pharmacies with symptoms of dyspepsia (3). The efficacy of extended counselling over usual care for patients on *Helicobacter pylori* eradication therapy was unclear, with one study finding improved adherence (4) and the second finding no effect on adherence, dyspepsia symptoms or *H. pylori* status (5). One study which assessed single session counselling against no counselling found no overall improvement in compliance and knowledge scores for patients discharged from hospital, although subgroup analysis revealed elderly patients discharged from the acute care facility did improve, while there was no effect on those discharged from the rehabilitation ward (6). A further study, with short term follow-up did not assess compliance rates, but does provide evidence of improvement in quality of life scores for people with dyspepsia symptoms following pharmacist counselling for pharmacy only medicines (3). The study with a longer follow-up period of three months, demonstrated no effect (5). Short-term follow-up is probably most appropriate for single session counselling, as sustained effects are unlikely to be observed without repetition of the messages.

One other study (2) was identified which was located within the hospital outpatient setting and assessed single session counselling at the point of dispensing plus the provision of written information, a compliance diary and follow-up telephone call with usual care (2). Usual care in this instance was a letter of referral to the patient's general practitioner recommending therapy. This study was not considered directly comparable to the others where usual care involved medication supply and short counselling sessions, as it is not clear from the study's report how many people in the control group actually went to their general practitioners and were provided with medication. If all patients in the control group did receive medication, the study results provide further evidence that single session counselling plus written material and compliance aids is effective for improving outcomes associated with limited duration therapy. The study focused on *H. pylori* eradication and found significantly higher *H.pylori* eradication rates in the intervention group (95% eradication) than the control (74% eradication) and better compliance in the intervention groups. Patients with *H. pylori* eradication had significantly lower dyspeptic severity scores than those that had persistance of the organism.

Multiple session education

Eight studies assessed multiple session education (Table 8.3). Two further studies assessed multiple session education with active self-monitoring and are discussed later.

HRQOL
Two multiple session education studies used health-related quality of life as an outcome measure. One study targeted patients with heart failure (9) and the second, patients with asthma (15). Both studies reported no effect on HRQOL scores. In both studies, however, sample sizes were small, and in the study by Grainger-Rousseau et al. (15) power calculations suggested the sample size was not sufficient to demonstrate effect.

Symptoms and surrogate end-points
The study focusing on chronic stable heart-failure assessed the impact of three month intensive medication counselling at home visits with the provision of written information and medication calendars (9) (level 1- method). This study used pulmonary and peripheral oedema (measured by a blinded physician) and breathlessness (rated by patients using a visual analogue scale) as outcome measures. The number of patients with peripheral oedema at the end of the study was significantly lower in the intervention group compared to the control ($p<0.05$). There was a significant within-group change for the intervention group for pulmonary oedema (significance between groups was not stated). There was a significant difference between the groups in favour of the intervention group for changes in breathlessness scores at the end of the study. The authors stated, however, that from a patient's perspective, the 4% improvement found in breathlessness scores may not represent a clinically significant change. Exercise test performance increased significantly for the intervention group compared to the control at the end of the study (at three months the distance to breathlessness increasing an average of 26 metres for the intervention group compared to a decrease of 19 metres for the controls $p<0.001$). Other surrogate outcomes measured in this study included jugular venous pressure and body weight, with no significant effects found.

One study using a patient-centred approach to information provision in which the information needs of the patient were assessed (8) (level 1+ method) measured the effect of the intervention on blood pressure (rated by blinded independent researchers). Amongst patients who had uncontrolled BP at baseline there was a significantly greater proportion of patients in the intervention group (36%) who had controlled BP at the end of the study than the control group (17%) ($p<0.05$).

One study assessing a weekly telephone counselling service conducted for 12 weeks to patients who had undergone cardiac surgery and were taking lipid-lowering medication used lipid profiles as a surrogate outcome measure (14) (level 1- method). There was a two-year follow-up period for this endpoint. Short term changes in lipid profiles at 6 and 12 weeks were not significantly different between the groups, however at one and two year follow-ups there was a significant difference in the mean reduction in total cholesterol, LDL and triglycerides between the groups. Changes in HDL cholesterol levels were not significant.

Symptoms were assessed as an outcome measure in the study examining monitoring, education or education plus monitoring for patients with asthma (15) (level 1- method). No significant differences in subjective asthma symptom scores were found, however, as mentioned previously, sample sizes were problematic in this study.

One study assessing a pharmacist counselling intervention for HIV positive patients receiving combination highly active antiretroviral therapy (HAART) (10) (level 1- method) found no significant difference in the proportion of patients achieving an undetectable viral load at 6-months (65% of intervention patients versus 55% of controls). The study had a moderate sample size that may have limited the ability to detect a statistically significant difference.

Compliance
All but one of seven studies assessing the effectiveness of multiple education sessions and utilizing compliance as an outcome measure found improvements in compliance. Improvements in compliance compared to control were found for patients with heart failure (9), renal transplant patients (16), patients on antihypertensive medication (8), those on anti-retroviral therapy (10), those on lipid-lowering therapy (14) and elderly patients (7). A study assessing a 12-week intervention of telephone counselling found no significant differences in short-term compliance with lipid-lowering medications (at 6- and 12-weeks), however significant differences in long term compliance (at one and two years) were seen (14). Compliance for patients taking antihypertensive medication was improved in a group receiving education based on the needs of the individual patient (8) as was adherence to anti-retroviral therapy in patients receiving detailed counselling followed by ongoing support. (10). One study (11) used a "nine-category risk assessment profile" which included "medication taking behaviour" as one category. There were no significant differences between groups for this endpoint.

Device use
One randomised controlled trial assessed pharmacist education on metered dose inhaler (MDI) technique in patients with asthma (15). The study which compared education only, monitoring only or education plus monitoring with a control group found significant improvements in MDI technique for the education only group when scored by blinded assessors (15) (level 1- method).

Knowledge
Change in medication knowledge was only used as an outcome measure in two studies. In the study for patients with heart failure, improvements were found in awareness of name, purpose, dose and adverse effects (9). Studies assessing home visits to elderly patients (7) found no significant differences for knowledge scores.

Multiple session education plus active self-monitoring

One study focussed on multiple session education plus active self-monitoring (12). In one arm of a second study (15) self-monitoring was also undertaken. This study had very small and probably inadequate sample sizes and so no conclusions can be drawn from the results (15). The study focussing on multiple session education and self-monitoring (12) (level 1+ method) provides strong evidence for the effectiveness of this approach in people with heart failure. The 12-month study assessed the effect of education provided to patients with congestive heart failure along with strategies for patient-self-monitoring. It found an overall difference in disease-specific quality of life scores at the 9-month follow-up visit. The effect was not sustained at 12-month follow-up. Four of the 8 domains of the SF-36 (physical functioning, vitality, mental health and social functioning) were significantly different in favour of the intervention group at the 12-month follow-up. Baseline values for physical functioning had been higher in the intervention group (12). Medication knowledge scores

(p=0.00265) and compliance (p=0.039) both improved in the intervention group. No effect was demonstrated on the exercise test, body weight, blood pressure, pulse for FVC at 12 months. The intervention group had less hospitalisations than the control group (p=0.006).

Comment

There is good evidence for the effectiveness of multiple session education improving patient outcomes with medication.

Level 1+ evidence has demonstrated ongoing pharmacist counselling is effective in improving blood pressure control and compliance (8). There is also level 1+ evidence that demonstrates ongoing patient education delivered by the pharmacist, with active self monitoring and liaison with community practitioners where required, improves health related quality of life, medication knowledge and compliance, and reduces hospitalisations and improves quality of life in people with heart failure (12).

Level 1- evidence is available to further support these findings. Randomised controlled trials (level 1-) have demonstrated the effectiveness of multiple session education for improving adherence in patients on anti-retroviral therapy (10), cholesterol therapy (14), and in the elderly (7) and those receiving therapy for heart failure (9). The intervention was also found to assist symptoms, with improvements observed in people with heart failure (9) and improve surrogate end-points, with improvements in total cholesterol levels.

Table 8.1 Single session counselling at the point of dispensing for limited duration therapy

Reference	Level	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Extended counselling for prescription medicines compared with usual care							
Stevens et al, 2002 (5)	1-	Single-centre Primary care USA	Patients with dyspepsia and positive breath test for *H. pylori* receiving 7 day course *H. pylori* eradication therapy	15 minute counselling session plus follow-up telephone call. Control group received five minute counselling.	148 intervention & 154 control 3 month follow-up	Dyspepsia symptoms *H. pylori* status Adherence	No effect on Dyspepsia symptoms and *H.pylori* status at 3 months. Self-reported adherence at 8 days similar in both groups, although higher in the intervention group.
Lee et al., 1999 (4)	1-	Single-centre Ambulatory health centre of HMO USA	Adults with peptic ulcer disease or dyspepsia receiving two weeks of triple therapy	10 to 15 minute counselling session plus printed information, medication calendar and pocket sized pillbox. Follow-up telephone call within three days	61 intervention and 55 control Follow-up at 2 weeks	Adherence	The proportion of patients completing 90% or more of their medication was significantly different between the groups: 54/61 (89%) intervention patients versus 37/55 (67%) control patients ($p< 0.01$).
Extended counselling for pharmacy medicines compared with usual care							
Krishnan and Schaefer, 2000 (3)	1-	Multi-centre Community pharmacies Germany	Patients presenting to a pharmacy requesting pharmacy medication for dyspepsia or help for dyspepsia symptoms	Medication counselling plus instruction on diet and posture	114 intervention and 84 control Follow-up at 1 week	Quality of life	Increase in quality of life scores over the one week course of the study were greater in the intervention group compared to the control ($p<0.001$).
Single session counselling for prescription medicines at point of dispensing compared to letter of referral							
Al-Eidan et al., 2002 (2)	1-	Single-centre Outpatient unit Ireland	Adults with gastritis, duodenitis or ulceration and a positive *H. pylori* breath test	Medication provided plus 10 minute counselling session plus printed information and compliance diary Control group received normal care, which was a letter to their GP recommending treatment	38 intervention and 38 control Follow-up at 10 days, 1 month and 6 months	Dyspepsia symptoms *H. pylori* status Use of antisecretory medications	Severity scores for dyspeptic symptoms and use of antisecretory medications (most commonly H_2-receptor antagonists) were significantly lower for *H. pylori* eradicated patients than *H. pylori* persistent patients at 1 and 6-months after treatment. Comparison between groups was not presented. Better H. pylori eradication rates in the intervention group ($p=0.027$)

Table 8.2 Single session counselling for long-term therapy

Reference	Level	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Williford and Johnson, 1995 (6)	1-	Single-centre Hospital USA	Patients discharged to home on at least one medication	Verbal medication counselling when receiving discharge medication (15 minutes). Control patients received no counselling.	31 intervention and 29 control Follow-up at 6 weeks	Medication knowledge and compliance	The median medication knowledge-compliance score was 90.7 for intervention patients compared to 75.4 for control patients, which was not statistically significant. Sub group analysis showed for patients discharged from the acute-care facility (10 intervention patients, 5 control) the intervention group had a significantly higher median knowledge-compliance score (91) compared to control (75) ($p=0.02$).
Bynum et al., 2001 (13)	1-	Community setting USA	Adolescents attending rural schools with a diagnosis of asthma and previous use of MDI	Telepharmacy counselling sessions included verbal instructions and demonstrations by the pharmacist for any required correction to MDI technique.	36 patients (final numbers in each group not reported) Follow-up at two to four weeks	MDI technique	Baseline scores for MDI technique were 3.8 for the intervention group and 4.1 for control. The mean total follow-up scores were 6.7 for the intervention group and 4.9 for the controls. From pre-test to follow-up, the intervention group had more improvement in the MDI technique than controls ($p<0.001$).

Table 8.3 Multiple session education

Reference	Level of evidence	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Knobel et al., 1999 (10) cited in Haddad et al., 2002 (17)	1-	Single-centre Hospital outpatient clinic Spain	Patients receiving antiretroviral therapy with a viral load of 5000 copies per ml	Detailed education including discussion of lifestyle issues from a pharmacist at the point of initial dispensing followed by continual phone support, plus monthly visit to hospital	60 intervention 110 control Follow-up at 6 months	HIV viral load Adherence	Proportion of patients achieving undetectable viral load at 6 months was 65% for intervention patients versus 55% for controls (p=0.18). "Correct adherence" was achieved by 77% of intervention patients and 53% of controls (p=0.002).
Goodyer et al., 1995 (9)	1-	Single centre hospital outpatients England	aged 70 years or older with chronic heart failure and administered their own medications	Three domiciliary visits at two to four week intervals, including verbal counselling, printed information and medication calendars	42 intervention and 40 control Follow-up occurred two to four weeks after last domiciliary visit (approx two to four months)	HRQOL Symptoms Knowledge Compliance	Peripheral oedema improved with 81% of intervention patients had no peripheral oedema compared to 49% in the control ($p<0.05$). Pulmonary oedema improved significantly. No significant differences for HRQOL scores. Significant improvement in breathlessness scores ($p<0.05$). No effect on pulse rate, jugular venous pressure or body weight. Exercise test scores improved significantly ($p<0.001$). Mean compliance at the end of the study was 93% for intervention compared to 51% for controls ($p<0.001$). Knowledge scores improved significantly concerning awareness of name, purpose, dose and adverse effects of medication
Sidel et al., 1990 (11)	1-	Community setting, USA	65 years and over at risk of medication related problems	Two home visits over a six to eleven month period, providing individualised medication information, including written information, plus review of medication kept in the home and contact with the patient's physician if necessary.	92 intervention and 104 control Follow-up unclear. Study period at least 11 months.	Medication use and behavioural patterns	No effect. Improvements seen in both groups, but no differences between groups.

Reference	Level of evidence	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Begley et al., 1997 (7)	1-	Community setting England	75 years and over, taking three or more medications and at least two dosage times a day	Five home visits and counselling over twelve months (Group A) compared to home visits but no counselling (Group B) or no visits except at the beginning and end of the study (Group C). Counselling group also received written information if necessary.	61 Group A, 63 Group B and 66 Group C. Follow up 12 months	Compliance Knowledge Medication management issues	At the end of the study the mean percentage compliance values were 86 for group A, 75 for group B and 69 for group C (p=.0001). No effect on drug knowledge scores
Grainger-Rousseau and McElnay, 1996 (15)	1-	Health centre community pharmacy, Northern Ireland	6 years and over with a confirmed diagnosis of asthma	Compared education only, with education plus monitoring, compared to monitoring only, compared to control	Unclear, only 36 completed all assessments Follow-up six months	HRQOL Pulmonary Function Testing Inhaler technique	No effect on HRQOL or pulmonary function tests at studies end. The education only group had improvement in inhaler technique scores at all three intervention assessments ($p<0.005$), while the monitoring only group had an improved score only at the final assessment ($p<0.05$). The very small sample size (overall 36 subjects across 4 groups) limits any interpretation of study results, as sample unlikely to be large enough to show an effect, even if present.
Blenkinsopp et al., 2000 (8)	1+	Community pharmacies, England	Patients treated for hypertension	The intervention was delivered on three occasions at 2-month intervals, conducted by telephone if necessary. The pharmacist provided advice, verbal or written information or GP referral if required.	101 intervention 79 control 6 month follow-up	BP Adherence	For the 63 patients (28 intervention, 35 control) with uncontrolled BP at baseline the intervention patients were significantly more likely to have controlled BP after the study (35.7% intervention versus 17.1% control, $p<0.05$). Patient-self-reported compliance improved to 62.9% from 52.3% at baseline in the intervention group, versus 51.0% and 50.0% pre and post measures for the control group. ($p<0.05$). Prescription refill data also indicated improved compliance.

Reference	Level of evidence	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Chisholm et al., 2001 (16)	1+	Single centre Renal transplant clinic USA	Patients who had received a renal transplant	The intervention included counselling by a clinical pharmacist, verbally and/or in writing. Phone contact was provided so subjects could phone with any questions or concerns. Monthly follow-up at the clinic or by telephone was also provided. The control group had no contact with the clinical pharmacist	12 intervention and control 12 month follow-up	Adherence	Intervention patients had a significantly higher compliance rate of 96.1 ± 4.7% compared to controls at 81.6± 11.5% at the 12 month follow-up ($p<0.001$)
Faulkner et al., 2000 (14)	1-	Tertiary care hospital, USA	Patients had had cardiac surgery in the previous 7-30 days, had elevated fasting LDL levels and were prescribed lovastatin and colestipol in hospital	Intervention group patients received weekly telephone contact from the same pharmacist for 12 weeks.	15 intervention and 15 control 2 years follow-up	Lipid profiles Compliance	At 2 years: Total cholesterol: mean reduction 19.5% intervention versus 12.7% control ($p=0.03$). LDL: mean reduction 24.3% intervention versus 14.9% control ($p=0.02$). TG: mean reduction 10.2% intervention versus 3.9% control ($p=0.04$). Long-term follow-up found significantly higher percentage compliance with both drugs at 1 and 2 years ($p<0.05$).

Reference	Level of evidence	Setting	Target population	Education	Evaluable sample & follow-up	Measure	Effect
Multiple session education plus active self-monitoring							
Varma et al. 1999 (12)	Level 1+	3 hospitals Outpatient clinics Northern Ireland	aged over 65 years with a diagnosis of CHF	Patients in the intervention group received education from a hospital-based pharmacist about CHF and prescribed medications (including written information), encouragement to monitor their symptoms (using diary cards) and report results to community care practitioners, and comply with medications. If required, the pharmacist liaised with hospital physicians to simplify the patients' medication regimen and community physicians and community pharmacists. Patients in the control group received standard care.	83 patients randomised 42 intervention, 41 control, with 26 intervention and 23 control at 12 month follow-up.	HRQOL Doctor call outs, hospital admissions and emergency room visits; Two-minute walk test, BP, pulse rate, body mass index (BMI), forced vital capacity (FVC) Patients' drug knowledge, compliance with medications	Intervention patients had a trend to better Minnesota Living with Heart Failure scores, with the significant difference only seen at 9-month visit ($p=0.04$). SF-36 scores were higher for physical functioning; social functioning, mental health and vitality at 12 months ($p<0.05$). No effect on the two-minute walk test . The intervention group had a higher mean BP throughout the study. No significant differences in BMI, pulse rate, FVC. Self-reported compliance showed no differences, however, record data (n=23) showed significant improvement in compliance ($p=0.039$). Medication knowledge was significantly better than control group throughout the study (including baseline). Fewer hospital admissions (14) compared to controls (27) ($p=0.006$). Higher number of doctor call–outs and emergency room visits for the intervention group, but not statistically significant.

Single versus multiple session education

No controlled trials undertaken in the community setting were located that assessed the effectiveness of single session education versus multiple session education.

One-to-one versus group education

One key question facing pharmacy is whether the provision of education is better in the one to one format, or if group education would suffice in some circumstances. Only one randomized controlled trial meeting the inclusion criteria was located that had assessed one to one education against group education.

The study involved 41 patients randomised to three groups, one-to-one education, versus group education versus a control group (18) (level 1-). Eligible patients were those with diabetes. Endpoints monitored included blood glucose levels and the number of hypo- or hyperglycaemic episodes. The presentation of the results, however, did not allow the significance of differences between the two intervention groups to be assessed as many of the scores for the groups receiving any sort of education were pooled. With the scores of the two different education groups amalgamated there were some improvements in average weekly blood glucose levels for the intervention groups compared to the control.

This study does not provide an answer to the question of how one-to-one education compares to group education. Controlled studies assessing the effectiveness of group education by pharmacists seems to have not been published in the literature, nor were any full reports of unpublished studies located. Given that in practice, pharmacists are often asked to talk to consumer groups, it would be beneficial to undertake some research into the effectiveness of this approach.

Economic assessment

A randomised controlled trial showed that patient counselling by a hospital pharmacist when dispensing *Helicobacter pylori* eradication treatment increased significantly the eradication rate and compliance compared to the control group, who received a letter of referral to their GP recommending therapy (2). The data indicated that £8402 would be needed for *Helicobacter pylori* eradication in 100 patients using the study treatment regimen plus counselling, while an additional £3026 would be needed for *Helicobacter pylori* eradication using the study treatment regimen without counseling because of the increase in GP consultations and drug costs due to the higher treatment failure. It should be noted, however, that it is not clear from the study's report how many people in the control group actually went to their general practitioners and were provided with medication. If all patients in the control group did receive medication, the validity of the economic assessment is improved.

No other economic studies were located, which limits any conclusions that can be drawn on the cost-effectiveness of patient education by pharmacists.

Australian research

There is a lack of published research in the Australian community setting since 1990 assessing the impact of pharmacist education services on patient outcomes. One study

indicated it measured the impact of educational home visits on patient outcomes including hospital readmission rates, however the study report was descriptive only, the results for the outcome measures were not presented (19).

Two hospital-based studies were located, which did not meet the inclusion criteria for this review, as they included within hospital education. However, they are described here, because they do provide level 1- evidence for the effect of pharmacist-led education for improving medication knowledge (level 3 outcomes) and level 2 evidence for improving compliance (level 3 outcomes) in the Australian setting. One of the studies (level 1- method) assessed the effect of the addition of ward pharmacist counselling to routine discharge counselling to medication knowledge (level 3 outcomes) (20) and the other (level 2 method) assessed the effect of a pharmacist-led group education session, followed up by individual patient counselling on compliance rates (level 3 outcomes) (21).

A randomised controlled trial (level 1-) assessing the impact of additional ward pharmacist counselling to routine discharge counselling was undertaken in two separate two week periods in July and August 1990 in a large teaching hospital in Melbourne. Any patients, apart from those discharged from the intensive care and psychiatric units were eligible to participate. Subjects were randomly assigned, using computer generated numbers, to intervention or control groups. The control group received medication counselling at discharge, while the intervention group received medication counselling throughout the hospital stay and at discharge. Follow-up occurred on the same day. Patients' knowledge about their medication was assessed using a standard questionnaire. The pharmacist undertaking the follow-up assessment was not blinded to subject allocation, increasing the potential for bias in this study. Data for evaluation were available for 96 patients in the intervention group and 86 patients in the control group. Results revealed that the intervention group had significantly better knowledge of drug name, dose and duration of therapy than the control group ($p<0.05$), with no difference observed for knowledge relating to action, side effects or special directions (20).

A comparative study (level 2) was undertaken in a New South Wales hospital, to determine the effect on compliance of group education plus individual discharge counselling versus discharge counselling alone (21). The group education consisted of the "Ed Med" Program (Education about medication), which was attended by eight or nine participants often accompanied by a family member, and covered issues some as brand and generic names of medicines, strengths, importance and reasons for directions, drug storage and expiry and drug interactions. This was followed by a 15-minute individual counselling session. Patients were also provided with an individualised medication care detailing the medications they were on, including the generic name, all brand names, strength and dose, the reasons for use and directions. The program was offered every second month, with a general health education program held on alternate months. The control group received this intervention, which did not include a discussion of medicines. Follow-up occurred at one and three months post discharge by a research assistant who was unaware of the study hypothesis and patient allocation. Initial enrolment included 149 subjects in the intervention group and 119 in the control. At the three-month follow-up there were 77 in the intervention group and 71 in the control group. The percentage of patients with severe non-compliance was 26% in the intervention group and 39% control, which was not significantly different. Subgroup analysis of those taking four or more medicines revealed a significant difference in severe non-compliance rates, at 32% and 55% of the intervention and control groups respectively.

Comment

A number of randomised controlled trials have now been undertaken to assess the impact of pharmacist education services. The methods used to provide these services are varied and end-points (except for compliance) are variable, which to some extent reflects the different target groups in which the studies have been performed. No randomised controlled studies included in this review used adverse drug events as an outcome measure.

Taken together the results of studies assessing one-to-one educational interventions suggest both single session and multiple session education are effective, with stronger evidence and better outcomes for effectiveness of multiple session education. There is currently a lack of published controlled studies assessing the impact of small group education delivered by pharmacists for patients or consumers.

Overall, there is little evidence that pharmacist education interventions provide any sustained impact on quality of life measures, however only four of the level 1 method studies reviewed here used this as an outcome measure. Additionally, there is also a question as to whether the quality of life instruments utilised thus far are sensitive enough or appropriate as an outcome measure of the service.

The majority of level 1 method studies assessing pharmacist education services have used compliance as an outcome measure (level 3 outcome) with the majority finding a significant impact of pharmacist education in terms of improving compliance. It is recognised that studies assessing the effect of education or other services on compliance rates should also include patient health outcomes or surrogate outcomes measures (22). Future studies in this area should include appropriate level 1 and 2 outcome measures.

The level 1 method studies reviewed here were conducted in Europe (including the UK) and in the United States. There is a lack of published research examining the impact of pharmacist education services on patient outcomes in the Australian community setting. Further controlled studies examining the effect of pharmacist education services in the Australian health care system are needed. These studies should include patient health outcome measures or at least surrogate outcome measures and follow-up periods of at least 6 months. Studies assessing telephone and video counselling services to patients living in rural areas in the United States have provided some evidence for the effectiveness of these services. These pharmacist services could be studied further in the rural/remote community setting in Australia.

Studies excluded

Studies were excluded if they used both a pharmacist and another health care professional to conduct the educational service (23).

Studies reviewed but excluded due to the lack of a control group included:
Narhi et al., 2001 (24)
Sarkadi and Rosenqvist, 2001 (25)
Newman and Hanus, 2001 (26)
Hawksworth et al., 2000 (27)
Diamond and Chapman, 2001 (28)
Baran et al., 1999 (29).

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9. Education services for health care professionals

The Service

Pharmacists may provide education services to individual health care professionals (one-to-one) or to a group of health professionals. These services are often provided at "outreach visits" which involve visits to the health care provider in their practice setting to deliver educational messages which aim to improve practice (1). A number of studies have assessed educational services provided by pharmacists that are described as "detailing". The term "detailing" refers an educational approach based on principles of communications theory and behaviour change (2). Detailing interventions may involve identifying baseline knowledge and barriers to change, developing focussed educational programs, clearly defining objectives, providing authoritative and unbiased sources of information, encouraging involvement of the physician (or other health care professional) in the educational session and highlighting and reinforcing important messages (2).

Studies included

Studies were included if they described education services provided by pharmacists to physicians or other health care professionals. Studies which described educational outreach visiting or "detailing" (with or without the provision of additional materials such as prescribing guidelines, promotional leaflets, mailed education campaigns) were included if the face-to-face visiting was conducted by a pharmacist. Studies that described outreach visiting conducted by a multidisciplinary team or a physician and a pharmacist were excluded. Studies were also excluded if it was unclear whether a pharmacist had conducted the educational visit.

Studies were included if conducted in one of the following settings: community (e.g. general practice), aged care or other long-term care facilities, hospital outpatient or ambulatory care clinics. Studies describing interventions directed at physicians prescribing medications for hospital inpatients were excluded.

Studies must have included at least one measure of health care provider performance or a health care outcome including changes in prescribing (quality and/or quantity), changes in medication use, health care provider's medication knowledge, patient hospital admissions, mortality, morbidity or surrogate health endpoints. Studies that only reported physician/health care provider satisfaction with or opinion of a service as an outcome measure (level 4 outcomes) were excluded.

It should be noted, there is a Cochrane review of educational outreach visits (1). The Cochrane review differs from the review reported here in that in includes educational outreach visits delivered "by a trained person to a health provider in his or how own setting", which may involve persons other than pharmacists as the education provider. This review focuses solely on studies were a pharmacist provided the education.

Study design

Nine randomised controlled trials (level 1 method) were located that met the review inclusion criteria. Studies were conducted in North America, Europe and Australia. Eight of these

studies compared face-to-face educational services (with or without other strategies such as printed materials or guidelines) with no intervention. One study (3) compared a control (no intervention) with provision of mailed prescribing guidelines only and with mailed prescribing guidelines plus two educational visits from a pharmacist. Nine non-randomised controlled studies (level 2 method) were also located which were conducted in North America, Europe and Australia (4-12). In keeping with the use of the highest available level studies to determine evidence, only level 1 method studies were used to assess evidence for the effectiveness of the service. Findings of the level 2 method studies are, however, summarised in Appendix II Tables 6 and 7.

Eight of the randomised controlled studies (level 1 method) assessed educational services targeted to physicians working in the community setting (including general practices or community health care centres).

The educational services targeting physicians working in the community setting provided either individual (one-to-one) or group academic detailing sessions. Five of the eight studies targeting physicians involved individual education sessions (3, 13-16), two involved group education (17, 18) and in one study visits were conducted either individually or in groups (19) (Pers comm. M.Eccles, Jan 6, 2003). There was either one (13-16) or two (3) education sessions delivered in studies assessing individual education services. One of the two studies assessing group education involved four educational sessions (17) while the other involved two sessions for each of the prescribing guidelines presented (18). A single visit was conducted in the study assessing either group or individual education (19). The type of pharmacist conducting the intervention also varied in the different studies. Three studies used trained community pharmacists to conduct education (3, 18, 19), one used a clinical pharmacist (14) while other studies described the pharmacist as a research or study pharmacist. In one study, the pharmacist received specialist training in techniques used by pharmaceutical company representatives (15).

All eight randomised controlled trials targeted the prescribing behaviour of physicians. Two studies targeted prescribing of antimicrobial agents (13, 14), two non-steroidal anti-inflammatory drugs (NSAIDs) (3, 15), one angiotensin converting enzyme (ACE) inhibitors (16), one lipid-lowering medications (17) and one medications for *Helicobacter pylori* eradication (19). One study assessed education for four different guideline topics: aspirin as antiplatelet therapy, ACE inhibitors for heart failure, use of NSAIDs in osteoarthrits and choice of antidepressants for managing depression (18).

Most studies used other strategies in addition to the face-to-face pharmacist education sessions to change prescribing behaviour. These included development and distribution of specific prescribing guidelines (3, 14, 16, 18), promotional-style materials (15, 18), an educational video (17) and an educational mailing campaign (13).

One randomised controlled study (20) involved provision of education to physicians and nursing staff working in nursing homes. In this study, clinical pharmacists visited physicians individually while group educational sessions were provided for nursing staff (nurses and aides). It was not clear, however, whether a clinical pharmacist conducted the group sessions. This study also targeted prescribing behaviour focussing on psychoactive medications and in addition to the clinical pharmacist sessions used educational materials that targeted factors that had been identified to influence prescribing in the target group (social marketing techniques) (20).

The unit of randomisation in the controlled trial designs was the individual practitioner, the practice, the nursing home or the geographical area. Studies were judged to have more rigorous methods where randomisation occurred by practice/nursing home or by geographical area rather than the individual practitioner to minimise the risk of cross-contamination between control and intervention practitioners. Studies were also assessed to have more rigorous methods (level 1+) if independent or blinded researchers were employed to take baseline and follow-up outcome measures and where the pharmacists implementing the intervention did not have contact with the control group. Studies were judged to have significant potential for bias (level 1- method) if the pharmacist delivering the intervention assessed the outcome measures. Studies that used administrative databases for prescribing or dispensing rates were considered to have less chance of bias, than those using self-recording by the general practitioner. One of the limitations of administrative databases is some countries however, is the complete capture of medication use and the lack of medication use by indication, which potentially confounded some study results. Although randomisation was generally achieved through valid randomisation procedures such as computer generated random number tables, one study employed a "coin-toss" (17). Randomisation procedures such as a "coin-toss" may introduce more potential for bias, however, the randomisation procedure was not used to determine the level of bias in this review (that is, whether a study method was 1+ or 1-) because a number of articles did not describe the randomisation procedure that had been used.

Study outcomes

Most of the randomised controlled studies (level 1 method) used changes to prescribing as outcome measures (level 3 outcome). This included changes in the quantity, costs or doses of medications targeted through the educational intervention, changes in the prescribing of "recommended" medications and those that were "not recommended" and assessment of the percentage of prescriptions complying with the recommended guidelines. Only one study (20) undertaken in a nursing home assessed level 1 patient outcome measures.

Evidence for effectiveness of practice

Pharmacist education to health practitioners in the aged-care setting has been shown to improve psychoactive drug use without adversely impacting on patient outcomes. However, only one level 1 trial conducted since 1990 was located and more research is required in this setting

Educational outreach visits to medical practitioners in the community setting targeting specific drug classes (level 1+ and level 1-) for which there are recognised problems with use have been found to improve medication use.

Two studies (level 1+ method), both assessing group education delivered by a pharmacist, have shown improvements in medication use, one finding increased use of lipid-lowering medications for hyperlipidaemia and the other improving use of aspirin as anti-platelet therapy. The latter trial found greater effect for small group (1 or 2 practitioner) practices than the larger practices, suggesting one-to-one education may be more beneficial. The other level 1+ trial, using one-to-one visits, reported no effect, however, the baseline use of the target drugs was already good. The level 1- trials also provide evidence of the effectiveness of the approach, although results are modest and improvements were not seen for all drugs targeted. Some improvement in prescribing of NSAIDs by GPs was found in a study (level 1- method) that assessed a single outreach visit plus promotional materials to encourage rational prescribing. There were also improvements in antibiotic use in two studies (level 1- method), one of which involved a pharmacist visit as part of an extensive mail campaign, the other which involved educational visits plus distribution of therapeutic guidelines. The two level 1- studies which found no effect, included one which aimed to increase use of ACE inhibitors, however, baseline data revealed existing use was already high, so improvements may be difficult to obtain. The second aimed to improve use of *Helicobacter pylori* eradication therapy and while no effect was observed, the outcome was monitored with an administrative dataset, which did not enable medication use by indication to be monitored, which may have confounded the results.

Educational outreach visits have been extensively studied in the Australian setting, with level 1- evidence demonstrating improvements in antibiotic use and NSAID use. Level 2 evidence supports this finding with improvements seen in antibiotic use and NSAID use, with the latter also being associated with reduced hospitalisations for peptic ulcer.

There is currently limited economic data evaluating the cost-effectiveness of pharmacist education to physicians. Only two randomised controlled trials compared medication costs in the intervention group with the control, with only one of these providing evidence of reduced medication costs. Further studies are needed.

Educational sessions by pharmacists in the aged-care setting

Evidence for efficacy for changes in health outcomes (level 1 outcomes)

Only one study (20) (level 1+ method), which targeted prescribing of psychoactive medications in nursing homes, assessed level one patient outcomes (Table 9.1). The study used outcome measures of functional status (including mental status, memory, anxiety, depression, behaviour and sleep problems) which were assessed by a research assistant blinded to the study design. These outcomes were measured for patients who had received an antipsychotic, benzodiazepine or hypnotic in the month before the intervention and who had a "psychoactive-drug-use score" (a measure of potentially inappropriate medication use) of 1 or more at baseline. Following the intervention most measures of functional status remained unchanged in both groups. Among patients who had received antipsychotic medications there was a non-significant trend towards less deterioration in mental status for the intervention group compared to the control (rate ratio 0.7, 95% confidence interval 0.4 to 1.1), and a non-significant trend towards less memory deterioration (rate ratio 0.6, 95% confidence interval 0.3 to 1.0). There was, however, also a significantly greater proportion of these patients in intervention homes who reported worsening of depressive symptoms (rate ratio 2.0, 95% confidence interval 1.1 to 3.9). Among patients who had received benzodiazepines or antihistamine hypnotic medications there was a non-significant trend for a lower proportion the intervention group reporting anxiety compared to the control group (rate ratio 0.4, 95% confidence interval 0.2 to 1.0). There was, however a significantly greater proportion of the intervention group which showed deterioration in memory compared to the control (rate ratio 2.1, 95% confidence interval 1.1 to 4.2). The small sample sizes available for measurement of clinical outcomes may have accounted for the lack of statistically significance differences in clinical outcomes.

Evidence for efficacy for changes in prescribing (level 3 outcomes)
The study by Avorn et al (20) (level 1+ method) also assessed the effect of an academic detailing intervention on the prescribing of psychoactive medications for nursing home residents. This study involved the use of social marketing techniques to identify factors influencing prescribing, individual education sessions targeting physicians with high prescribing rates and also involved group education sessions to nursing staff at the homes. Using a psychoactive drug use index which measured both quantity and inappropriateness of medication use a significant reduction was found in the intervention nursing homes compared to the control homes (27% reduction in intervention homes versus 8% reduction in control homes, p=0.02).

The Avorn study was the only level 1 study located assessing pharmacist education sessions to staff in the aged-care setting. One level 2 study was located, which is presented in Appendix II Table 6. This study showed that patients of nursing homes where staff received educational sessions by a pharmacist used less hypnotics than a comparison group. The results should be interpreted with caution, however, as no pre-intervention comparative data were available, thus it is unclear how comparable intervention and control nursing homes were at baseline.

Table 9.1 Randomised controlled trial of educational services by pharmacists in aged-care settings

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Avorn et al., 1992 (20)	1+	Nursing homes USA	The educational intervention was a program to reduce the use of psychoactive drugs in nursing home residents. Factors that influenced prescribing of psychoactive drugs were explored through interviews with nursing home staff not included in the study and a systematic literature review. These were used to develop printed educational materials that were mailed to physicians caring for patients in intervention nursing homes in a series of three mail-outs. Physicians identified as having high rates of psychoactive drug prescribing at baseline were targeted in three face-to-face academic detailing sessions with a clinical pharmacist. Four educational sessions were also held for groups of nurses and nurse assistants from each intervention nursing home (it was not stated if these sessions were conducted by the clinical pharmacist).	6 intervention and 6 control nursing homes. 349 patients in the intervention group and 329 control. Data was collected for 1 month before and after the intervention	Level 1 i)mental status ii)memory iii) measures of anxiety, depression, behavior, sleep problems Level 3 psychoactive drug use	Scores on the index of psychoactive drug use declined significantly more in the intervention nursing homes (27% decrease, from 1.87 to 1.36) compared to the control homes (8% decrease, 1.74 to 1.60) (p=0.02). Clinical outcomes were determined for patients who had received an antipsychotic, benzodiazepine or hypnotic in the month before the intervention and who had a psychoactive-drug-use score of 1 or more at baseline. Among patients who had received antipsychotic medications there was a trend towards less deterioration in mental status in the intervention group (n=36 for intervention n=43 for control, rate ratio 0.7, 95% CI 0.4 to 1.1). There was also a trend towards less memory deterioration (n=36 intervention, n= 39 control, rate ratio 0.6, 95% CI 0.3 to 1.0). However, there was a greater proportion in the intervention group that reported worsening of depressive symptoms (n=27 intervention, n=33 control, rate ratio 2.0, 95% CI 1.1 to 3.9). Anxiety, sleep disturbances and behaviour were not significantly different. In patients that had received benzodiazepines or antihistamine hypnotic medications prior to the intervention a greater proportion of the intervention group showed memory deterioration (n=26 intervention, n=24 control, rate ratio 2.1, 95% CI 1.1 to 4.2). However, a lower proportion reported anxiety (n= 22 intervention, n= 23 control, rate ratio 0.4, 95% CI 0.2 to 1.0). The authors state that the small sample sizes may have accounted for the lack of statistically significant differences in clinical outcomes.

Educational sessions by pharmacists to medical practitioners in the community setting

Individual (one-to-one education)

The five randomised controlled trials that involved individual (one-to-one) educational sessions between a physician and pharmacist showed variable effects on prescribing (Table 9.2). Three of the studies (13-15) showed improvements in at least one the prescribing outcome measures. The study by Newton-Syms et al. (15) (level 1- method) which assessed a single outreach visit plus promotional materials to encourage rational prescribing of NSAIDs amongst GPs found a significant increase in the use of the first line recommended agent (ibuprofen) for the intervention group compared to the control ($p<0.001$). Differences for the second and third choice agents (piroxicam and indomethacin), however, were not significant between the groups. An Australian study (13) (level 1- method) that involved an extensive mail campaign to GPs to improve antibiotic prescribing with a single visit from a pharmacist to discuss the campaign messages found a significantly greater improvement for the intervention group in the proportion of prescriptions for antibiotics that complied with the recommended guidelines. Another Australian study by Ilett et al. (14) (level 1- method) involved a single visit by a clinical pharmacist in addition to prepared guidelines to influence prescribing of antibiotics. There was a significant within group increase for the intervention group in the median number of prescriptions per GP for two of the recommended antibiotics but no significant change for the control group. There was also a significant within group increase in the prescribing of two antibiotics that were not recommended in the guidelines for the control group. The between group significance was not reported, however, limiting the conclusions that can be drawn from the study.

The remaining two studies assessing individual education found no significant differences between groups for changes in prescribing. A study (level 1+ method) comparing provision of guidelines aimed at improving NSAID prescribing with or without visits from a trained community pharmacist (3) found no changes in the volume of prescribing of the three recommended NSAIDs. Despite a low participation rate among practices (only 20 of the 51 invited practices agreeing to be involved), a power calculation suggested there was sufficient power to detect a 6% difference between the groups. Good prescribing practices with respect to NSAIDs amongst participating practices at baseline may have limited the capacity of the intervention to produce a significant improvement (3). The other study assessing pharmacist detailing to encourage ACE inhibitor prescribing for specific patients with heart failure (level 1- method) (16) found no significant effects on prescribing. Although a power analysis was not reported, there was a high baseline level of ACE inhibitor utilisation in both groups.

Group education

Both of the studies assessing group education interventions by pharmacists for physicians showed some improvements in prescribing outcomes (17, 18) (Table 9.2). The study by Freemantle et al (18) that assessed the delivery of four guideline topics (with two educational visits per guideline topic) found a modest overall increase of 5.2% (95% confidence interval 1.7% to 8.7%) in the proportion of patients treated in accordance with the guidelines. The

guideline concerning the use of aspirin as an antiplatelet therapy was the only individual guideline for which the difference was reported as significant with an average of 7% increase in the proportion of patients treated in accordance with it. Although this study was described as a group education intervention some practices included only one medical practitioner. An analysis by the authors indicated that smaller practices (with one or two practitioners) had a statistically significant increase in the proportion of patients treated according to guidelines while those in the larger practices did not (18). The study by Diwan et al. (17) assessed the impact of four education sessions presented to groups of physicians on prescribing of lipid lowering drugs for patients with hyperlipidaemia. There was a significant increase for the intervention compared to the control in the number of prescriptions per month per health care centre for female patients aged 35-65 years. For other patient groups (men 35-65 years and patients over 65 years) the differences were not significant. There were also reported significant increases in the number of prescriptions for first line lipid lowering therapy for the intervention group, although between group comparisons were not presented.

Individual or group education

One randomised controlled study (19) (level 1- method) where educational sessions about prescribing guidelines for *Helicobacter pylori* eradication were delivered either individually or to groups of physicians, found no significant effect on the prescribing of the indicator medications metronidazole or omeprazole as a result of the intervention (Table 9.2). The administrative database used to monitor overall drug use was unable to detect drug use by indication and assessments were on overall use of omeprazole and metronidazole, leading to the potential for the results to be confounded by use of the medications for other indications.

Economic assessment

Two controlled trials compared the medication costs in the intervention group with the control group for pharmacist education to physicians in the community setting.

One randomised controlled trial assessed the impact of academic detailing on cost of antibiotic prescriptions in Western Australia (14). There was an increase in antibiotic prescriptions between the pre- and post-intervention periods which was stated to have been due to a seasonal increase in antibiotic prescribing. However, the increase was smaller in the intervention group than in the control group ($16,130 savings for 3 months) with lower prescribing rates for cefaclor and roxithromycin by the intervention group accounting for 82% of the overall savings.

One randomised controlled trial assessed the impact of mailed guidelines and academic detailing on cost of NSAID prescriptions in England (3). There were no statistically significant differences between the 3 groups when comparing the differences in prescription costs for 12 months before and after the interventions.

Although educational services and academic detailing are widely implemented in Australia, there is very limited economic evaluation of these activities.

No economic evaluations were presented in the study assessing pharmacist education in the aged-care setting.

Australian research

The provision of pharmacist education services to physicians in the community setting in Australia has been tested with two randomised controlled studies as described above (13, 14). Six non-randomised controlled (level 2 method) studies were also located which were undertaken in the Australian community setting. Five of these studies assessed a one-to-one educational intervention delivered by a pharmacist (5, 9-12), and one study assessed delivery of either individual or group education (4). A non-controlled study assessing outcomes before and after an educational intervention (level 3 method) was also located (21).

Level 2 studies

Three studies (level 2 method) undertaken in the general practice setting in Tasmania used a similar methodology to assess the impact of a single educational visit by a pharmacist in addition to mailed educational materials on antibiotic prescribing for urinary tract infections (UTIs) (12), NSAID prescribing for rheumatic disorders in elderly patients (11) and allopurinol dosage prescribing (10). In each of these three studies the southern region of the state served as the intervention region with the north and north-west regions serving as the control. Printed educational materials were mailed to general practitioners practising in the intervention area after which they were contacted to arrange an educational visit from the study pharmacist. One-to-one educational visits were conducted between the GPs and the pharmacist. Outcomes measured were changes in prescribing of the target medications using both pharmacy complete dispensing data and data obtained from the Drug Utilization Sub-Committee (DUSC) of the Pharmaceutical Benefits Advisory Committee (level 3 outcomes).

In the study assessing the educational intervention targeting antibiotic prescribing for UTIs (12) there were improvements in both the control and intervention regions in the prescribing of the recommended first-line agents (amoxycillin-potassium clavulanate, cephalexin and trimethoprim) compared to amoxycillin (3g single dose) and co-trimoxazole. The change in prescribing seen in the intervention region was significantly greater than that in the control region. The study that assessed an educational intervention for improving NSAID prescribing in elderly patients (11) used the ratio of dispensing of defined daily doses of NSAIDs to paracetamol as the outcome measure. There was a decline in the ratio (representing improved prescribing) in both the control and intervention regions, with the improvement in the intervention region being significantly greater than the control. The impact of the intervention to improve allopurinol dosage prescribing in accordance with the renal function of the patient was measured by the percentage of prescriptions for allopurinol that were for the 100 mg (lower dosage) form (10). The increase in the percentage of the lower dose form dispensed from the intervention region was significant while the increase in the control region was not significant. The improvement for the intervention region was not significantly different from that for the control region, however.

Another study conducted in South Australia assessed the impact of an ongoing teaching-hospital based educational outreach service that was provided to community doctors by clinical pharmacists (9). Clinical pharmacists prepared written materials as a source of unbiased information about NSAIDs and the information was externally reviewed. Doctors (GPs and specialists) receiving the service were visited by the clinical pharmacists and provided with copies of the written materials. Educational information provided at the visits was tailored to suit the individual needs of the doctor. Outcome measures (which included hospital admissions for upper gastrointestinal ulceration or perforation events and NSAID use) were compared between the area in which the service was provided and an adjacent comparison area in which the service was not provided. Using discharge diagnosis codes (ICD-9-CM codes) a gradual decrease in the rate of hospital admissions for upper gastrointestinal ulceration or perforation was seen in the intervention region between 1992 (when visits began) until 1997 while there were no notable changes in the comparison region over the same period. In the 5 years since the beginning of the service there were aggregate reductions of 9% in PBS NSAID dispensing and 28% in unit sales of NSAIDs to pharmacies in the intervention area relative to the comparison area.

A study conducted in the general practice setting in Melbourne (4) assessed whether educational outreach provided by a hospital pharmacist as part of a Coordinated Care Trial could improve prescribing of medications for *Helicobacter pylori* eradication or NSAIDs by 40 GPs who had accepted an invitation to receive the service. The intervention involved academic detailing carried out either at one-to-one visits or small group visits. Peer-reviewed educational materials were also provided at the visits. A control group of GPs who did not receive the service was used to compare prescribing patterns for 3 months before and after the visits. The database used for analysis was the co-ordinated trial data set, which only included patients registered for co-ordinated care. This resulted in only a small number of patients and thus prescriptions being available for analysis, which limited the findings of the study. For the intervention group there was a decrease in the number of NSAID prescriptions from 35 pre-intervention to 16 post-intervention, while the number of prescriptions for the comparison group increased from 11 to 14. The results were not statistically significant. Results for *H. pylori* eradication were not reported.

A study undertaken in two government areas of Sydney (5) assessed an educational intervention to reduce overall medication usage in older people. The intervention did not target any specific medical condition or class of drugs. Eligible patients were 60 years or older, taking prescribed medication and living at home. The educational intervention was provided to GPs of the enrolled patients in the intervention area by a trained pharmacist academic detailer. The intervention involved two visits and the distribution of printed promotional-style materials. Educational messages concerned the importance of reducing overall medication use through rational drug review with an emphasis placed on the high prevalence of drug-related hospital admissions among the elderly. Prescription medication usage was assessed at visits to patients 4, 8 and 12 months after initial contact. There were no significant differences between the control and intervention groups in the number of medications prescribed at any of the study time periods. There were also no significant differences when medications for the treatment of chronic conditions were analysed separately.

Level 3 studies

A study undertaken in Northern Tasmania assessed an educational program for GPs designed to involve GPs in community education and to improve the use of medications in older people (21). A pharmacist was contracted by a Division of General Practice to develop the educational materials and prescribing guidelines and to provide two academic detailing sessions for GPs to cover issues relating to the use of medications in older people. The program was managed by a multi-disciplinary team and also involved the provision of a resource and education package to help participating GPs to develop and deliver education sessions to other health care professionals and to older people and their carers and two continuing medical education seminars conducted by local specialist geriatricians. A multiple choice questionnaire was developed by the project pharmacist to assess the change in knowledge of general practitioners with respect to "therapeutic issues" in older people. Randomly selected medical records of 20 older people from each of the 13 participating GPs were collected at the initial and follow-up detailing sessions to assess prescribing according to a set of indicators. Pre-post assessments of knowledge for 11 GPs showed an increase in the mean score from 74.8% to 84.7% ($p=0.06$). Assessment of medical records of patients who resided in nursing homes found significant reductions in the median number of medications prescribed per patient and in the number of patients taking a psychoactive medication or NSAID. There was also a non-significant trend for reduction in the median number of medications per patient for community-based patients.

Comment

Nine randomised controlled studies (level 1 method) evaluating education services provided by pharmacists to health practitioners have now been undertaken. Most of these studies, however, have measured effectiveness in terms of changes to prescribing (level 3 outcomes) without assessing the impact of the intervention on patient outcomes.

Only one level 1 trial was located that assessed pharmacist education to health practitioners in the aged-care setting. The trial (level 1+ method) focussed on psychoactive medication use, and used social marketing techniques to identify factors influencing prescribing, individual education sessions by clinical targeting physicians with high prescribing rates and also group education sessions to nursing staff at the homes. It found significant improvements in prescribing (level 3 outcome) without adversely affecting patient outcome measures (level 1 outcomes).

Studies assessing education delivered by a pharmacist to physicians in the community setting suggest the service has an impact on medication use, although the results are variable. Two studies (level 1+ method), both of which used group education delivered by a pharmacist, have shown improved prescribing, one improving use of lipid-lowering medications for hyperlipidaemia and the second providing evidence for improved use of aspirin as anti-platelet therapy. The latter trial found greater effect for small group (1 or 2 practitioner) practices than the larger practices, suggesting one-to-one education may be more beneficial. The other level 1+ trial reported no effect, however, the baseline use of the target drugs was already good. The level 1- trials also provide evidence of the effectiveness of the approach, although results are modest and improvements were not seen for all drugs targeted. Some improvement in prescribing of NSAIDs by GPs was found in a study (level 1- method) (15) which assessed a single outreach

visit plus promotional materials to encourage rational prescribing. There were also improvements in antibiotic use in two studies (level 1- method), one of which involved a pharmacist visit as part of an extensive mail campaign (13), the other which involved educational visits plus distribution of therapeutic guidelines (14). The two level 1- studies which found no effect, included one which aimed to increase use of ACE inhibitors (16), however, baseline data revealed existing use was already high, so improvements may be difficult to obtain. The second aimed to improve use of *Helicobacter pylori* eradication therapy (19) and while no effect was observed, the outcome was monitored with an administrative dataset, which did not enable medication use by indication to be monitored, which may have confounded the results.

Further support for the effectiveness of academic detailing delivered by pharmacists comes from an earlier landmark study (22) published pre-1990. This randomised controlled study assessed whether academic detailing could reduce prescribing of targeted medications propoxyphene, cerebral and peripheral vasodilators and cephalexin. The study compared three groups: no intervention (control), individual educational visits to physicians plus printed promotional materials ("unadvertisements") or printed materials only. The academic detailers who conducted educational visits were six clinical pharmacists and one pharmacologist. Principles from communications and education theory and behaviour change research were used in the development of the printed materials and the training of the academic detailers. Post-intervention, there was a significant (14%) reduction in the prescribing of the target medications by physicians receiving the educational visits plus printed materials compared to the controls ($p<0.0001$). There was no significant change for the physicians receiving the educational materials only.

Collectively, the level 1 studies provide evidence that pharmacist education in the community setting does have a modest impact on medication use, where the intervention is targeted to specific drugs classes and where the use is known to be inappropriate.

Table 9.2 Randomised controlled studies of educational outreach services by pharmacists for medical practitioners in the community setting

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Studies involving individual (one-to-one) education						
Educational visits plus guidelines						
Ilett et al., 2000 (14)	1-	General practice setting Perth, Western Australia	A clinical pharmacist was used as a 'therapeutics adviser' to influence prescribing of antibiotics by general practitioners. An expert panel developed guidelines in line with published Australian guidelines. A summary version was prepared as a chart. GPs in the intervention group received a 10-15 minute visit from the adviser who briefly discussed the recommendations and provided a copy of the chart. The control group did not receive the visit or the chart,	56 intervention, 56 control. Prescribing patterns (Health Insurance Commission data) 3 months before & post-intervention	Level 3 Antibiotic use	For the intervention group there were significant increases in the median number of prescriptions per GP for doxycycline (p=0.0001) and amoxycillin 250mg (p=0.03) post-intervention compared with the pre-intervention period. Both of these antibiotics were "recommended" agents in the practice chart. While the number of prescriptions for these two antibiotics was not significantly different for the control group (p values for between group comparisons were not presented). For the control group there was a significant increase in the number of prescriptions for cefaclor (p<0.03) and roxithromycin (p<0.03), both of which were antibiotics that were not recommended. .
Watson et al., 2001 (3)	1+	General practice setting, Avon, England	Practices were randomised to one of three groups: i) control; ii) mailed guidelines; iii) mailed guidelines plus two educational outreach visits from a trained community pharmacist. The intervention aimed to improve prescribing of NSAIDs. Therapeutic guidelines were developed with local practitioners. Two visits were conducted approximately 3 months apart. The educational visits promoted the guidelines, tailored according to each GP's attitude/opinion towards NSAID prescribing. Visits lasted no more than 10 minutes.	20 general practices Practice-level prescribing analysis and cost (PACT) data for 12 months pre- and post-intervention.	Level 3 NSAID use	No statistically significant differences were detected between the three groups for the primary outcome measure. Practices that received the educational outreach visits prescribed 2.1% (95% CI –0.8 to 5.0) more of the three recommended NSAIDs than the control practices and 1.6% (95% CI –1.4 to 4.7) more than those that received the guidelines only. Good prescribing amongst the participating practices at baseline (79% of NSAID prescribing accounted for by the three recommended NSAIDs) may have limited the capacity for the intervention to provide improvement.

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Educational visits plus promotional materials						
Newton-Syms et al., 1992 (15)	1-	General practice setting Leeds, England	GPs receiving the intervention were provided with information about NSAIDs in a single short "sales" interview by a pharmacist trained to work as a medical representative. Promotional materials to convey the educational messages were also developed in conjunction with medical specialists and a marketing consultant. Materials were used as detailing aids by the pharmacist and were left with the GP following the interview. The control group did not receive any notification about the study and was not visited by the pharmacist.	101 intervention and 217 control Prescription Pricing Authority data and government prescribing data for the 5 months pre and post intervention.	Level 3 NSAID use	After the educational intervention the median PI ratio* for ibuprofen (the first choice recommended agent) increased significantly in the intervention group from 0.20 to 0.24 (P<0.005), while the PI value for the control group decreased from 0.18 to 0.16 (p< 0.005). The median PI for piroxicam (the second choice agent) decreased significantly in the control group after the intervention period but was not significantly different in the intervention group. There were no significant changes in the PI values for indomethacin. * Prescribing index (PI) ratio = ratio of prescribing costs for recommended NSAID : the cost of prescribing non-recommended NSAIDs plus recommended NSAID.
Pharmacist visit as part of mailed education campaign						
De Santis et al., 1994 (13)	1-	General practice setting Rural and metro Victoria, Australia	GPs who agreed to participate in the intervention locations received an educational mailing campaign based on the Victorian *Antibiotic Guidelines* recommending the use of narrow rather than broad spectrum antibiotics for the management of tonsillitis. The campaign was initiated with a brochure. A project pharmacist visited GPs in the intervention group to discuss the messages of the brochure. The visit was followed by another five mailings.	43 intervention, 30 control GP self-recorded pre- and 5 months post-intervention diaries.	Level 3 Antibiotic prescriptions	The percentage of prescriptions consistent with the recommendations improved from 60.5% pre-intervention to 87.7% post-intervention for the intervention group. There was also improvement in the control group from 52.9% pre-intervention to 71.7% post-intervention. The improvement in the intervention group was significantly greater than the control (p<0.05).

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Educational visits to physicians following use of pharmacy records to identify patients						
Turner et al., 2000 (16)	1-	Community setting Canada	Interviews with physicians were undertaken to identify patients being treated for CHF in both groups and to identify cases of CHF from those receiving an ACE inhibitor. Intervention physicians were visited regarding the use and dosage of ACE inhibitors and angiotensin II receptor antagonists for CHF. Consensus guidelines on the management of CHF were also provided at the visit.	109 physicians (from 72 practices) were randomised. Data for 51 patients in the control group and 91 patients in the intervention group. Follow-up at 3 months	Level 3 ACE inhibitor use	There were no statistically significant changes in the rate of prescribing of ACE inhibitors between the first and second interviews for the intervention or control groups (p value not given). There were, however, high baseline levels of ACE inhibitor use (78% control group, 79% intervention group). There were no significant changes in the dosage of ACE inhibitors between the two interviews (p=0.14).
Educational visits to physicians delivered as either single session or group session						
Freemantle et al., 2002 (18)	1+	General practices in 12 health authorities, England	Educational outreach on visits on two of four guideline topics. The guidelines related to i) the use of aspirin as antiplatelet therapy; ii) the use of ACE inhibitors in heart failure; iii) the use of NSAIDs for pain due to osteoarthritis; iv) the choice of antidepressants in the management of depression. Trained community pharmacists provided two educational visits on each topic to the general practices. Pharmacists were given copies of guidelines, summary sheets and promotional materials (it was not clear if all of these were given to GPs at the visits).	69 practices, data represented 11,326 patients and the work of 162 GPs. Random samples of 25 patient records for those who met inclusion criteria for each of the 4 guidelines pre-intervention and 3 to 11 months post-intervention	Level 3 Proportion of patients treated in accordance with guideline recommendations	Overall the educational visits were found to improve the proportion of patients treated in accordance with the guidelines. Intervention odds ratio of 1.24 (95% CI=1.07 to 1.42). Visits for the aspirin guideline were associated with statistically significant improvement (OR= 2.11, 95% CI 1.76 to 2.54), with an average 7% increase in the patients managed in line with the recommendations. Visits for the antidepressant guideline and ACE inhibitor guideline were associated with a 4% and 2% increase in treatment according to recommendations, respectively (statistical significance was not stated). In contrast, visits for the NSAID guideline were associated with a 3% reduction in treatment in accordance with guidelines (OR=0.73, 95% CI 0.56 to 0.94). Practices with one or two practitioners in the intervention group was associated with an odds ratio of 1.73 (95% CI 1.28 to 2.33), and an average improvement of 13.5% (95% CI 6% to 20.9%). In larger practices the effects were non-significant.

Reference		Setting	Description of the intervention	Evaluable sample and follow-up	Study outcomes	Results
Educational visits to physicians delivered as either single session or group session						
Hall et al., 2001 (19)	1-	General practice setting Single health district, England	Consensus guidelines for the management of *Helicobacter pylori* were developed locally & sent to all practices. A trained community pharmacist provided a single outreach visits to intervention practices, at which the pharmacist saw as many of the GPs as possible either as a group or individually. The pharmacist also offered to conduct an audit to identify patients that may benefit from *H. pylori* eradication therapy.	19 intervention and 38 control prescribing analysis and costs (PACT) data) at least six months pre and post intervention	Level 3 Omeprazole and metronidazole prescribing	No significant change in the use of omeprazole associated with the intervention (change -0.02 dose units, 95% CI -0.12 to 0.08). The effects on metronidazole prescribing were also non-significant. The high use of omeprazole for indications other than *Helicobacter* eradication may have confounded results.
Educational visits to general practitioners delivered as group sessions						
Diwan et al., 1995 (17)	1+	Community health care centres Sweden	Physicians at intervention centres received four 30-minute academic detailing sessions over a five-month period. An educational video on hypercholesterolaemia was also provided for later viewing.	60 intervention group centres and 56 control group centres. Five months pre-intervention and 12 months post intervention follow-up	Level 3 Prescribing of lipid-lowering medications	The mean number of prescriptions for first-line lipid-lowering medications per month and per health centre increased by 20% in the intervention centres (from 0.6 prescription pre-intervention to 0.74 post-intervention, p=0.03) compared to a decrease from 0.49 to 0.47 prescriptions in the control centres over the same period (between group p value not given).

Studies excluded

Studies were excluded if they used either a pharmacist or physician to conduct the educational service (23, 24) or used both a pharmacist and a physician (25-28).

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10. Drug Information Services

The Service

Drug information services are specialist services that provide drug information and answer general and specialist enquiries concerning medicines and their use.

Studies included

Studies were included in this section if they focused on the provision of a stand alone drug information service, i.e. drug information provided separately from another pharmacist service. Studies must have utilised patient outcomes or changes in medication use as an outcome measure.

Studies that incorporated provision of drug information as part of the education service during medication supply, pharmaceutical care or medication review services were excluded and are dealt with in other sections of this report.

Study design

A systematic review of the provision of drug information services by pharmacies was published in 2002 by Hands et al. (1). The search, encompassing Medline, Embase, Pharmline and International Pharmaceutical Abstracts, included any studies published since 1980, which had assessed drug information services and patient outcomes. Studies which had assessed operational systems or endpoints excluding patient outcomes were excluded. Pharmacy schools and drug information services in the UK were also contacted to detect any unpublished studies.

The review found only six published and one unpublished study meeting the inclusion criteria. No studies were located which had used a randomised controlled trial design. One study was an ecological study comparing existence of a drug information service within a hospital with mortality rates (level 3 for evidence). The other six study designs (level 3 evidence for method) included a review of the drug information logs (detailing type of request and information provided) plus a follow-up questionnaire or interview to the enquirer asking for details concerning perceived usefulness of the information, action taken and/or patient outcomes. Independent corroboration or review of the actions taken occurred in three of these studies, through an audit of the medical record or through review by an independent panel (level 3 outcomes). Two of the studies were prospective, the remaining were retrospective.

No further studies of the effect of drug information services on patient outcomes have been located since this systematic review was published.

Study outcomes

Patient outcomes were determined by self-report from the enquirer asking for details concerning perceived patient outcomes. Independent panel review of the information provided and likely

outcomes if the information had not been provided occurred in two studies included in the review (level 3 outcomes).

Evidence for effectiveness of practice

No controlled studies have been undertaken assessing the effect of drug information services.

Uncontrolled studies (level 3) suggests drug information services may contribute to improved patient outcomes as measured by enquirer self-report.

No study has examined actual patient outcomes in relation to drug information services. In considering future research in this area, it should be recognised that drug information services are an important component of any countries overall strategy for improving use of medicines. It may not be appropriate to expect drug information services, studied in isolation from other service provision of which they are an integral part, to demonstrate benefit.

Economic assessment

The only economic study we located was uncontrolled and was not included in this review (2).

Australian research

The evaluation of drug information services in Australia does not generally appear in the published medical literature, but is in unpublished reports. There have been evaluations of the National Medicines Weeks Phone In Service, which were one-off services employing experienced pharmacists and general practitioners to provide drug information for consumers. The service ran for one day only in 1996, two days in 1997 and for five days in 1998. The evaluation of these services was limited to process evaluation including monitoring the number of participants, types of enquiries, participant satisfaction and actions taken as a result of the advice, measured via follow-up surveys, as well as the accuracy of the information provided, measured by simulated callers using standardised scenarios (3). Process evaluations of the Therapeutics Advisory and Information Service which is operated by the National Prescribing Service have also been undertaken and are reported in the National Prescribing Service Evaluation Reports (4, 5). These reports indicate numbers of calls and types of enquiries. Process evaluation of the Queensland Medication Help-line is also reported annually.

We did not locate any Australian studies assessing drug information services provided by community pharmacists. A review of consumer drug information services undertaken in 1998 by the University of Newcastle also failed to locate any studies assessing outcomes associated with consumer drug information services. The study did include surveys of consumers and providers about their drug information needs (6).

Comment

No rigorous research demonstrating causal relationships between the provision of drug information services and patient outcomes has been undertaken. Level 3 evidence, obtained from studies reviewing drug information provided and participant perception of impact, with or without independent review, suggests drug information services are likely to have an influence on patient outcomes, as measured by perceived or probable impact on outcomes (level 3 evidence for outcomes). Because of the methods employed, an assessment of the size of the effect of the intervention is not possible. All studies in the systematic review had been conducted overseas (USA, UK & Canada). Data from Australia are limited to measures of service utilisation, types of enquiries made and enquirer satisfaction with service.

There is a limitation of reviewing services as an isolated, independent activity, which should be borne in mind when interpreting the findings presented here. Drug information services are a necessary part of health care provision and generally intended to be only part of the overall service provided by pharmacies. Systematic reviews of interventions to improve prescribing have demonstrated that the provision of drug information alone may change knowledge or awareness, but does not necessarily change behaviour (7). It is noted, however, that the provision of information is an important component of an overall strategy for improving use of medicines (7). In a similar vein, it may not be appropriate to expect drug information services, studied in isolation from other service provision of which they are an integral part, to demonstrate benefit.

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11. Pharmacist participation in therapeutic decision making

The service

Pharmacists can take an active role in the decision-making process about a patient's therapy. This is a collaborative process in which the pharmacist works as part of a team with physicians and other health care professionals.

Studies included

For the purposes of this review studies were included if they assessed the impact of a pharmacist's involvement in the decision-making process about a patient's therapy in collaboration with other healthcare professionals. Studies used a team-approach to care rather than simply the conduct of a medication review by the pharmacist with recommendations made and discussed with the prescriber. Studies were included if they were conducted in the community setting, outpatient clinics or extended-care facilities.

Studies assessing services for hospital inpatients were excluded. Studies which compared care by a multidisciplinary team against a control were excluded if it was not possible to assess the individual impact of pharmacist involvement.

Two further criteria for inclusion in this review were:

- The existence of a control or comparison group
- Endpoints included at least one patient outcome, which could include any of the following: hospital admissions, adverse events, mortality, quality of life, symptoms, surrogate health endpoint (e.g. BP control, cholesterol, BGL), changes in medication use, knowledge or compliance (level 1, 2 or 3 outcomes).

Study design

Two randomised controlled trials (level 1 method) were located which compared patient management by a pharmacist-physician team with management by a physician only (1, 2). The two studies were conducted in the same hospital outpatient clinic in Hawaii, USA. One study assessed a program that encouraged team-work between pharmacists and physicians to manage adult patients with elevated total cholesterol levels (1), the other study assessed a teamwork approach for the management of patients with uncontrolled hypertension (2). The studies are summarised in Table 11.1.

Study outcomes

Surrogate outcome measures (level 2 outcomes) were used in the two studies. These included:

- Total cholesterol levels
- Proportion of patients achieving goals for LDL cholesterol
- Changes in blood pressure (systolic and diastolic BP)
- Number of patients achieving blood pressure goals

Evidence for the effectiveness of the service

There is sound evidence from two randomised controlled trials (level 1+) of the effectiveness of pharmacist involvement in therapeutic decision making with a physician in improving patient outcomes measured by the surrogate endpoints of cholesterol and blood pressure in the USA.

However, both studies were undertaken in the one clinic and more rigorous research in other settings and other countries is still required.

Economic analyses have not yet been undertaken

Evidence for the effectiveness in improving level 2 outcomes (surrogate endpoints)

Both studies provide evidence (level 1+) for the effectiveness of pharmacist involvement as part of therapeutic decision making. In the study targeting patients with elevated cholesterol levels, a greater decline, by a mean of 44 mg/dL (or 1.1 mmol/L), was seen in the intervention group compared to the control group, which had a mean decline of 13 mg/dL (or 0.3 mmol/L). The difference between the groups was significant ($p<0.01$). There was a higher rate of success in achieving LDL cholesterol lowering goals in the intervention group (43% of patients) than the control group (21% of patients), $p<0.05$. The study targeting patients with hypertension also found positive results with 55% of patients in the intervention group achieving blood pressure goals compared to 20% in the control group ($p<0.001$).

Other endpoints were not reported.

Economic assessment

No economic outcomes were reported for the included studies (level 1 method)

Australian research

Two studies were located which assessed the involvement of a pharmacist in an Aged Care Assessment Team (ACAT) in the Australian health care setting (3, 4). These studies assessed outcomes for a cohort of elderly patients seen by an ACAT and for a subsequent cohort seen by an ACAT that included a clinical pharmacist (level 3 method). In the first study (3), the pharmacist worked with the other members of the team in the assessment of the patient, interviewed the patient to discuss their medications and collect data and collaborated with the team geriatrician and the patient in making decisions about medication changes. There were 100 control and 93 intervention patients. Baseline data and outcomes were collected at the initial ACAT assessment, after leaving the influence of the ACAT and 30 days after leaving the ACAT. The pharmacist intervention was reported to improve compliance with medication changes recommended by the geriatrician. There was 75% compliance with recommendations to cease a drug for the control group compared to 97% compliance for the intervention group at the last follow-up visit. Compliance with recommendations to start a drug was higher in the intervention

group (100%) than the control group (93%). Significantly more patients in the intervention group received a review of their medications by the geriatrician than the control group (p=0.02). In the second study (4) the clinical pharmacist reviewed medications, identified problems, discussed and recommended medication changes to the team geriatrician and answered medication-related queries from patients or members of the team. Quality of life (measured using the SF-36 and the Assessment of Quality of Life instruments) was used as an outcome measure with follow-up conducted one month after the patient was seen by the team. There were 390 patients assessed by a metropolitan ACAT (215 control, 175 intervention) and 369 assessed by a rural ACAT (205 control, 164, intervention). There were no statistically significant differences in changes in quality of life scores over time between the groups in either the metropolitan or rural setting. There were also no significant differences between the groups for the number of medications started or ceased in either setting.

There have been two randomised controlled trials (level 1 method) that have assessed the effectiveness of case conferencing in the Australian setting (5, 6), however, these trials compared case conferencing, which included the involvement of a pharmacist, against no case conferencing. In these instances it is not possible to evaluate the contribution of the pharmacist in the case conference to the patient outcomes.

Comment

There is sound evidence from two randomised controlled trials (level 1+) of the effectiveness of pharmacist involvement in therapeutic decision making with a physician in improving patient outcomes, as measured by the surrogate endpoints of cholesterol and blood pressure. However, both studies were undertaken in the one clinic and more rigorous research in other settings and other countries is still required to determine the broader applicability of the service. In addition both studies examined pharmacist and physician conferences, the involvement of pharmacists in larger multidisciplinary case conferences has still to be assessed. Research in the Australian setting is still required, as are rigorous economic evaluations.

Table 11.1 Randomised controlled trials of pharmacist involvement in therapeutic decision-making

Reference	Level	Setting	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Bogden et al., 1997 (1)	1+	Primary care outpatient clinic, Hawaii, USA (Single centre)	Assessed a program that encouraged team-work between pharmacists and physicians to manage adult patients with elevated total cholesterol levels. For the intervention arm the pharmacist routinely advised and interacted with physicians about the best course of pharmacological management at each patient visit. Activities undertaken by the pharmacist included medication history taking, patient education, and recommendation to physicians on drug selection, dosage and monitoring. The control group received standard medical care.	47 intervention, 47 control 6 months follow-up	Level 2 Total cholesterol levels; Proportion of patients achieving goals for LDL cholesterol lowering	Total cholesterol levels for the intervention group declined by a mean of 44 mg/dL (or 1.1 mmol/L) while the decline for the intervention group was 13 mg/dL (or 0.3 mmol/L). The difference between the groups was significant ($p<0.01$). There was a higher rate of success in achieving LDL cholesterol lowering goals in the intervention group (20/47 intervention patients (43%) versus 10/47 controls (21%), $p<0.05$).
Bogden et al., 1998 (2)	1+	Primary care outpatient clinic, Hawaii, USA (Single centre)	Assessed the effect of a pharmacist and physician teamwork approach on management of patients with uncontrolled hypertension. The intervention groups received coordinated input from a pharmacist into their care (as described above for Bogden et al 1997). Control patients received normal medical care.	49 intervention, 46 control 6 months follow-up	Level 2 Target BP Changes in systolic and diastolic BP	Number of patients achieving blood pressure goals was 27/49 (55%) in the intervention group and 9/46 (20%) in the control group ($p<0.001$). This difference remained significant using an intention-to-treat analysis with a "worse case scenario" ($p<0.01$). Diastolic BP declined an average of 14 mmHg in the intervention group and 3 mmHg in the control group ($p<0.001$). Systolic BP declined by an average of 23 mmHg in the intervention and 11 mmHg in the control ($p<0.01$).

Ongoing studies

An ongoing controlled study was located which involves pharmacist participation in therapeutic decision-making for patients with major depression (7)

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12. Pharmacist involvement in non-prescription medicine use

The service

Pharmacists in many countries are actively involved in providing advice, assistance and recommendations regarding non-prescription medication use. In some countries, some medicines are restricted to pharmacist or pharmacy only sale because of the perceived additional benefit pharmacists can provide in achieving quality use of medicines.

Studies included

Studies were included in this section if they were controlled studies which assessed patient outcomes associated with pharmacist involvement in the provision or use of non-prescription medicines, not prescribed by another health practitioner.

Study design

One randomised controlled trial (1) (level 1- method) assessed the impact of pharmacists' advice and counselling on the outcomes of self-medication in patients with dyspepsia. Thirty-six urban and rural community pharmacies in Germany were randomly assigned to the intervention or study group. It is not clear if pharmacists knew their group allocation. Pharmacists from intervention pharmacies received a training programme including guidelines on counselling patients with dyspepsia. The control pharmacists received no training. Eligible patients were those who presented to the pharmacy asking for a specific pharmacy medication for dyspepsia or who requested help for dyspepsia. In intervention pharmacies patients received medication counselling, and instruction on diet and posture. Control pharmacies provided standard care. Follow-up was conducted one week later to monitor changes quality of life. It appears the questionnaire was given to the patient by the community pharmacist. More questionnaires were returned from intervention than control pharmacies (114 intervention, 84 control).

Study outcomes

The outcome measured was quality of life using the validated Gastrointestinal-Quality-of-Life Index (level 1 outcome).

Evidence for effectiveness of practice

There has been a lack of controlled trials assessing the effect of pharmacist involvement in non-prescription medicine use. Only one randomised controlled trial (level 1-) was located, which had positive outcomes, as measured by health related quality of life, in the short term for people with dyspepsia.

No controlled trials assessing patient outcomes undertaken in the Australian setting were located.

Further rigorous research, including economic evaluation, is required.

The one randomised controlled trial that was located demonstrated improvements in quality of life measures for both groups over the study period. The increase in quality of life scores over the one week course of the study were significantly greater in the intervention group compared to the control ($p<0.001$).

Further supporting evidence

Three uncontrolled studies were located which provide some support that the involvement of pharmacists in non-prescription medication use may be positive. In an uncontrolled study (level 3 method) Sclar et al. (2) assessed the effects of pharmacy consultation on purchasing decisions related to over-the-counter (OTC) medicines and quantified prevention of adverse medication-related outcomes. Consultations were provided by 55 pharmacy interns in their final year of training in 23 pharmacies in Washington, USA. The intern conducting the consultation documented patient details and outcomes of the consultation. Consultations were provided for 745 patients of which 317 (43%) changed their intended purchase as a result of the pharmacist consultation. Thirty-two (4.2%) customers were referred to a physician. The number of potentially prevented adverse outcomes related to medications was assessed by examining each customer's self-reported medications, medical conditions and the OTC product the customer had originally intended to buy. It was reported that adverse outcomes were prevented in 53 customers (7.1%) by the pharmacy consultation. It is not clear, however, whether the consultations were independently reviewed, and what criteria were used to judge whether or not an adverse outcome had been prevented.

Dreyer et al. (3, 4) conducted an uncontrolled study (level 3 method) to assess the incidence, extent and outcomes of interventions by a random sample of 155 community pharmacists in South Africa. Interventions made for both non-prescription and prescription medications were examined. To assess the outcomes of pharmacist-initiated OTC therapy, every tenth patient was telephoned three days after the intervention. A standard questionnaire was used to "establish the consequences of pharmacist interventions on the course of the patient's condition". Of the 472 patients assessed for outcomes 297 (63%) reported their condition was vastly improved, 142 (30%) reported it was somewhat improved, 21 (4.5%) reported no change and 12 (2.5%) reported their condition was worse when asked to "describe your condition today". Four hundred and three patients (85%) reported that it was not necessary to see a doctor due to worsening of their condition. A limitation of this study is that the pharmacists carrying out the intervention also carried out the follow-up assessment. It is also unclear how these results would differ from a control population.

Another study by Nichol et al. (5) (level 3 method) conducted in a community pharmacy in California assessed the impact of counselling on OTC medication by a trained intern pharmacist on customer's purchasing decisions. It was found that 33% of customers reported buying a different OTC medication as a result of consultation with the intern pharmacist. Nearly 15% purchased an additional medication and 6% decided not to purchase an OTC medication.

The focus of this review was studies that assessed changes to patient outcomes. Other endpoints such as workload transfer may also be valid when assessing the value of pharmacist services related to non-prescription medicines. Two pre-post studies (level 3 method) conducted in the United Kingdom (6, 7) have assessed the workload transfer away from general practitioners (GPs) when community pharmacists manage patients with self-limiting conditions.

Economic analysis

No studies (level 1 method) meeting the review inclusion criteria which presented economic outcomes were located.

Australian research

No controlled studies undertaken in the Australian setting were located that had assessed patient outcomes.

Comment

There is currently a lack of good evidence world-wide determining the effectiveness of the involvement of pharmacists in non-prescription medicine use. Only one study was located, and while it does provide evidence of improved health outcomes in the short term, further research is required before conclusions can be drawn about longer term outcomes, outcomes for other diseases and outcomes in other countries.

The lack of rigorous research assessing the effect of professional pharmacist services for over-the-counter medicines is of concern. Use of over-the-counter (OTC) medicines has been found to be less than optimal. An Australian survey of 500 mothers of children aged 0 to 12 years found that while most mothers reported responsible self-medication practices and that they followed dosage instructions precisely, one in ten mothers admitted that when they use analgesics, sedating antihistamines and compound cough and cold formulas they usually increase the recommended dosage 'just for good measure'. This same group of mothers admitted to using analgesics for behavioural purposes: "12% of mothers admit to administering 'Panadol' when their child is upset…"(8). Research commissioned by SmithKline Beecham found that 67% of consumers surveyed were unaware of complications associated with ibuprofen. There was also little awareness of its contraindications even amongst consumers with conditions contraindicating use of ibuprofen (9). Another Australian study assessing use of OTC analgesics found dosage and frequency of doses above the manufacturer's recommendation, prolonged use without medical supervision, non-analgesic use of pharmacist only (S3) and pharmacy only (S2) analgesic products and limited pharmacist interaction regarding S3 analgesics to be problematic (10).

It becomes apparent from the evidence highlighting less than optimal medication use, that structures are necessary to support appropriate medication use. While not all countries have provision for pharmacist-only or pharmacy-only medicines, many do to ensure appropriate use of over-the-counter medicines. It may be that there has been a lack of research in this area because historically it has been a privilege of the profession. However, the continuation of this privilege is not necessarily assured. The provision of pharmacist-only and pharmacy-only medicines, at least in Australia, has been under-review recently (11). If professional pharmacy is to maintain the privilege of pharmacist-only and pharmacy-only medicines, it is likely that further rigorous evidence will be necessary to maintain the conviction of policy makers is this area.

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13. Smoking Cessation Services

The Service

Smoking cessation programs offered by community pharmacies aim to assist consumers to quit smoking. The programs generally include patient assessment, counselling, documentation and ongoing follow-up. Nicotine replacement therapy or referral as appropriate are also usually included. The programs are generally implemented within community pharmacies.

Studies included

Studies were included in this section in they had provided a program run by a pharmacist with the aim of improving smoking cessation rates. Studies could be located in community pharmacies or hospital outpatient settings. Studies must have utilised some measure of smoking cessation rates as an outcome measure.

Study design

Three randomised, controlled trials assessing smoking cessation interventions based in community pharmacies were located (level 1) (Table 13.1). Two were undertaken in the UK (1, 2) and one in Australia (3). The method of randomisation differed across studies. One study used the pharmacy as the unit for randomisation (2), with all subjects attending the one pharmacy allocated to either intervention or control group with subjects unaware of allocation (level 1+). In one study (1), the subjects were allocated to groups within the pharmacy. This latter system has significant potential to bias the results, with the pharmacist responsible for delivering the intervention being aware of the group to which the subject was allocated (level 1-). The third study involved recruitment within the hospital setting and subjects randomly allocated to one of two intervention groups (hospital based or community based) or the control groups (3). In this instance the hospital pharmacist responsible for recruiting subjects, also undertook the hospital intervention, as well as the follow-up with subjects from all groups, leading to potential for bias. All studies assessed the effect on smoking cessation of a support program, with or without use of nicotine replacement therapy offered by the community pharmacist. All programs included counselling, documentation and ongoing follow-up.

Study outcomes

Outcomes measured were self-reported smoking cessation at 12 months, with or without urinary cotinine levels (level 2 outcome). Subjects lost to follow-up were assumed to have lapsed. Outcomes were usually assessed by interview or written survey.

Evidence for effectiveness of practice

Currently, there is a lack of good evidence for the effectiveness of smoking cessation programs in community pharmacy. This has been due to studies failing to recruit sufficient samples, or studies with open designs where the pharmacist delivering the intervention is aware of group allocation and interacts with both groups, leading to potential for significant bias

One randomised controlled trial undertaken in the UK (level 1-) has demonstrated a causal relationship between the provision of smoking cessation services and smoking cessation rate (level 2), although this study had significant potential for bias. Two other randomised controlled trials (level 1+ and level 1-) failed to demonstrate effect, although both failed to recruit sufficient sample sizes.

Only very limited economic evaluation has been undertaken, involving 2 pharmacies only, thus no conclusions can be drawn about the cost-effectiveness of the service at this stage.

Only one randomised controlled trial found a statistically significant difference between control and intervention groups (1), with 14.3% of the 265 subjects in the intervention group reporting 12 months abstinence (supported by urinary cotinine measurements) compared to 2.7% of the 219 subjects in the control group ($p<0.001$). However, in this study consumers were randomly allocated to intervention or control group. Because all pharmacists were trained to utilise the intervention and aware of the purpose of the study, randomisation by consumer, rather than by pharmacy, has the potential to bias the results. The other two studies failed to recruit enough subjects to demonstrate significance (2, 3). Trends towards significance were observed in a UK study with 12% of subjects reporting nine-months continuous abstinence compared with 7.4% in the control group (2) but this did not reach statistical significance. Similarly, trends towards significance were also reported in the Australian study (3), with 24% of subjects in the hospital intervention arm, 19% in the community pharmacy arm and 4.6% in the control arm reported continuous abstinence at 12 months ($p=0.225$). The lack of significant result in these studies is not necessarily because of failure of the intervention. Power calculations for both studies suggested much larger sample sizes were required.

Economic assessment

A cost-effectiveness analysis of the pilot study underpinning the work of Maguire et al. (1) has been undertaken (4). Only 2 community pharmacies were involved. The cost per life-year saved was found to vary from £181.35 to £772.12 for women and £196.76 to £351.45 for men (1997 prices). Incremental costs have not been calculated.

Australian research

A randomised controlled trial of the effectiveness of smoking cessation programs has been undertaken in the Australian setting (3). As detailed above, trends towards effect were noted, however, failure to recruit sufficient sample sizes meant non-significant results were

obtained. Research undertaken without a comparison group (level 3 method) in a community pharmacy setting suggests the service may assist smoking cessation (5).

Comment

One randomised controlled trial undertaken in the UK (level 1-) has demonstrated a causal relationship between the provision of smoking cessation services and patient outcomes (level 2), although this study had significant potential for bias. Two other randomised controlled trials (one in Australia and one in the UK) have failed to demonstrate significant results primarily because of the failure to recruit sufficient sample sizes, but both studies demonstrated trends towards improved smoking cessation rates.

There is a lack of strong evidence concerning the implementation of smoking cessation programs within community pharmacies. Trials to date have had problems recruiting sufficient participants. The smoking cessation programs reviewed in this section all included interventions that aimed to improve cessation rates. Behavioural change theory suggests that participation in programs is more likely when participants are at the "contemplation, trial or action" stage of change (6). It may be that cessation programs must also be supported by programs, either delivered locally or nationally, that raise awareness of the need for change, to move participants from the pre-contemplation stage of change to the trial and action stages to facilitate participation.

Table 13.1 Randomised controlled trials assessing pharmacist smoking cessation services

Reference	Level	Setting	Intervention	Evaluable sample and follow-up	Study outcomes	Results
Maguire et al., 2001 (1)	1-	Community pharmacies UK	The intervention included training workshops, use of the "Pharmacists' Action on Smoking module, which utilised a face-to-face counseling with structured follow-up and included documentation proforma, and ongoing follow-up for at least four weeks. Nicotine replacement therapy may have been supplied if appropriate.	265 subjects in the intervention group; 219 subjects in the control group. 12 month follow-up	Level 2 Self-reported abstinence at 12 months supported by urinary cotinine measurements	14.3% of the 265 subjects in the intervention group reporting 12 months abstinence (supported by urinary cotinine measurements) compared to 2.7% of the 219 subjects in the control group ($p<0.001$)
Sinclair et al., 1998 (2)	1+	Community pharmacies Scotland	The intervention involved training for pharmacists and pharmacy assistants in and subsequent use of the Pharmacy Support Program for smoking cessation, which included counseling follow-up and documentation proforma	224 subjects in the intervention group; 268 subjects in the control group. Nine month follow-up	Level 2 Self-reported abstinence	12% of subjects reporting nine-months continuous abstinence compared with 7.4% in the control group ($p=0.089$). Power calculations suggest at least 538 subjects required in each group to demonstrate significance.
Vial et al., 2002 (3)	1-	Hospital and community setting Adelaide Australia	The intervention included nicotine replacement therapy with weekly follow-up visits for a maximum of 16 weeks delivered by the hospital or community pharmacist, depending on group allocation.	3 groups; 35 subjects in the hospital based intervention arm, 34 the community pharmacy intervention arm and 33 in the control group. 12 month follow-up	Level 2 Self-reported abstinence	24% of subjects in the hospital intervention arm, 19% in the community pharmacy arm and 4.6% in the control arm reported continuous abstinence at 12 months ($p=0.225$). Power calculations suggest at least 100 subjects required in each group to demonstrate significance

Excluded studies

Studies reviewed but excluded from this review because of lack of comparison groups included:

Kennedy et al., 2002 (7)
Zillich et al., 2002 (8)
Smith et al., 1995 (9)

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14. Pharmacist immunisation services

The Service

Pharmacist services related to immunisation that are described in the international literature include:

a) immunisation advocacy programs in which the pharmacist identifies patients requiring immunisation and provides information and education with the aim of raising awareness and improving vaccination rates;
b) administration or provision of vaccinations in the pharmacy setting to improve vaccine access.

In the USA, community pharmacists are permitted to administer vaccinations (1).

Immunisation advocacy

Studies included

For the purposes of this review we included studies that aimed to improve immunisation rates or immunisation access through immunisation advocacy (provision of information and education).

Services provided for hospital outpatients or patients discharged from hospital were included. Immunisation services provided to hospital inpatients only were excluded.

Study designs

Two randomised controlled trials (level 1 method) were located which assessed the impact of education and recommendations provided by a pharmacist on immunisation rates. The methods and findings of the studies are summarised in Table 14.1. One study targeted consumers (2), while the other targeted health care providers and consumers compared to consumers alone (3). The study targeting consumers was conducted in the USA (2) and assessed whether provision of mailed information from community pharmacies could improve influenza vaccination rates amongst patients at risk. The other study (3) conducted at a hospital in Canada assessed whether pharmacist intervention could improve pneumococcal and influenza vaccination rates amongst patients discharged from hospital who had undergone cardiac surgery. The study involved three groups: discharge counselling about immunisation by a pharmacist only, pharmacist counselling plus liaison with the patient's community pharmacist and pharmacist counselling plus liaison with the patient's community pharmacist and physician (through a discharge letter and care plan). There was no control group without pharmacist intervention. Both studies were rated level 1- for method due to the lack of blinded outcome assessment.

Other studies located which assessed the impact of pharmacist immunisation advocacy lacked control or comparison groups (level 3 method) (4). In keeping with the use of the highest available evidence studies to provide evidence for the effectiveness of the practice, only randomised controlled trials (level 1 method) were reviewed.

Study outcomes

Both studies (level 1- method) measured the proportion of patients immunised as the outcome measure (level 3 outcome).

Evidence for effectiveness of the service

One only study (level 1- method) was found which assessed the effect of a community pharmacist initiated mail-out to consumers for improving vaccination rates. It found a significant increase in the proportion of at-risk patients receiving influenza vaccinations following the mail-out campaign.

Another study (level 1-) assessed whether targeting consumers and the consumers' community health professionals improved vaccination rates compared to pharmacist counselling alone. It found no difference for pneumococcal and influenza vaccination rates when a hospital pharmacist provided a letter and plan to a patient's community pharmacist or to their community pharmacist and physician, however the consumers in the control group who received pharmacist counselling only, had improved immunisation rates at the study's completion compared to baseline.

Further studies of rigorous methodology (level 1 method) are required to evaluate pharmacist-services to improve immunisation rates. The existing evidence suggests the services should target consumers and that the additional targeting of community health providers makes no further difference.

Cost-effectiveness is still to be evaluated.

Further rigour needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation.

Research in the Australian setting was not located. Given existing high immunisation rates in Australia, any research undertaken in the Australian setting needs to be evaluated to ensure no detrimental effect on overall immunisation trends.

Evidence for effectiveness (level 3 outcome)

In the study assessing whether the provision of mailed information from community pharmacies could improve influenza vaccination rates amongst patients at risk (2) there were 125 patients in the intervention group and 134 patients in the control group who had not been immunised at the time of the pharmacy mail-out. At the end of the study there was a significantly higher proportion of the intervention group (31%) than the control group (18%) who had been vaccinated for influenza ($p=0.013$).

In the study comparing three types of pharmacist interventions for patients discharged from hospital (3) there were no significant differences in the vaccination rates between groups for either the pneumococcal or influenza vaccination at three months post-discharge. The authors stated that an immunisation campaign provided by the Ministry of Health at the same time as

the study could also have influenced vaccination rates. Due to the lack of a control group receiving no pharmacist intervention it is not possible to assess the extent to which this other campaign influenced vaccination uptake in the study groups.

Economic assessment

No level 1 studies were located that had assessed the cost-effectiveness of immunisation advocacy.

Australian research

No studies assessing the impact of pharmacist services on immunisation rates in the Australian health care setting were located. One study investigated the feasibility of immunisation service provision in Australian community pharmacies (4). This study included assessment of stakeholder attitudes, availability of materials to train pharmacists, current legislation, professional indemnity issues and strategies for service promotion (4). Another study described a multidisciplinary service to provide vaccinations to paediatric inpatients and outpatients in an Australian hospital (5). The program resulted in thirty patients (16 outpatients and 14 inpatients) receiving vaccination who were either behind the recommended vaccination schedule or who had not received their initial course of a recommended vaccination. The pharmacy department role included supply and recording of vaccination details.

Comment

Evidence from randomised controlled trials (level 1 method) that pharmacist immunisation advocacy services improve vaccination rates is limited to one trial. One study (level 1-method) found a significant increase in the proportion of at-risk patients receiving influenza vaccinations following a mail-out campaign from community pharmacies which advised patients about their influenza risk and where they could obtain vaccination. The second study assessed whether the addition of liaison with community care providers to pharmacist counselling concerning immunisation had any effect. It found no difference compared to counselling alone in the administration rates for pneumococcal and influenza vaccination rates when a hospital pharmacist provided a letter and plan to a patient's community pharmacist or to their community pharmacist and physician, suggesting this additional service is not warranted. The lack of a control group receiving no intervention prevents assessment of the impact of the pharmacist counselling alone. The vaccination rate improved in all groups compared to baseline.

Further studies of rigorous methodology (level 1 method) are required to evaluate pharmacist-services to improve immunisation rates. Further rigor needs to be incorporated into the assessment of patient outcomes including assessment by independent researchers, blinded to subject allocation. Further research is required to assess the impact of pharmacist services on immunisation rates in the Australian health care setting and to ensure they have no negative impact on overall immunisation rates.

Excluded studies

Studies reviewed but excluded from this review because of lack of comparison groups included: Van Amburgh et al., 2001 (6).

Administration of immunisations by pharmacists

Studies included

For the purposes of this review studies were included if they assessed provision of pharmacy-based or pharmacist-managed immunisation programs including the administration of vaccinations in pharmacies. Services provided for hospital outpatients or patients discharged from hospital were included. Immunisation services provided in hospital were excluded.

Study designs and outcomes

No controlled trials (level 1 or 2 method) assessing outcomes from a pharmacy-based immunisation program were located. Studies located lacked control or comparison groups or correlated cross-sectional surveys in different states in the USA (level 3 method).

In an uncontrolled study (level 3 method) Ernst et al. (7) assessed a community based influenza vaccination program in a rural area of Iowa, USA. These authors assessed whether administration of influenza vaccinations by a pharmacist (after counselling the patient and screening for contraindications) in a community pharmacy setting increased access to vaccination in the rural area and the number of at-risk patients immunised. Records of all immunisations were kept. The pharmacist administered 343 doses of the vaccination during the 7-week study. No adverse effects were reported or observed. There were 110 patients (32%) who had not been immunised in the previous year. Of these, 61% reported they would not have gone elsewhere to get the vaccine.

Grabenstein et al. (1) (level 3 method) measured association between availability of pharmacist immunisers in 2 US states (Washington State in which pharmacists could administer vaccinations and Oregon in which they could not) and influenza vaccination rates amongst adults in the area. Influenza vaccination rates were assessed by a survey sent to adults in the two states. Eligible subjects from two target groups were identified from pharmacy records: those aged 21-64 years that received certain target prescription medicines used in conditions that indicate a need for influenza vaccination and those aged 65 or above taking any prescription medication. A total of 4,403 randomly selected eligible subjects (2,211 Washington, 2,192 Oregon) were sent a self-administered survey about beliefs and behaviours related to vaccination. The response rate was 51% in the Washington cohort and 55% for the Oregon cohort. Between the years 1997 and 1998 the increase in influenza vaccination rates was 4.7% more in Washington than Oregon for the over 65 year group, this difference was not significant, however ($p=0.20$). In the younger age group taking medications for chronic diseases the net increase for Washington compared to Oregon was 10.6% which was borderline significant ($p=0.05$).

Evidence for the efficacy of the service

There is currently a lack of evidence supporting administration of immunisation by pharmacists. No controlled studies have been located.

Australian Research

There were no studies located assessing pharmacy-based administration of immunisations in the Australian health care setting.

Comment

Studies assessing community pharmacy administration of immunisations have been undertaken in the US community setting where pharmacists are authorised to administer vaccinations. There is currently a lack of evidence from controlled trials (level 1 and 2 method) for the effectiveness of the service in improving immunisation rates and patient health outcomes.

Table 14.1 Randomised controlled trials assessing pharmacist immunisation advocacy services

Reference	Level	Setting	Patients, description of the service	Evaluable sample and follow-up	Outcomes	Results
Grabenstein et al. 1993 (2)	1-	Three community pharmacies North Carolina, USA	Patients aged 65 years or older at risk of influenza. The intervention group was mailed information from the pharmacy about influenza vaccinations and where the patient could obtain vaccination. Control patients received information about poison prevention. A reminder postcard was sent to both groups after 2-3 weeks. Although study pharmacists were advised not to initiate discussions with any patients about vaccination, they could discuss it if asked by patients in either group.	There were 125 patients in the intervention group and 134 patients in the control group who had not been immunised at the time of the pharmacy mail-out 2 month follow-up	Level 3 Proportion of patients immunised	. At the end of the study there were 39/125 (31%) intervention group patients and 24/135 (17.9%) controls who had been vaccinated (p=0.013) (reported as RR 1.74 (95% CI 1.11 to 2.72).
Gutschi et al., 1998 (3)	1-	Hospital and community Ottawa, Canada	Eligible patients were discharged from hospital following cardiac surgery who had not received both the pneumococcal and influenza vaccinations in the previous two years. Patients were randomised to one of three groups: i) discharge counselling (information and recommendations about influenza and pneumococcal vaccination) (group 1); ii) discharge counselling plus follow-up letter and a care plan addressed to the patient's community pharmacist (group 2); iii) discharge counselling plus follow-up letter and care plan to patient's physician and community pharmacist (group 3).	There were 135 evaluable patients (44 in group 1, 44 in group 2 and 47 in group 3). Follow-up at 3 months	Level 3 Proportion of patients immunised	There were increases in both influenza and pneumococcal vaccination rates compared to baseline for all 3 groups with no significant differences between the groups. For pneumococcal vaccination the percentage of increase in vaccination rate from baseline was 43%, 36% and 46.8% for groups 1, 2 and 3, respectively (p=0.594). For influenza vaccination the percentage increase was 66%, 80% and 70% for groups 1, 2 and 3, respectively (p=0.347). The authors state that a pneumococcal vaccination program run by the Ontario Ministry of Health at the same time could also have influenced vaccination rates. It was not possible to assess the extent to which this influenced vaccination in the study group.

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15. Other services

Other services that were considered for this review included clinical interventions, hospital in the home services, screening and monitoring services.

Clinical interventions

There is a large literature base describing and evaluating clinical interventions provided by pharmacists. This literature is usually referring to the detection of errors, actual or potential or inappropriate medication use identified by pharmacists during their routine practice. For example, the detection of an inappropriate dose, drug-interaction, allergy or contraindication identified and rectified during routine dispensing. This practice is widely recognised as a professional pharmacist service. Despite an extensive review of the literature, we did not locate any controlled studies evaluating this service in terms of patient outcomes. Nearly all of the published literature incorporates a prospective or retrospective method where all interventions are documented and subsequently reviewed, usually by an independent panel, which makes an assessment about the likely impact on patient outcomes in the presence and absence of the intervention, such as in the studies of Caleo et al., 1996 (1), Hulls and Emmerton, 1996 (2), Hawkesworth et al., 1999 (3), Needham et al., 2002 (4) and Whitehead et al., 2002 (5). The likely economic benefit is also often included as part of the assessment, such as in the studies of Rupp, 1992 (6), Fincham and Gottlob, 1997 (7), Knapp et al., 1998 (8) and Benrimoj et al., 2000 (9). This method, however, did not meet our criteria for inclusion in this review. The rigorous methods encompassed in this review that probably provide most insight into the effectiveness of this practice are the medication review services. Unfortunately, the two randomised controlled studies under-taken in the out-patient setting used a passive method for alerting physicians to recommended interventions and no effect was observed (10, 11). Randomised controlled trials of medication review services in the out-patient setting using active methods for engaging with physicians about pharmacist recommendations are required to provide evidence for the effectiveness of this service.

Hospital in the home

Hospital in the home services are a relatively new service and despite an extensive literature review, we did not locate any controlled studies that had assessed the involvement of a pharmacist in this service. Descriptive studies have been reported such as those of Triller et al., 2000 (12) and Dedden et al., 1997 (13). Currently, the continuity of care studies post-hospital discharge provide the best insight into the likely benefit of pharmacists in these circumstances. This suggests pharmacist involvement would be advantageous to patient outcomes and that further rigorous research of this service is required.

Screening

While pharmacist involvement in screening services has been examined (14, 15) and it is possible for pharmacists to undertake screening services such as blood pressure, blood cholesterol and blood glucose measurement, the benefits of this to the overall health system are still currently unclear. A critical review of the literature relating to community pharmacy involvement in health development published in 2001 (16) concluded that there was insufficient evidence to determine whether screening activities in community pharmacies are an effective use of resources. We did not locate any controlled studies that had assessed

pharmacist delivered screening services in terms of patient outcomes. We recognise it may be impractical to assess pharmacist involvement in screening services with patient outcomes as the endpoint as it would require large samples. The research concerning the provision of screening services by pharmacists needs to encompass both the capacity of pharmacists to provide the service and the actual or potential impact of the provision of this service by pharmacists on overall screening rates. This is particularly relevant in countries where established screening services exist and are supplied by other providers.

Monitoring services

Another professional service involves community pharmacists monitoring surrogate endpoints for specific disease states. These services aim to improve the proportion of patients achieving target levels for these surrogate endpoints such as blood pressure and cholesterol levels. Two randomised controlled trials (level 1 method) which assessed pharmacist services to relating to patient monitoring were located (17, 18).

A study conducted in the USA (17) (level 1- method) assessed a program in which patients at risk of coronary artery disease were identified through the community pharmacy prescription database and were subsequently invited to attend a screening day in the pharmacy. Patients whose LDL cholesterol and triglyceride levels were not at goal levels were randomly assigned to the intervention or control group. The intervention group was followed in a pharmacist-directed intervention which involved diet and exercise evaluation and instruction, ongoing cholesterol monitoring, drug therapy monitoring, patient education and collaboration with physicians. Intervention group patients were seen in the pharmacy every 1-2 months during the study period. A total of 51 patients were randomised to the study (25 intervention, 26 control). In the intervention group 8 patients (32%) reached their cholesterol goals compared to 4 patients (15%) in the control group (level 2 outcome). The result did not reach statistical significance ($p=0.08$), however, inadequate numbers of subjects may have limited the ability to detect a significant difference. Compared to baseline values the mean LDL levels decreased for the intervention group (baseline 156.4 mg/dL, post-test 153.0 mg/dL), whereas mean LDL levels increased for the control group (baseline 145.2 mg/dL, post-test 152.2 mg/dL) (level 2 outcome). The differences between the groups were not statistically significant. There were no significant differences between the groups for mean total cholesterol, HDL or triglyceride levels.

Another study conducted in the USA by Mehos et al. (18) (level 1- method) evaluated the impact of a pharmacist-initiated home blood pressure monitoring intervention. Patients with uncontrolled hypertension who were taking at least one antihypertensive medication were randomised to intervention or control groups. All patients received counselling on antihypertensive medication and lifestyle modification while the intervention group patients were provided with a blood pressure monitor and instructed on how to use it. A clinical pharmacist contacted intervention patients at one to two monthly intervals to assess BP response and if necessary to refer the patient to their physician. Follow-up continued for 6 months. Patients in the control group received routine care with assessment at the end of the study. Thirty-six patients completed the study (18 intervention, 18 control). There were no significant differences between the groups for changes in scores of health-related quality of life (measured by SF-36 instrument) over the course of the study (level 1 outcome).
There was a significant difference between the groups for reductions in diastolic BP (level 2 outcome), with intervention patients having a mean reduction of 10.5 mm Hg versus a reduction of 3.8 mm Hg for the control group ($p=0.022$). The mean reduction in mean arterial

pressure (level 2 outcome) was also significantly more in the intervention group patients (12.7 mm Hg) than the controls (4.9 mm Hg) (p=0.01). Differences in the reduction in systolic BP were not significantly different between groups.

Taken together, the results of these two studies provide equivocal evidence for the effectiveness of pharmacist monitoring services. At present there is stronger evidence for pharmaceutical care services (Chapter 2) for improvement of surrogate outcomes. No economic analyses were located for these studies of monitoring services.

Pharmacist prescribing

Services that included pharmacist prescribing of prescription medicines as part of the intervention are reviewed in the chapter on pharmacist-managed clinic services. No randomised controlled studies (level 1 method) evaluating pharmacist prescribing of prescription medicines as the sole intervention on patient outcomes were located. Pharmacist prescribing of over-the-counter medicines is reviewed in the non-prescription medicines chapter.

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16. Conclusion

This review of the value of professional pharmacist services was commissioned by the Pharmacy Guild of Australia to inform ongoing research and strategic planning for the development of professional pharmacist services in the community setting both within Australia and internationally.

This review encompasses the depth and breadth of the research effort published in the English language since 1990 to support professional pharmacy practice in the community and evaluates the strength of the evidence for the effectiveness of professional pharmacist services, in terms of consumer outcomes, and where possible, the economic benefit. A small number of unpublished reports are also included. This review encompasses over 70 randomised controlled trials evaluating professional pharmacist services that have monitored patient outcomes as the end-point for the study.

Evidence for effect

There is clear evidence across a number of different settings for the effectiveness of pharmaceutical care services, continuity of care services post-hospital discharge, pharmacist education services to consumers and pharmacist education services to health practitioners for improving patient outcomes or medication use.

Pharmaceutical care services (level 1- for method) have shown a reduction in adverse drug events (level 1 outcome), an improvement in medication appropriateness (level 1+ for method, level 3 outcome), a reduction in medication problems (level 1- for method, level 3 for outcomes), improvements in signs, symptoms for people with asthma (level 1+ and level 1- for method, level 1 for outcomes), an improvement in combined all-cause mortality and non-fatal heart-failure related events in patients with heart failure (level 1+ method, level 1 outcome), improvements for surrogate end-points such as blood pressure, glycosylated haemoglobin and cholesterol levels in some studies (level 2 for outcomes) and measures of improved management of cholesterol risk (level 3 outcome). The variability observed in study results across studies, particularly with multi-centre trials suggests future work needs to focus on how to maximise service delivery, including uptake by pharmacists and targeted delivery to those in need and for whom outcomes can be improved.

There is sound evidence (level 1-) that pharmacist implemented continuity of care services post hospital discharge that include active patient follow-up and are targeted to high-risk patients improve patient outcomes including reducing hospital readmissions (level 1 outcomes), numbers of medication related problems, as well as improving medication knowledge and adherence (level 3 outcomes).

The results of studies assessing one-to-one educational interventions suggest both single session and multiple session education are effective, with stronger evidence and better outcomes for effectiveness of multiple session education. There is level 1+ evidence supporting the efficacy of multiple session education for improving blood pressure and compliance in patients with hypertension and compliance in renal transplant patients. Multiple session education was also found to be effective (level 1-) in improving adherence in the elderly, and those on lipid-lowering therapy, therapy for chronic heart failure and anti-retroviral therapy. It was also found to be effective (level 1-) for improving the symptoms of heart failure and for improving lipid profiles in those with existing heart disease. Multiple

session education plus active self-monitoring was found to be effective (level 1-) for reducing hospitalisation, improving quality of life and improving compliance in patients with heart failure. Single session counselling via telepharmacy has been shown to be effective in the short term for improving metered dose inhaler technique. Single session counselling was also found to improve quality of life measures for patients presenting to community pharmacies with symptoms of dyspepsia. The efficacy of extended counselling over standard counselling for patients on *Helicobacter pylori* eradication therapy, the only subject studied, is unclear, with two studies finding conflicting results. There is currently a lack of published controlled studies assessing the impact of small group education delivered by pharmacists for patients or consumers.

Pharmacist education to health practitioners in the aged-care setting has been shown to improve psychoactive drug use without adversely impacting on patient outcomes. However, only one level 1 trial was located and more research is required in this setting.

Educational outreach visits to medical practitioners in the community setting targeting specific drug classes (level 1+ and level 1-) for which there are recognised prescribing problems have been found to improve medication use. Two studies (level 1+ method), both assessing group education delivered by a pharmacist, have shown improvements in medication use, one finding increased use of lipid-lowering medications for hyperlipidaemia and the other improving use of aspirin as anti-platelet therapy. The latter trial found greater effect for small group (1 or 2 practitioner) practices than the larger practices, suggesting one-to-one education may be more beneficial. The other level 1+ trial, using one-to-one visits, reported no effect, however, the baseline use of the target drugs was high. The level 1- trials also provide evidence of the effectiveness of the approach, although results are modest and improvements were not seen for all drugs targeted. Some improvement in prescribing of NSAIDs by GPs was found in a study (level 1- method) that assessed a single outreach visit plus promotional materials to encourage rational prescribing. There were also improvements in antibiotic use in two studies (level 1- method), one of which involved a pharmacist visit as part of an extensive mail campaign, the other which involved educational visits plus distribution of therapeutic guidelines. The two level 1- studies which found no effect, included one which aimed to increase use of ACE inhibitors, however, baseline data revealed existing use was already high, so improvements may be difficult to obtain. The second aimed to improve use of *Helicobacter pylori* eradication therapy and while no effect was observed, the outcome was monitored with an administrative dataset, which did not enable medication use by indication to be monitored, which may have confounded the results.

There is more limited evidence, but still positive evidence, for the effectiveness of pharmacist managed clinics, pharmacist review of repeat prescribing and pharmacist participation in therapeutic decision making in improving patient outcomes. Evidence for these services is often limited to one or two countries.

Studies assessing pharmacists' review of the continuing need for repeat prescriptions demonstrated (level 1-) that patient outcomes were no different to usual care, which was usually provided by a physician. It is not yet clear, however, if these findings can be applied to all disease states, and further evidence is required. Studies have only been undertaken in the UK setting, which also limits the generalisability of the results to other countries, where health systems may differ considerably

Two randomised controlled trials (level 1- method) provide evidence for the effectiveness of pharmacist-managed hypertension clinics for improving blood pressure measurements (level 2 outcomes) in adult patients with essential hypertension in the USA health setting. Level 2 evidence suggests pharmacist managed clinics can improve HbA1C levels for patients with diabetes, improve lipid levels for those with coronary artery disease, and reduce major haemorrhagic events for those on anticoagulant therapy.

There is sound evidence from two randomised controlled trials (level 1+) for the effectiveness of pharmacist involvement in therapeutic decision making with a physician in improving patient outcomes, as measured by the surrogate endpoints of cholesterol and blood pressure. Both studies, however, were undertaken in the one clinic and more rigorous research in other settings and other countries is still required to determine the broader applicability of the service. In addition both studies examined pharmacist and physician conferences, the involvement of pharmacists in larger multidisciplinary case conferences has still to be assessed. Research in the Australian setting is still required, as are rigorous economic evaluations.

New professional services that have not yet been adequately evaluated include pharmacist administration of vaccines, pharmacist involvement in pre-admission clinics and pharmacist participation in hospital in the home services.

Pharmacist involvement in pre-admission clinics appears to be a relatively new service and consequently little research has been undertaken in this area. Level 2 evidence from one UK study suggests pharmacist involvement in pre-admission clinics may reduce error rates, but poor methodology limits any conclusions that can be drawn. Admission to hospital is a point where continuity of care can break down. Future research in this area should not necessarily limit the service to patient assessment prior to admission, but also include liaison services with community care providers, which is co-ordinated with the post-discharge continuity of care service to support the entire continuum of care for the patient.

No controlled studies were located assessing pharmacist participation in hospital in the home services on patient outcomes. The results from the continuity of care studies post hospital discharge support the notion that pharmacist participation in hospital in the home services would be beneficial and highlights the need for rigorous research in this area.

Further studies of rigorous methodology (level 1 method) are required to evaluate pharmacist services to improve immunisation rates. The existing evidence suggests the involvement of community pharmacists as advocates for immunisation services, improves vaccination rates, although this is limited to evidence from one randomised controlled trial. The evidence suggests the education should target consumers and that the additional targeting of community health providers makes no further difference to vaccination rates. Controlled studies assessing pharmacist administration of vaccines on overall immunisation rates and patient outcomes are still required.

There were some areas of established pharmacy professional practice for which rigorous controlled studies were either not located or only a small number were located with equivocal results. More research is still required to establish best practice for medication review in aged-care facilities and medication review in the outpatient setting, as well as pharmacist participation in pharmacist-only and pharmacy-only medicines use. In addition, more

research is required concerning pharmacist involvement in smoking cessation services and screening services.

There are only a limited number of controlled studies conducted world-wide assessing medication reviews in nursing homes. Best practice is not yet clear with studies reporting mixed results. Only one study (level 1-) reported finding a decrease in mortality, with a second (level 1-) finding no effect, although insufficient sample sizes and the lack of sufficient follow-up may have contributed to this finding. Given the significant potential for problems and ultimately harm to patients in aged-care facilities, from inappropriate medication use, it seems apparent that there is great need for further rigorous research in this area to establish best-practice.

Currently, evidence for the effectiveness of medication review (review of medication charts and case notes) is lacking. Only two randomised controlled trials were located, and neither provides evidence for the effectiveness of the service. Both studies relied on written communication to physicians as the main method to communicate the review recommendations. This is a passive method of engagement and may have contributed to the lack of effect observed in the study outcomes. Hospital-based drug utilisation evaluation studies which have involved active engagement with physicians concerning the reviews findings suggest medication review can be effective. Future study of medication review in the outpatient setting should examine whether a more active process of engagement with physicians has any effect.

No rigorous research demonstrating causal relationships between the provision of drug information services and patient outcomes has been undertaken. Level 3 evidence, obtained from studies reviewing drug information provided and participant perception of impact, with or without independent review, suggests drug information services are likely to have an influence on patient outcomes, as measured by perceived or probable impact on outcomes (level 3 evidence for outcomes). There is a limitation of reviewing services as an isolated, independent activity, which should be borne in mind when interpreting the findings presented here. Drug information services are a necessary part of health care provision and generally intended to be only part of the overall service provided by pharmacies. Systematic reviews of interventions to improve prescribing have demonstrated that the provision of drug information alone may change knowledge or awareness, but does not necessarily change behaviour. It is noted, however, that the provision of information is an important component of an overall strategy for improving use of medicines. In a similar vein, it may not be appropriate to expect drug information services, studied in isolation from other service provision of which they are an integral part, to demonstrate benefit.

There is currently a lack of rigorous research determining the effectiveness of the involvement of pharmacists in non-prescription medicine use. Only one level 1 method study was located, and while it does provide evidence of improved health outcomes, as measured by health related quality of life, for people with dyspepsia in the short term, further research is required before conclusions can be drawn about longer term outcomes, outcomes for other diseases and outcomes in other countries.

Currently, there is a lack of good evidence for the effectiveness of smoking cessation programs in community pharmacy. This has been due to studies failing to recruit sufficient samples, or studies with open designs where the pharmacist delivering the intervention is

aware of group allocation and interacts with both groups, leading to potential for significant bias.

Methodological limitations

Common methodological limitations observed in a number of studies included the open allocation of subjects to intervention or control groups and the assessment of outcomes by reviewers who were aware of the group allocation of subjects. Methodological rigour would be improved if the pharmacists providing the intervention were unaware of the group allocation of subjects, or alternatively, the pharmacy is used as the unit of allocation, steps are taken to avoid cross contamination between pharmacies and subjects are unaware of pharmacy allocation. In addition, independent reviewers blinded to subject group allocation, should be utilised to monitor outcomes. One further methodological consideration is the type of end-point monitored. The variability in end-points used in the studies considered in this review often made it difficult to synthesise findings. In addition, health related quality of life measures were commonly utilised, often demonstrating no effect, which raises questions of whether this is due to the lack of effect of the service, or the lack of sensitivity of the measure. By comparison, adverse drug events were seldom utilised as an outcome measure, even where the aim of the study was to reduce medication misadventure. Where adverse drug events were monitored as an endpoint, variable methods were used and explicit criteria for assessing adverse drug events often omitted, despite their existence. Given that the focus of professional pharmacist services is to improve medication use and reduce medication misadventure, it is likely that adverse drug events are a more sensitive outcome indicator of the effect of pharmacist services than quality of life measures. It would seem appropriate to give further consideration to incorporating adverse drug events, assessed by independent panels utilising explicit criteria, more commonly as an outcome measure of the services.

Economic analysis

Economic evaluation of the value of pharmacist professional services is limited. There were 19 studies with a randomised controlled trial design, including 9 studies with minimal economic input, 8 descriptive economic studies and two full economic evaluations. Studies with minimal economic output looked at drug costs exclusively without considering any other costs. Descriptive economic studies compared a variable range of health care costs. Studies that were excluded from this analysis where mainly studies which were not randomised and presented other serious shortcomings such as a lack of control group or failure to demonstrate statistically significant outcomes (see Appendix III Table 1). Almost half of the studies (9 studies) assessed the impact of the pharmaceutical care services and 3 assessed the medication review services. We located only one or two studies for any other pharmacist services that were reviewed in this report.

Nine studies assessed the impact of pharmacist professional services on drug costs. Six studies showed a significant reduction in drug costs associated with the provision of pharmacist professional services. Two studies did not show a difference between the intervention and the control groups. All 3 studies done in Australia showed a decrease in medication costs associated with the provision of domiciliary based medication reviews (1), medication reviews in nursing homes (2) and academic detailing (3). Further studies would be needed to establish for how long these savings are maintained and how frequently medication reviews should take place. None of these 3 studies showed an association between reduction in drug costs and improvement of clinical outcomes.

Eight studies were descriptive economic studies and included comparisons of various health care resources between the intervention and control groups. Only 2 studies showed a reduction in health care costs and four studies did not show this effect (no statistical results for 2 studies).

Two studies were full economic evaluation studies. The clinical relevance of the cost/effectiveness ratio used in the first study is difficult to appreciate as it was expressed per unit change in the Medication Appropriateness Index that is not commonly used. The second cost-effectiveness study related to smoking cessation services in a pilot study in 2 community services. These results cannot be reasonably extrapolated all smoking cessation services.

Other studies citing economic evidence for value of pharmacy professional services were located, however, very often they were based on studies that had not shown an effect on patient outcomes or were not controlled designs. Economic studies were excluded if there had been no demonstrable effect on patient outcomes.

Given the scarcity of economic studies for most types of clinical pharmacist services, it is difficult to comment on their impact on drug costs, health care resource costs or cost-effectiveness. Most of the evidence comes from pharmaceutical care studies and medication review studies. There is some evidence that these interventions can reduce drug costs. Further studies would be needed to establish for how long these savings are maintained and how frequently these interventions should take place. We have not located any full economic evaluation study on the cost/effectiveness of these services.

Overall, this review demonstrates that there is considerable high quality evidence to support the value of professional pharmacy services. The world-wide research effort has evaluated the majority of professional services currently provided by pharmacists and, importantly, demonstrated improvements in outcomes for patients. Improvement in economic analyses is still required. Where the evidence is sound, however, it should now become a high priority to implement these services more broadly within a country's health system.

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Appendix I

Search terms used to identify published studies about professional pharmacist services.

Multiple searches were conducted in MEDLINE, International Pharmaceutical Abstracts, Current Contents, Australasian Medical Index (via AUSTHealth) and the Cochrane Library. Terms were searched as subject headings, keywords. Due to differences in subject heading structures between the different databases, the subject heading searches differed in the various databases. The search terms used in each database are detailed below.

MEDLINE (via Ovid) 1990- Oct 2002

Pharmacist or Pharmacists
Pharmacy
Pharmaceutical care
Counsel or counselling
Intervention or interventions
Clinic or clinics
Pre-admission or preadmission
Screening
Drug Information
Academic detailing
Medication review
Medication management

Drugs, non-prescription (subject heading)
Drug Information Services (subject heading)
Patient education (subject heading)
Education, medical, continuing (subject heading)
Community pharmacy services (subject heading)
Pharmacy service, hospital (subject heading)

International Pharmaceutical Abstracts 1990- Oct 2002

Pharmacist or pharmacists
Pharmacy
Pharmaceutical care
Smoking cessation
Intervention or interventions
Medication review
Medication management
Clinic or clinics
Pre-admission or preadmission
Screening
Hospital in the home

Interventions (subject heading)
Pharmacists, community interventions (subject heading)
Pharmacists community, services (subject heading)

Pharmacists community, patient education (subject heading)
Pharmacists community, patient information (subject heading)
Pharmacists community, tests, laboratory (subject heading)
Pharmacy services, community (subject heading)
Pharmacy services, ambulatory care (subject heading)
Pharmacy services, home health care (subject heading)
Pharmaceutical care, pharmacy services (subject heading)
Pharmaceutical care, pharmacy community (subject heading)
Pharmaceutical care, pharmacy practice (subject heading)
Health care home (subject heading)
Ambulatory care, pharmacy services (subject heading)
Pharmacists, hospital ambulatory care (subject heading)
Drugs, over-the-counter (subject heading)
Prescriptions pharmacists, community (subject heading)
Pharmacists, education (subject heading)
Education, physicians (subject heading)
Patient education (subject heading)
Nursing homes (subject heading)
Residential care facilities (subject heading)

Current contents 1998-Oct 2002

Pharmacist or pharmacists
Pharmacy or pharmacies
Medicine or medicines or medication
Over-the-counter or non-prescription or nonprescription
Counsel or counselling
Education
Drug information
Academic detailing
Pharmaceutical care
Clinic or clinics
Pre-admission or preadmission
Screening
Medication review
Medication management
Intervention or interventions

Australasian Medical Index 1990- Oct 2002

Pharmacist or pharmacists or pharmacist- or pharmacists-
Pharmacy or pharmacies
Over-the-counter or non-prescription or nonprescription
Schedule or schedule-
S2 or S3 or S2-S3 or S2S3 or S2-3
Drug Information
Counsel or counselling
Academic detailing or academic detail
Education or education-
Intervention or interventions

Medication review
Medication management
Professional
Service or services
Clinic or clinics
Pre-admission or preadmission
Screening

The Cochrane Library (Accessed 15 October 2002)

Pharmacist (no restrictions)
Pharmacists (MESH heading)

Appendix II

Controlled studies, that were not randomised, were generally not discussed in the body of this report because the highest level evidence available was used to make conclusions about the efficacy of the services evaluated. Level 2 studies, however, were reviewed as part of this research. Summary tables of all Level 2 studies reviewed follow.

Table 1. Level 2 pharmaceutical care studies

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Pharmaceutical care studies targeting general patient populations at risk of drug-related problems				
Blakey and Hixson-Wallace, 2000 (1)	Level 2 Non-randomised, controlled Geriatric ambulatory care clinic, Atlanta, USA	Targeted patients with polypharmacy (5 or more medications per day) and chronic disease states. Intervention included pharmacist interview with the patient, evaluation of DRPs, generation of an electronic progress note, discussion with the physician and follow-up. The control group received usual medical care in the clinic	Level 3 Medication use	The intervention was provided 106 patient visits and 144 received usual care. There was mean reduction of 3.4 agents per patient in the intervention group compared to a mean decrease of 0.4 agents per patient in the control group at the end of the study ($p<0.0001$). However the control group had a significantly lower of number of medications at the start of the study.
Pharmaceutical care for specific disease states				
Knoell et al., 1998 (3)	Level 2 Pre-post, non-randomized control group, (alternately assigned) Specialty pulmonary medicine outpatient clinic of a large midwestern hospital, USA	Eligible patients were adults with a diagnosis of asthma. All patients were given a peakflow meter for use in the study. The intervention group received pharmaceutical care. The pharmacist interacted directly with the patient and their physician (pulmonologist) at clinic visits. This included chart review by the physician and pharmacist, consultation between the physician and pharmacist, interventions and education. The pharmacist met with the patient and introduced an individualised self-management plan to the patient. One follow-up visit was also conducted. The control group received physician (pulmonologist) care. Outcomes were measured at baseline and 45 days after the first clinic visit. 100 patients (45 intervention, 55 control) were included in the study.	Level 1 HRQOL (SF-12 and the disease specific asthma quality of life [AQLQ] questionnaire); Hospitalisations, emergency department visits, physician visits Level 3 Compliance with asthma inhaler medications and monitoring	Scores for the AQLQ improved in both groups in 45 days. There was a greater percentage in the experimental group than the control group who had "moderate" change (change greater that 1.0 unit) or "large" change (change greater 1.5 units) in AQLQ scores but the difference was not significant between the groups. Both groups showed improved SF-12 scores in most domains except the mental component score (compared to baseline at 45 days). Although the intervention group showed a trend towards greater improvement, a significant difference in improvement between the groups was not seen. Both groups had fewer emergency department visits, hospitalisations and physician visits, there were no significant differences between the groups, however. Patients in the intervention group were more likely to use their peakflow meter to monitor asthma ($p<0.004$), and to have established a personal "best peak value" recording ($p<0.004$). Medication compliance was not different between the groups.

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Pharmaceutical care for specific disease states (cont.)				
Schulz et al., 2001 (2)	Level 2 Non-randomised controlled trial Community pharmacies. Hamburg, Germany Multi-centre	48 pharmacies were involved in the study. 26 intervention pharmacies and 22 control (pharmacies choice). Eligible patients were those with asthma (identified by medications or self reports). In intervention pharmacies, trained pharmacists were asked to provide pharmaceutical care in one-to-one meetings with patients in counselling rooms. Meetings were scheduled at six-week intervals over a 12-month period and involved the pharmacist detecting drug or health related problems and working in cooperation with the patient's physician to resolve them. The pharmacist also assessed the patient's inhaler technique, and provided education where necessary. Patients were also instructed on how to use a peak flow meter. Patients of control pharmacies received usual care. Patients completed questionnaires at baseline, 6, and 12 months. A total of 242 patients were recruited (161 intervention, 81 control). There were 101 intervention patients and 63 control patients that completed the study according to the study criteria, and which were included in the analysis.	Level 1 Health-related quality of life (SF-36 and the German version of the "Living with Asthma" questionnaire). Level 2 Lung function tests (FEV_1 and PEFR). Level 3 Patient's inhalation technique (using a 7-point checklist); Patients' knowledge of asthma and drug therapy (using a questionnaire); Self-efficacy (self-management skills and ability to cope with asthma)	The mental summary scale of the SF-36 questionnaire was significantly improved in the intervention group compared to the control group (p=0.003), however the physical summary scale showed no difference (p=0.490). Asthma-specific quality of life scores improved significantly for the intervention group compared to the control (physical symptoms p=0.04, psychological distress p=0.001, functional status p=0.011). The FEV_1 lung function test improved from baseline for both the intervention and control group but there was no significant difference between the groups at 12 months. There were no significant differences in PEFR values measured in the pharmacy between the intervention and control groups. PEFRs measured at home by patients (intervention group only) remained unchanged from baseline in the morning, but evening values improved significantly. The patients' inhalation technique was significantly improved compared to the control group (p=0.001) There was no significant difference between the intervention and control groups with respect to knowledge of asthma and drug therapy at 6 or 12 months. At 12 months, the improvement in knowledge compared to baseline was significant for the intervention group. Significant improvement in self-efficacy was found for the intervention group compared to baseline at 6 months (p=0.019) and 12 months (p=0.001).

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Pharmaceutical care for specific disease states (cont.)				
Watanabe et al., 1998 (4)	Level 2 Non-randomised, Controlled trial Hospital in Tokyo, Japan Single-centre	Asthma patients treated with medication were eligible. Intervention group were inpatients of the hospital at enrollment, patients in the control group were inpatients or outpatients of the hospital. The intervention group received pharmaceutical care during and after their hospitalisation. Participants were evaluated over a 12-month period. 176 patients were enrolled, 15 patients received the intervention, the remaining 161 patients served as controls.	Level 1 Emergency room/urgent care visits Level 2 Plasma theophylline concentrations Level 3 Asthma medication use	Patients in the intervention group had a significantly reduced mean frequency of emergency/urgent care visits compared to before they received the service (No comparison with control group provided). Mean plasma theophylline concentration (used by the investigators to measure compliance) was significantly higher in the intervention group (no comparison with the control group was given). Compared to the control group the patients in the intervention group were prescribed significantly more inhaled anti-inflammatory medications, anti-allergic, leukotriene receptor antagonists, thromboxane A2 receptor antagonists and synthesis inhibitors.

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Preventative care				
Carter et al., 1997 (5)	Level 2 Controlled with group allocation by site (non-random) Primary care clinic, rural Illinois, USA	Randomly selected patients with essential hypertension within a study and control site were eligible. Trained community pharmacists delivered the intervention which included reviewing medical records, face-to face interventions with physicians, nurses, and patients, blood pressure measurement, assessment of drug-related problems and compliance, preparation of written progress notes (including a plan and recommendations), provision of patient education. Intervention patients returned for monthly scheduled visits to the pharmacist for 6 months. Controls were assessed at baseline and 6-months received only traditional pharmacy service including brief counselling and normal medication dispensing services. 51 patients were included (25 intervention, 26 control).	Level 1 HRQOL (SF-36) Level 2 BP (measured by pharmacist) Level 3 Quality of prescribing (assessed by blinded panel)	Significant improvements within group (compared to baseline) in the intervention group scores for the SF-36 domains of "physical functioning", "physical role limitations" and "bodily pain" ($p<0.05$) while no significant changes for the control. Differences between groups not reported. Systolic BP was reduced in the study group from 151 mm Hg at baseline to 140 mm Hg at 6 months ($p< 0.001$, within group). Systolic BP for the control group was 145 mm Hg at baseline and 143 mm Hg at 6 months ($p>0.05$, within group). There were no significant differences between the groups Quality of prescribing scores for the blood pressure medication regimen appropriateness improved significantly within the intervention group over the course of the study from 8.7 to 10.9 ($p<0.01$), while there was no change for the control group (10.3 to 10.1).

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Preventative care (cont.)				
Erickson et al., 1997 (6)	Level 2 Controlled, non-randomised Internal medicine outpatient clinic, Michigan, USA	Assessed a pharmaceutical care intervention for patients 18 years or older diagnosed with essential hypertension and with uncontrolled BP. Patients were allocated to intervention or control groups by day of clinic attendance. The pharmaceutical care intervention included medical record review, drug history taking and assessment of patient specific drug-related issues, compliance and patient knowledge. Discussion of drug-related problems with physicians, laboratory monitoring and patient education were conducted. Intervention patients received the service at regularly scheduled clinic visits for approximately 5 months. Control patients received regular care without pharmaceutical care. 80 patients were enrolled (40 intervention, 40 control)	Level 1 HRQOL (SF-36 and a published disease-specific hypertension questionnaire) Level 2 BP (physician measured)	HRQOL scores (using data available from 28 intervention and 32 control patients) were not significantly different between groups for the either the SF-36 or disease-specific instrument. Within the intervention group there was a significant worsening of one domain (physical functioning) compared to baseline (p=0.03). For the intervention group there was a significant decrease in systolic BP compared to baseline (mean systolic 156.5 mm Hg baseline versus 144.5 mm Hg at 5 months, p=0.001 within group) while the change for the control group was non-significant (153.7 mm Hg baseline versus 151.0 mm Hg at 5 months, p=0.480. Between the groups the difference in BP change was borderline significant (p=0.05). Mean diastolic BP decreased significantly compared to baseline for the intervention group (91.6 mm Hg baseline versus 86.9 mm Hg at 5 months, p=0.01 within group) but the change was not significantly different from the control group (p=0.49).

Table 2. Level 2 continuity of care studies

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Lucas, 1998 (7)	Controlled trial, no randomisation. Retrospective medical chart review (Level 2). Single hospital	Group allocation was based on medical record documentation of bedside medication education. Where no documentation, the person was allocated to control group. Intervention consisted of bedside medication teaching by a clinical pharmacist. Patients discharged to the community were included. There were 143 and 142, respectively in the intervention and control group.	Level 1 Readmission within 30 days Drug-related readmission	No significant differences in hospitalisation rates. Twenty seven people in the intervention group had unplanned readmissions compared to 23 in the control group. Four admissions in the intervention group were considered to be possibly or probably drug related compared to 6 in the control group (although method for assigning this was poor).

Table 3. Level 2 studies assessing pharmacist-managed clinics

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Bozovich et al., 2000 (8)	Level 2 Pre-post with control group, non-randomised Clinic in a cardiology practice, North Carolina, USA	Patients with a diagnosis of coronary artery disease who were under the care of a single cardiologist attended pharmacist-managed clinic. The clinical pharmacist followed patients and developed a drug therapy decision making protocol which was approved by the cardiologist. The pharmacist selected lipid lowering therapies, and made therapeutic changes (cosigned by the cardiologist), provided patient education and evaluated barriers to compliance. A drug therapy plan was developed and followed-up at return visits. The control group came from the practice of a non-participating cardiologist and received usual care from the cardiologist Patients in both groups were followed for a minimum of 6 months	Level 2 Achievement of LDL cholesterol goals (according to National Cholesterol Education Program guidelines)	104 patients were enrolled and treated at the clinic (intervention group), 101 patients served as controls. There was a statistically significant increase in the number of patients in the intervention group that achieved their LDL cholesterol goal level from 34 patients (33%) at baseline to 72 patients (69%). The percentage of control group patients who achieved their LDL goal was also significantly increased from 25% of patients at baseline to 50% at 6-months. Intervention group patients were more likely to achieve their LDL goal than control patients (p=0.016).
Foss et al., 1999 (9)	Level 2 Non-randomised, controlled Anticoagulation clinic in a Veterans' Affairs Medical Center, Denvar, Colorado, USA Single centre	Pharmacist-operated anticoagulation clinic. Pharmacists were given the authority by medical staff to write prescriptions for warfarin, to adjust doses and to undertake laboratory monitoring. Pharmacists also provided education to patients and encouraged them to contact the pharmacist with any questions or concerns. Patients were referred to the clinic by their doctor. Over a 9-month period the outcomes for patients in the clinic were compared to a "usual care" group (patients from the center with an active prescription for warfarin, but who were not attending the clinic).	Level 1 Percentage of patients admitted to the medical center due to bleeding; Percentage of patients with thromboembolic complications; Percentage of patients with any medical complication.	During the 9-month period 443 patients were followed in the clinic, while 197 patients with active warfarin prescriptions received usual care. During the 9-month period 1.1% of the clinic patients and 2.0% of the usual care patients were admitted to the medical center for bleeding (admissions to another outside hospital were not included in the analysis). Of the clinic patients 0.9% had thromboembolic complications compared to 3.1% of the usual care group. The percentage of patients with "any complication" was 2.0% in the clinic group compared to 5.1% in the usual care group. Tests for statistical significance were not performed.

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Wilt et al., 1995 (10)	Level 2 Retrospective chart review, with a control group Anticoagulation monitoring service in an academic-based family practice setting, Florida, USA Single-centre	This study evaluated a pharmacist-managed anticoagulation monitoring service which provided monitoring and education for patients using warfarin who were referred by their physician. Patients attended the service weekly, then fortnightly until their warfarin regimen was stabilised. All stabilised patients were seen 4-6 weekly for laboratory testing (prothrombin times and INRs) and counselling. Outcomes for patients attending the pharmacist service were compared with those using warfarin and receiving usual care from their physician. The length of follow-up varied between patients, therefore statistical comparisons were expressed as event rates (person-years per event)	Level 1 Number of thromboembolic and haemorrhagic events; Unplanned clinic visits, emergency room visits, hospital admissions	The intervention group included 60 person-years of warfarin therapy, the control group included 28 person-years. No major haemorrhagic or thromboembolic events were recorded for the intervention group. Significantly fewer major haemorrhagic events in the intervention group than the control (> 60 person-years per event for intervention group compared to 5.6 person-years per event for the control group). Significantly fewer thromboembolic events (> 60 person-years per event for intervention group compared to 2.8 person-years per event for the control group). The number of minor haemorrhagic events was not significantly different between groups. No events in the intervention group that led to unplanned clinic visits, emergency room visits or hospital admissions. For the control group, however, there were 14 unplanned clinic visits, 11 hospital admissions and 10 emergency room visits. The differences between the groups were statistically significant.
Yanchick, 2000 (12)	Level 2 (Diabetes arm) Cohort comparison group Primary care setting, military hospital, Oklahoma, USA Single-centre	Evaluation of a clinic established to initiate and monitor treatment plans for patients with various chronic diseases. The outcomes for patients with diabetes were reported in with a comparison group (physician-only monitoring). Chart review was conducted to measure patient outcomes over a 1-year period and to compare outcomes with physician-only monitoring before the clinic and during the same period.	Level 2 Glycosylated haemoglobin; Level 3 Completion of laboratory tests and examinations according to American Diabetes Association (ADA) standards	190 patients with diabetes received pharmacist monitoring 185 received physician monitoring. For the physician monitoring group 45% of patients were judged to have met ADA for testing and examinations compared to 99% in the pharmacist monitoring group. During the year the mean glycosylated haemoglobin level was 7.6% for the pharmacist-monitored group compared to 9.05% for the physician-monitored group, however baseline levels were not provided (a value of “less than or equal to 8%” was the target).

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Lee and Schommer, 1996 (11)	Level 2 Prospective, parallel longtitudinal study with matched treatment and control groups (matching on the basis of review of medical records from previous 6-months) Anticoagulation clinic in a University medical center, Ohio, USA Single centre	This study examined whether a pharmacist-managed anticoagulation clinic would reduce the rate of warfarin-related hospital readmissions. Inpatients or outpatients referred to the clinic were given counselling by a pharmacist at the initial visit. Patients were monitored through follow-up telephone calls or clinic visits at an interval determined by the pharmacist.All patients discharged from the hospital who were taking warfarin and referred to the clinic over a 4-month period were included in the intervention group. Outcomes were compared with a control group randomly selected from a list of patients discharged from the same hospital, taking warfarin, but who were not referred to the clinic. Patients were followed for 90 days after discharge to assess outcomes.	Level 1 Warfarin-related hospital readmissions including emergency room visits	There were 68 clinic (intervention) patients and 68 controls. Patients from the 2 groups were matched for relevant medical history and indication for warfarin use, resulting in 31 matched pairs. The matching process resulted in the exclusion of patients who had experienced warfarin-related bleeding or a warfarin-related hospital admission in the 6 months before the study. Significantly fewer patients in the intervention group experienced a warfarin-related hospital readmission during the 90-day study period. Ten of the 31 control patients (32%) had a total of 15 warfarin-related readmissions, while 3 of the intervention group (10%) had one readmission each.

Table 4. Level 2 studies assessing medication review services in the aged-care setting

Reference	Study design, setting	Subjects, intervention, follow-up period	Study outcomes	Results
Quality of Medication Care Group, 1999 (13)	Level 2 Non-randomised. Controlled Nursing Homes, Australia	This study was a National Evaluation of Medication Review Services in Australian Nursing Homes was undertaken to examine the effectiveness and outcomes of the government-funded medication review service in its first year of operation. Accredited pharmacists provided medication review services to high level care residential aged care facilities. Outcomes for patients in facilities receiving the medication review service where compared to those in facilities that did not.	Level 1 Mortality rate; Measures of disability, Hospitalisation rate; Transfers to the community; Level 3 Medication use Level 4 Uptake of the service; Opinions of nursing home staff, health professionals servicing the facilities and consumer/resident groups.	No significant difference in outcomes data were reported for facilities with medication review services compared to those without the service, however, there was a trend towards improved outcomes and reduced medication use. It was found that medication use was significantly reduced in those residents whose general practitioner reported having "an effective professional relationship with the accredited pharmacist". Staff involved with the service responded positively and the five consumer organisations and 25 residents/relative groups that responded to the survey all believed that a review of medications was worthwhile. The service was taken up by 1,556 (52%) of all aged-care facilities, the equivalent of 81,760 beds.
Rumble, 1996 (14)	Level 2 Controlled trial, group allocation according to site Aged care hostels, Tasmania, Australia Multi-centre	This project evaluated the effect of consultant pharmacy services that included monthly medication chart reviews for a six-month period, notification of the prescriber if a drug-related problem was detected and provision of education about medications and compliance aids for residents. Residents who received the intervention were randomly selected from two hostels in the Hobart area, while the control group was randomly selected from the three hostels in a different part of the state (Launceston). A nurse consultant blinded to group allocation performed interviews to determine life satisfaction. Assessments were made at baseline and six months	Level 1 Life satisfaction, using the Sickness Impact Profile (SIP) Level 3 Number of medications and the number of doses taken by the residents;	The project included 119 elderly hostel residents from five aged care hostels. Life satisfaction scores (based on data from 41 intervention and 36 control residents who completed both interviews) revealed significant improvements in psychological measures in the intervention group compared with baseline ($p=0.005$ within-group), however, the total SIP score did not change significantly over the course of the study. For the control group there was a significant decline in the total SIP score compared to baseline ($p=0.047$, within group). Statistical tests for between group differences were not reported. There were no significant differences in medication use between groups reported.

Table 5. Level 2 studies assessing pharmacist education services to patients

Reference	Study design, setting	Description of the patients, intervention	Study outcomes	Results
McPherson et al., 2000 (15)	Level 2 Non-randomised, matched control group Clinic of a Veterans' Affairs Medical Center Miami, USA	Assessed a brief medication counselling and behavioral intervention conducted by a pharmacist (PharmD) on adherence to combination antiretroviral medication and prophylactic therapy in HIV-positive men who were assessed as being "non-adherent". Intervention patients were aged 32-67 years and included African-Americans (74%), Hispanics (14%) and non-Hispanic whites (12%). The intervention involved individual meetings between the patient and the pharmacist (20-25 mins) at monthly intervals for 5 months. The pharmacist provided focused counselling including information about the condition, each of the medications, barriers to adherence and self-management of medications. A weekly pill organiser was provided the pharmacist educated the patient on its use. A control group matched for demographic factors, CD4 cell counts and criteria of non-adherence received usual treatment. Outcomes were assessed at baseline and post-intervention.	Level 1 Number of opportunistic infections; Number of hospitalisations (from medical records) Level 3 Level of medication adherence measured as: Number of prescribed medications refilled; Number of missed clinic appointments (from medical records)	There were 21 intervention patients and 21 matched controls. The results do not state the time period over which the baseline and post-intervention data was collected. Mean hospitalisation rate: pre- intervention: 0.76 intervention and 0.76 control post-intervention: 0.33 intervention versus 1.04 control ($p<0.05$) Opportunistic infections: Data not presented, stated that an increased use of medication post-intervention was associated with a lower number of opportunistic infections ($p<0.05$) Medication refill compliance: Pre-intervention: 47% intervention, 54% control Post intervention: 76% intervention ($p<0.01$ compared to pre-intervention), 39% control (p value for between group comparison not given) Clinic appointment compliance: Pre-intervention: 60% intervention, 79% control Post-intervention: 76% intervention ($p<0.05$ compared to pre-intervention), 73% control (p value for between group comparison not given)

Table 6. Level 2 studies assessing pharmacist education services in the aged-care setting

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Eide and Schjot, 2001 (16)	2	Nursing home setting Bergen, Norway	Five nursing homes that had participated in a survey of hypnotic use in 1995 received the intervention. Two further nursing homes acted as the control. The study pharmacist provided written and oral information on the rational use of hypnotics. Meetings with nursing home staff including physicians, nurses and directors involved discussion of the results of the 1995 survey that showed high rates of hypnotic usage in the homes. The pharmacist also met with individual physicians and nurses to discuss use of hypnotics. Control homes received "traditional pharmaceutical care" services from the same pharmacist.	The numbers of patients in the 5 intervention homes were 187, with 79 patients in the two control homes. Baseline data not collected, follow-up unclear.	Level 3 Change in use of hypnotic medications	Comparison between the intervention and control homes for hypnotic use in the year 2000 showed the proportion of patients that used hypnotics was 44% of control and 24% of intervention patients ($p<0.01$). There was also a significantly higher proportion of control patients (10%) than intervention patients (3.7%) using more than one hypnotic ($p<0.05$). A higher proportion of patients in the control home received their hypnotic medication earlier in the evening than recommended (control 63%, intervention 13%, $p<0.01$). These results should be interpreted with caution as pre-intervention baseline results were not measured, thus, the comparability of groups is unclear.

Table 7. Level 2 studies assessing pharmacist education services to physicians in the community setting

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Studies involving individual (one-to-one) education						
Peterson et al., 1997 (17)	2	General practice setting Tasmania, Australia	GPs in the intervention region were mailed educational materials to encourage rational prescribing of antibiotics for the management of acute, uncomplicated UTIs. Two weeks after the mail-out GPs practicing in the intervention region were telephoned to arrange an educational visit by the study pharmacist.	A total of 169 GPs were visited and detailed. Pharmacy dispensing data and Health Insurance Commission dispensing data were compared pre and post-intervention	Level 3 Antibiotic use	Pharmacy dispensing data revealed relative prescribing of the first-line agents was significantly higher in the intervention region after the intervention period ($p< 0.01$). Prescribing of the recommended agents compared to the antibiotics not recommended rose significantly in both regions after the intervention period with the improvement seen in the intervention region being significantly greater than the change for the control region ($p<0.0001$).
Peterson et al., 1996 (18)	2	General practice setting Tasmania, Australia	The GPs in the target region were sent educational materials encouraging the rational prescribing of NSAIDs for rheumatic disorders in elderly patients. An educational visit followed.	A total of 117 GPs received the educational visit. Dispensing data were compared pre and post-intervention	Level 3 NSAIDs and paracetamol use	The ratio of dispensed defined daily doses (DDDs) of NSAIDs : paracetamol declined from 3.00 (pre-intervention) to 2.59 (post-intervention) in the intervention region, while in the control region the decline in the ratio was less (from 3.16 to 2.92). The improvement was significantly greater in the intervention region compared to the control ($p<0.0001$).
Peterson and Sugden, 1995 (19)	2	General practice setting Tasmania, Australia	The GPs in the target region were sent educational materials emphasising the need to adjust allopurinol dosages in accordance with the renal function of the patient. An educational visit followed .	A total of 125 GPs received a visit from the pharmacist. Dispensing data (for 100mg and 300mg allopurinol dosage forms) were analysed pre- and post-intervention	Level 3 Allopurinol use	Allopurinol in the lower dosage (100mg) form dispensed for the intervention region increased from 14.8% pre-intervention to 22.1% post-intervention($p<0.05$). For the control region the change was less, from 13.8% pre-intervention to 16.9% post-intervention ($p>0.20$). The improvement for the intervention area was not significantly greater than that for the control ($p>0.20$).

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Studies involving individual (one-to-one) education (cont.)						
May et al., 1999 (20)	2	Community medical practices Adelaide, South Australia	Participating medical practitioners were visited twice (approximately 6-8 wks apart) by an experienced clinical pharmacist. The medical practitioner also received printed written materials as a source of unbiased information about NSAIDs. The written materials were prepared by the clinical pharmacists and externally reviewed. The educational information was tailored to suit the individual practitioner.	Of the 236 medical practitioners in the intervention area, 210 (89%) received an initial educational visit and 202 (86%) received the second visit. Outcome data was compared before and after the educational program in the intervention and comparison areas.	Level 1 Hospital admissions for upper gastrointestinal ulceration or perforation events with or without bleeding NSAID use	Between 1986 and 1992, before the educational service was started, there an increase in hospitalisation rates for people living in the intervention area with a principal diagnosis of upper GI ulceration or perforation from an estimated 0.10 to 0.20 per 1000 population. After the visits began in 1992 there was a gradual decrease to 0.06 per 1000 population by 1997. In the comparison area there were no notable changes in the 11-year observation period. An approximate 95% confidence interval for the change point in the intervention area included the period of the educational visits. During the 5 years since the program began, relative to the comparison area, aggregate reductions of 9% (in PBS NSAID dispensing) and 28% (in unit sales to pharmacies) were seen.
Atkin et al., 1996 (21)	2	Sydney, NSW, Australia	Patients were 60 years or older, taking prescribed medication and home-dwelling. The education intervention was provided to GPs of the enrolled patients by a trained pharmacist academic detailer. Printed promotional-style educational materials were also produced. Educational messages concerned the importance of reducing overall medication use through rational drug review. Follow-up detailing was carried out.	39 control prescribers (treating 77 patients) and 51 intervention prescribers (treating 131 patients). Follow-up at 4, 8 and 12 months after initial contact.	Level 3 Relative reduction in prescribing	There were no significant differences between the control and intervention groups in the number of medications prescribed at any of the study time periods (p=0.19). There were also no-significant differences when medications for the treatment of chronic conditions were analysed separately (p=0.21).

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Studies involving group education						
Farris et al., 1996 (22)	2	Family practice clinics Michigan , USA	The intervention program targeted oral antihistamines and antibiotics. It included market research techniques, peer comparison prescribing feedback, the use of a physician opinion leader, printed materials. Face-to face group detailing sessions were conducted for prescribing physicians and nurse practitioners. Detailers were academic pharmacists with clinical pharmacy training.	Two family practices (one urban, one rural; 41 HMO physicians) intervention. Comparison groups were i) seven clinics in the same geographical area ii) all other HMO clinics claims data were compared between two consecutive 3-month periods post intervention and from the same period the previous year.	Antihistamine and antibiotic prescribing	For the intervention group there was a small reduction in the prescribing of the non-sedating antihistamines (terfenadine and astemizole) compared to the previous year in both study periods. There was a reduction of 2.1% and 3.2% in study periods 1 and 2, respectively. Within each of the two comparison groups there was an increase in the rate of prescribing of the non-sedating antihistamines compared to the previous year in both study periods. For the 7 other HMO practices in the same area there was a 17.1% and 7.3% increase in prescriptions for the two antihistamines in study periods 1 and 2, respectively. The group of other HMO physicians had increases of 17.9% and 5.0% in study periods 1 and 2, respectively. (Statistical analyses for differences between groups were not reported) The ratio for limited spectrum : total antibiotics improved in the intervention group in both study periods (reflecting an increase in the prescribing of limited spectrum agents) compared to the same period the previous year. The increases were 2.6% and 13.6% in study periods 1 and 2, respectively. The ratio also improved in the comparison group containing the 7 other HMO practices in the same area, the increase in the second period was lower then that for the intervention group (statistical significance not reported, 5.4% and 1.4% increases for periods 1 and 2, respectively). In the second comparison group (remainder of HMO physicians) the ratios decreased (worsened) by 9.5% and 3.2% in periods 1 and 2, respectively.

Reference	Level	Setting	Intervention	Evaluable sample	Study outcomes	Results
Studies involving group or one-to-one education						
Alvarez et al., 2001 (23)	2	General practice setting, outer Melbourne, Victoria, Australia	Assessed educational outreach provided by a hospital pharmacist to GPs as part of a Coordinated Care Trial. The intervention was provided to 40 GPs who accepted an invitation to receive the service. The pharmacist trained in academic detailing carried out either one-to-one visits (27 GPs) or small group visits (4 visits provided to 13 GPs). The topics discussed were *Helicobacter pylori* eradication and NSAID use. Peer-reviewed printed educational materials were also given to GPs at the educational visits.	Prescribing patterns were compared for the 3 months before and after the visits and compared to control group of 40 GPs	Level 3 Changes in prescribing of NSAIDs (measured as number of prescriptions and number of patients who had a prescription written)	Small numbers of prescriptions and patients limited the findings of the study. In the intervention group of GPs (n=40) there was a decrease in the number of NSAID prescriptions from 35 pre-intervention to 16 post-intervention, while the numbers increased for the control groups from 11 to 14. There were 18 patients of the intervention GPs who had a prescription written for an NSAID pre-intervention compared to 13 post-intervention. For the control GPs, 6 patients received an NSAID prescription pre-intervention compared to 7 post-intervention.
Studies comparing one-to-one and group education						
Hartlaub et al., 1993 (24)	2	Primary care group practice setting Colorado, USA	Targeted benzodiazepine prescribing for elderly (65 years or older) patients. The one-to-one educational intervention involved provision of written educational materials, a face-to-face educational visit (approx. 10-12 min) by a staff clinical pharmacist prescribing feedback, assistance with difficult cases, and a second follow-up visit by the pharmacist. The group educational intervention proved the same educational materials and an educational visit by a specialist drug information pharmacist.	Patients (all elderly members of the group practice) were monitored from 6 months before the intervention until 6 months after its completion.	Level 3 benzodiazepine prescriptions	There were no significant differences in benzodiazepine on-off status between groups when pre-intervention status, patient age, gender and or gender-by-preintervention status interactions were controlled. There was no significant effect from either intervention on the median dosage difference for benzodiazepines.

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Appendix III

Table 1. Studies which included economic data but have not been excluded from the economic analysis

Pharmaceutical care services
Three studies were excluded because there were non-randomised studies (1-3). In addition, one study had unbalanced groups and the results were impossible to interpret (1); one study included 15 patients only (2); in one study, there was no control group and the economic analysis was based on estimations of cost savings rather than on observational data (4).
Discharge liaison services
None
Pharmacist-run clinics
One study was excluded because it was a non-randomised study (5)
Pharmacist review of repeat prescribing
None
Medication review services
Two studies were excluded because there were non-randomised (6, 7). Moreover, all these studies failed to demonstrate statistically significant outcomes.
Patient education
None
Educational services
One study was excluded as drug costs were only used as a mean to calculate a "Prescribing index" (8).
Drug information services
One economic study was located that developed a model to determine potential cost savings that resulted from a drug information service (9). However, it was an uncontrolled study with several severe shortcomings.
Smoking cessation services
One study (10) assessing cost-effectiveness was located. However, it utilises the study by Smith et al., 1995 (11) to determine quit rates for the effectiveness of NRT plus pharmacists' smoking-cessation counseling. The study by Smith et al. was uncontrolled and excluded from the review for that reason.
A cost-effectiveness evaluation of the intervention by Sinclair et al.,1998. (12) has been reported (13). It was excluded from inclusion in this review, because of the failure of the primary study to demonstrate statistically significant outcomes.
Immunisation
None
Pharmacist-only medicines and over-the-counter medicines
None
Therapeutic decision making
None
Other
None

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