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Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns (Review)

Nkansah N, Mostovetsky O, Yu C, Chheng T, Beney J, Bond CM, Bero L

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TABLE OF CONTENTS

[Intervention Review]

Effect of outpatient pharmacists' non-dispensing roles on patient outcomes and prescribing patterns

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ABSTRACT

Background

The roles of pharmacists in patient care have expanded from the traditional tasks of dispensing medications and providing basic medication counseling to working with other health professionals and the public. Multiple reviews have evaluated the impact of pharmacist-provided patient care on health-related outcomes. Prior reviews have primarily focused on in-patient settings. This systematic review focuses on services provided by outpatient pharmacists in community or ambulatory care settings. This is an update of the Cochrane review published in 2000.

Objectives

To examine the effect of outpatient pharmacists' non-dispensing roles on patient and health professional outcomes.

Search methods

This review has been split into two phases. For Phase I, we searched the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register (January 1966 through March 2007). For Phase II, we searched MEDLINE/EMBASE (January 1966 through March 2008). The Phase I results are reported in this review; Phase II will be summarized in the next update.

Selection criteria

Randomized controlled trials comparing 1. Pharmacist services targeted at patients versus services delivered by other health professionals; 2. Pharmacist services targeted at patients versus the delivery of no comparable service; 3. Pharmacist services targeted at health professionals versus services delivered by other health professionals; 4. Pharmacist services targeted at health professionals versus the delivery of no comparable service.

Data collection and analysis

Two authors independently reviewed studies for inclusion, extracted data, and assessed risk of bias of included studies.

Main results

Forty-three studies were included; 36 studies were pharmacist interventions targeting patients and seven studies were pharmacist interventions targeting health professionals. For comparison 1, the only included study showed a significant improvement in systolic blood

pressure for patients receiving medication management from a pharmacist compared to usual care from a physician. For comparison 2, in the five studies evaluating process of care outcomes, pharmacist services reduced the incidence of therapeutic duplication and decreased the total number of medications prescribed. Twenty-nine of 36 studies reported clinical and humanistic outcomes. Pharmacist interventions resulted in improvement in most clinical outcomes, although these improvements were not always statistically significant. Eight studies reported patient quality of life outcomes; three studies showed improvement in at least three subdomains. For comparison 3, no studies were identified meeting the inclusion criteria. For comparison 4, two of seven studies demonstrated a clear statistically significant improvement in prescribing patterns.

Authors' conclusions

Only one included study compared pharmacist services with other health professional services, hence we are unable to draw conclusions regarding comparisons 1 and 3. Most included studies supported the role of pharmacists in medication/therapeutic management, patient counseling, and providing health professional education with the goal of improving patient process of care and clinical outcomes, and of educational outreach visits on physician prescribing patterns. There was great heterogeneity in the types of outcomes measured across all studies. Therefore a standardized approach to measure and report clinical, humanistic, and process outcomes for future randomized controlled studies evaluating the impact of outpatient pharmacists is needed. Heterogeneity in study comparison groups, outcomes, and measures makes it challenging to make generalised statements regarding the impact of pharmacists in specific settings, disease states, and patient populations.

PLAIN LANGUAGE SUMMARY

Non-traditional roles of outpatient pharmacists.

The role of pharmacists in the community includes more than dispensing medications. It involves identifying, preventing, and resolving drug-related problems, as well as encouraging proper use of medications and general health promotion and education.

This review found forty-three studies which evaluated non-traditional roles of pharmacists. In general, the data included in this review supported the roles of pharmacists in patient counseling, therapeutic management, and providing health professional education with the goal of improving patient process of care and clinical outcomes. Non-traditional roles of outpatient pharmacists improves health care outcomes. The data show that educational outreach visits may impact physician prescribing patterns.

BACKGROUND

In the past three decades, the roles of pharmacists in patient care have expanded from the traditional tasks of dispensing medications to working with other health professionals and the public. Multiple systematic reviews and meta-analyses have evaluated the impact of pharmacist-provided patient care on health-related outcomes (Machado 2007a; Machado 2007b). It is important to conduct systematic reviews in this area because both the results and quality of the original studies vary. Thus, a rigorous review enables us to assess the best available evidence on the effects of pharmacist interventions.

The systematic reviews conducted thus far have focused on care rendered in specific practice settings (for example, ambulatory care, community pharmacy, acute care, long-term/intermediate care) (Beney 2000; Blenkinsopp 2003; Christensen 2006; Horn 2006; Kaboli 2006; Kane 2003; Royal 2006; Singhal 1999; Tully 2000; Van Wijk 2005; Westerlund 2006), to specific patient populations (for example, geriatric, pediatric) (Hanlon 2004; Holland 2008; Rollason 2003; Sanghera 2006; van Eijken 2003), and in specified therapeutic areas (for example, anticoagulation, antibiotic utilization, asthma, diabetes, depression, heart failure, hypertension, immunizations, mental health, Parkinson's disease, tobacco cessation) (Dent 2007; Donovan 2006; Finley 2003; Hogue 2006; Holland 2005; Jenkins 1996; Lindenmeyer 2006; Machado 2007a; Machado 2007b; Manley 2002; McLean 2005; Ponniah 2007; Simonson 2007; von Gunten 2007). A few reviews have been conducted to evaluate the impact of pharmacist-provided care on specific health outcome criteria (for example, humanistic) (Pickard 1999; Pickard 2006; Schumock 1996; Schumock 2003). Although there is some overlap in the focus of previous reviews, there are also gaps in the types of interventions assessed (for example, pharmacist-care provided to socio-economically, ethnically, or linguistically diverse patient populations or patients with low health literacy). To our knowledge, there are no comprehensive systematic reviews thoroughly evaluating randomized controlled trials studying the impact of pharmacist-provided care in outpatient practice settings.

Because the impact of pharmacist-provided services in the hospital setting has been well-studied, this systematic review focused on services provided by outpatient pharmacists in community or ambulatory care settings. This review encompassed all outpatient pharmacist services targeted toward patients and health professionals, as well as all types of clinical disease states and health care process measures. This was an update to the previous Cochrane systematic review (Beney 2000) that incorporated the studies that have been published since 2000 as well as studies not included in the original review.

OBJECTIVES

The objective of this review was to examine the effect of outpatient pharmacists' roles on patient and health professional outcomes. Relevant health professional outcomes or healthcare practice measures included changes in prescribing patterns (for example, appropriateness of or prescribing, therapeutic duplication) and disease control (for example, disease-specific test ordering). Relevant patient outcomes included changes in clinical disease markers (for example, blood pressure) and humanistic quality of life outcomes.

We examined the following main hypotheses:

1. Does the delivery of patient-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of the same services by other health professionals?

2. Does the delivery of patient-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of no comparable services?

3. Does the delivery of health professional-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of the same services by other health professionals?

4. Does the delivery of health professional-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of no comparable services?

To test the above hypotheses, we examined the following comparisons.

1. Pharmacist services targeted at patients versus services delivered by other health professionals.

2. Pharmacist services targeted at patients versus the delivery of no comparable services.

3. Pharmacist services targeted at health professionals versus services delivered by other health professionals.

4. Pharmacist services targeted at health professionals versus the delivery of no comparable services.

METHODS

Criteria for considering studies for this review

Types of studies

Study designs that meet Effective Practice and Organization of Care Group (EPOC) inclusion criteria are randomized controlled trial (RCT), controlled clinical trial (CCT), controlled before and after study (CBA) and interrupted time series (ITS). In this area of research, it has historically been challenging to identify a substantial number of RCTs in the literature. In the original review and 2000 update, all study designs mentioned above were included. Due to the substantial increase in the number of published RCTs studying the effect of pharmacists' interventions on patient and health professional outcomes, we limited the current update to RCT study designs.

We included

RCTs randomizing:
patients;
pharmacists;
practices (pharmacies or medical clinics); or
geographical areas.

Types of participants

The participants for all comparative studies we included in this review were pharmacists (or pharmacies) who deliver services in outpatient settings other than, or in addition to, drug compounding and dispensing. We excluded studies involving services to patients in hospitals or skilled nursing facilities. We included studies of

pharmacists delivering services to outpatients in a clinic attached to a hospital or a day hospital.

Types of interventions

The types of interventions we included were any services delivered by pharmacists other than drug compounding and dispensing. When available we collected additional data on the content of each intervention including recipients, format, source, timing, setting, and cost.

Types of outcome measures

We included studies only if 1) reported primary outcomes were objective with respect to measurement of health care process measures or patient outcomes and 2) relevant and interpretable data were presented. We therefore excluded subjective outcomes (for example, self-reporting of symptoms, medication knowledge, satisfaction with pharmacist services) or outcomes for which reporting was incomplete (for example no numerical values reported, no baseline data provided). To minimize reporting bias, we excluded outcomes that were not primary. For studies that did not explicitly report which outcomes were primary, we included all objective and relevant outcomes.

We excluded adherence outcomes because there is another Cochrane review that assessed interventions to improve adherence (Haynes 2008). We also excluded resource-utilization and cost outcomes because these endpoints were recently assessed in another systematic review (Perez 2009).

Search methods for identification of studies

When the original review was performed, there were few randomized controlled trials evaluating non-dispensing roles of outpatient pharmacists. Studies were identified by electronically searching the EPOC Specialised Register, MEDLINE, EMBASE, PHARMLINE and International Pharmaceutical Abstracts from January 1,1966 through December, 1995. Professional librarians were consulted to advise on a broad search strategy for each database. In MEDLINE, broad searches using the MeSH headings 'pharmacy' and 'pharmacist' and each of the following publication types 'randomized controlled trial', 'controlled clinical trial', 'comparative study', 'follow up study', 'prospective study', and 'evaluation study' were performed.

The following journals were hand searched: *American Journal of Hospital Pharmacy* (1985 through 1995), *International Journal of Pharmacy Practice Research* (1987 through 1995), *Journal of Social and Administrative Pharmacy* (1987 through 1995), *Scanner* (a pharmacy abstract journal) (1987 through1995), and *The Pharmaceutical Journal* (1960 through1997). *The Pharmacy Practice Research Literature Index* (1984 through1994) compiled by Peter Abel and published by the UK Pharmacy Practice Research Resource Centre, University of Manchester, England, was also searched.

The reference lists of trials identified for the review, as well as other review articles on the extended roles of pharmacists, were checked. Non-English language publications, if found, were to be included in the review.

An attempt was made to identify unpublished studies and works in progress by searching, for 1990 through 1995, the published abstracts of the annual meetings of the American Society of Hospital Pharmacists, Health Service and Pharmacy Practice Research Conference (UK), Pharmacy Practice Research Sessions of the Royal Pharmaceutical Society of Great Britain Annual Conference, and proceedings of the UK Clinical Research Association.

For the 2000 update, relevant studies were located by searching the EPOC Specialised Register, electronically searching MEDLINE, and ongoing handsearching of the *International Journal of Pharmacy Practice Research* and *The Pharmaceutical Journal*.

Given the significant increase in publications in this area over the past several years, we split the search for this update. We will complete this update in two phases. Phase I (the current update) consists of studies identified in prior versions of this review and studies identified in the EPOC Specialised Register search (January 1966 through March 2007). Phase II (in progress) will include studies identified in prior versions of this review, the Phase I update, and studies identified through a MEDLINE and EMBASE (January 1966 through March 2008) search. Specific search criteria are included in Appendices.

Data collection and analysis

Selection of studies

Two review authors independently selected the trials to be included in the review. We resolved disagreements by discussion of the articles by at least two of the authors of the review.

Data extraction and management

We collected data using the EPOC Data Extraction Checklist. To streamline the data collection process, we built an online database on the Quesgen platform using the Data Extraction Checklist questionnaire. Two review authors independently extracted data for each study with a focus on outcomes and characteristics aimed at reducing bias. We discussed and reconciled differences in coding.

Assessment of risk of bias in included studies

Two review authors independently assessed the risk of bias of all studies eligible for the review using the EPOC Data Extraction Checklist. We adjudicated discrepancies by discussion of the studies. We assessed allocation concealment, blinding, follow-up of patients or health professionals (when applicable), baseline measurement, reliability of outcome measures, and protection against contamination. For included studies, the risk of bias characteristics are described in the Characteristics of included studies table. We identified studies with unit of analysis errors. No pooled data included unit of analysis errors.

Measures of treatment effect

We reported results for baseline (pre-intervention) and end-of-study (post-intervention) periods if available (see 'Outcomes Table' under Data and analyses). Where possible, we calculated pre-post intervention differences for each outcome for control and intervention groups, and the difference of pre-post intervention change between study groups (result interval). In all cases, we reported a more favorable outcome in the intervention group as a positive finding (that is where changes from baseline are in the intended direction) and vice versa as a negative finding. For quality of life outcomes, we did not report raw data for each quality of life domain; instead we listed each domain measured under the

'primary outcomes' column in the 'Outcomes Table' (under Data and analyses) and indicated in the 'significance' column which domains were significantly improved in intervention versus control groups during the course of the study. All outcomes included in this review are listed under the Characteristics of included studies and Data and analyses tables.

Assessment of heterogeneity

Among the included studies, there was great heterogeneity in comparison groups, intervention type, outcomes assessed, duration of intervention, length of follow-up, and measurement used for outcomes.

We attempted to perform a meta-analysis by subgrouping studies based on clinical disease state and outcome type. Unfortunately, there were insufficient data across the 43 included trials to perform subgroup analyses on all disease states.

There was a high degree of heterogeneity in the types of outcomes measured for each disease state. For example, in the four studies assessing disease control in patients with depression, one study used Brief Inventory of Depressive Symptoms (BIDs), Beck Depression Inventory (BDI), and Work and Social Disability Scale (WSDS) (Finley 2003), one study used BDI (Rickles 2005) and two studies used the self-rating Hopkins Symptom Checklist (SCL) (Brook 2003b; Capoccia 2004). Due to the different outcome measures and measurement units, we were unable to pool these outcomes into one analysis. The same issue was present in studies targeting patients with asthma, chronic obstructive pulmonary disease (COPD), heart failure, hyperlipidemia and anticoagulation therapy. In these cases, we were unable to perform a meta-analysis due to the reasons described above, as well as the small number of studies performed with these disease states. We present data separately for each of these studies.

Subgroup analysis and investigation of heterogeneity

For studies measuring blood pressure and glycosylated hemoglobin (HbA1C), we collected enough data points to potentially perform a pooled analysis. Although these groups of studies were comparable in terms of disease state studied and outcomes assessed, there was variability in intervention type and length of follow-up. To minimize heterogeneity in these pooled analyses, we included in the meta-analysis only studies with similar disease state, intervention type, and length of study.

Performing a pooled analysis for continuous outcomes requires pre- and post- means and standard deviations for outcome measures for both control and intervention groups. Reporting of standard deviations was incomplete; only three of the seven studies measuring systolic and diastolic blood pressures and one of the five studies measuring HbA1C reported standard deviations.

We considered two methods to yield a standard deviation for data pooling purposes: 1) calculating a standard deviation from a P value and 2) imputation (using the standard deviation reported in other studies included in the analysis). Standard deviations derived from P values resulted in a high degree of study heterogeneity ($I^2 > 80\%$). Imputation had the least effect on study heterogeneity ($I^2 = 0$). Given these observations, we chose the imputation method.

RESULTS

Description of studies

The prior update to this review (Beney 2000) identified 25 studies that met inclusion criteria. Six of the 25 included studies were pre-post designs, controlled by a separate site (Cody 1998; Lai 1998; Peterson 1995; Peterson 1997; Schaffner 1983; Tamai 1987), two were quasi randomized controlled trials (Erickson 1997; McKenney 1973), and the remainder were randomized controlled trials.

In Phase I of this update, we identified 107 publications that met our search criteria. Of these, 64 were excluded from the final analysis (see Characteristics of excluded studies and Excluded studies). All included studies were randomized controlled trials. One study was a before-and-after pragmatic randomized controlled trial (Hall 2001).

Characteristics of interventions

For study details see the Characteristics of included studies table.

Of the 43 included studies, seven studied pharmacist interventions targeted at health professionals (Diwan 1995; Freemantle 2002; Hall 2001; Ilett 2000; Stergachis 1987; Turner 2000; Watson 2001) and 36 reported on pharmacist interventions targeted at patients. In 11 of the 36 studies targeted at patients, the pharmacist intervention also targeted health professionals (Borenstein 2003; Choe 2005; Gattis 1999; Hanlon 1996; Jackson 2004; Mehos 2000; Sadik 2005; Schneider 1982; Sookaneknun 2004; Taylor 2003; Tsuyuki 2002). In most of these studies, pharmacists provided: a) oral or written recommendations to physicians regarding therapy modifications or resolution of medication-related problems and b) multiple follow-up visits with patients spanning several months (range: 1 month to 12 months). All but one of the included studies compared pharmacist services targeted at patients or health professionals versus provision of no comparable services (or usual care). One study (Hawkins 1979) compared pharmacist services with services provided by other health professionals. Eight of the 43 studies were randomized by clinical practice or region, with the remainder randomizing by individual patient or health professional.

In all seven studies targeted at health professionals, pharmacists conducted educational outreach visits at physician practices to promote guideline-based prescribing for certain medication classes including antibiotics (Ilett 2000) and nonsteroidal anti-inflammatory drugs (NSAIDs) (Freemantle 2002; Stergachis 1987; Watson 2001), and for certain disease states including *Helicobacter pylori* infection (Hall 2001), heart failure (Freemantle 2002; Turner 2000), and cardiovascular disease (Diwan 1995). Overall, pharmacists conducted one or two visits lasting 10 to 15 minutes within a study period ranging from 3 months to 24 months. Educational outreach visits are the focus of a Cochrane review (O'Brien 2007). This review evaluated all but two (Stergachis 1987; Turner 2000) of the seven studies identified above.

In 8 of 36 studies targeted at patients, the main focus of the pharmacist intervention was patient education (Barbanel 2003; Brook 2003a; Gonzalez-Martin 2003; Goodyer 1995; Paulos 2005; Rickles 2005; Sarkadi 2004; Van Veldhuizen 1995). One study evaluated the effect of home blood pressure monitoring on blood pressure control with the pharmacist providing telephone follow-up to assess blood pressures and response to therapy (Mehos 2000). In the rest of the patient-targeted

studies, pharmacist interventions were complex and commonly involved pharmaceutical therapy management consisting of pharmaceutical therapy optimization, monitoring of disease control and adverse drug reactions, identification of drug-drug interactions, compliance assessment, and patient education. Twenty-two studies took place in outpatient medical clinics, ten studies took place in community pharmacies (Barbanel 2003; Brook 2003a; Cody 1998; Park 1996; Paulos 2005; Rickles 2005; Sarkadi 2004; Sookaneknun 2004; Tsuyuki 2002; Weinberger 2002), one study took place at a home care agency (Meredith 2002), and two studies involved hospital pharmacists following recently discharged patients at home (Jackson 2004; Peterson 2004). The duration of the intervention ranged from 14 to 120 minutes with 1 to 22 intervention events conducted over the study period of 6 weeks to 23 months. Post-intervention follow-up was performed in two trials to assess duration of intervention effect after the studies were completed (Odegard 2005; Sarkadi 2004).

In most patient-targeted studies, controls were 'usual care' groups in which patients continued to receive standard care from primary care health professionals; the usual care differed from the service provided by the pharmacist to the intervention group. In three of the seven studies targeting health professionals, control groups received no intervention (Diwan 1995; Ilett 2000; Turner 2000). In two of the other health professional-targeted studies, control groups received a non-pharmacist intervention. In one study, the control group received a non-targeted intervention (Freemantle 2002), and in the other study, the control group received mailed practice guidelines, but not the educational outreach visit by the pharmacist (Hall 2001). Two studies had more than one control group (Watson 2001; Weinberger 2002). In the first study, which targeted health professionals to study the effect of an intervention composed of mailed practice guidelines and education outreach visits by the pharmacist, the first control group received no intervention while the second control group received mailed practice guidelines (Watson 2001). In the second trial, which targeted patients with asthma and COPD, the first control group received usual care while the second control group received home peak flow monitors but not follow-up by the pharmacist (Weinberger 2002).

Characteristics of health professionals delivering the intervention

In all studies, interventions were performed by either practicing pharmacists, pharmacy residents, or doctor of pharmacy students. In most studies, 1 to 4 pharmacists performed the intervention, but some studies involved more than 10 pharmacists across multiple practices (Bond 2000; Brook 2003b; Diwan 1995; Freemantle 2002; Malone 2001; Rickles 2005).

Target population

In six of seven studies targeted at health professionals, participants were selected based on location. Two studies selected participants from general practices within one or more health authorities (Freemantle 2002; Hall 2001) and four studies selected participants within a specific region (Diwan 1995; Ilett 2000; Stergachis 1987; Turner 2000). In one of seven studies, participating practices were selected based on their use of a specific computer system (Watson 2001).

Of the 36 studies targeting patients, 27 studies selected participants based on the clinical disease state; some studies included patients from more than one disease state. The following clinical disease states were represented across the included studies: asthma (Barbanel 2003; Gonzalez-Martin 2003; Weinberger 2002), COPD (Solomon 1998; Weinberger 2002), depression (Brook 2003a; Capoccia 2004; Finley 2003, Rickles 2005), diabetes (Choe 2005; Clifford 2005; Hawkins 1979; Jaber 1996; Odegard 2005; Sarkadi 2004; Van Veldhuizen 1995), heart failure (Gattis 1999; Goodyer 1995), hyperlipidemia (Bogden 1997; Paulos 2005; Peterson 2004; Tsuyuki 2002) and hypertension (Borenstein 2003; Hawkins 1979; Mehos 2000; Okamoto 2001; Park 1996; Schneider 1982; Solomon 1998; Sookaneknun 2004). Additionally, five studies selected participants based on characteristics other than the clinical disease state; these studies focused on patients with high risk of medication related problems (Malone 2001; Taylor 2003), home care patients (Meredith 2002), patients with repeat prescriptions (Bond 2000), and patients on warfarin therapy (Jackson 2004).

The number of participants ranged from 21 to 6000 patients and 17 to 112 health professionals. Nine studies included fewer than 50 participants, 14 studies had between 50 and 100 participants, 12 studies had between 101 and 500 participants and eight studies had more than 500 participants. One study targeted pediatric patients (Gonzalez-Martin 2003) and the rest of the studies targeted adults, with nine studies focusing on elderly patients 65 years of age and older.

Risk of bias in included studies

Characteristics aimed at reducing bias are listed in the 'risk of bias' table under each study table in the Characteristics of included studies section. See Figure 1 and Figure 2 for graphic representations of the data presented below.

Figure 1. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

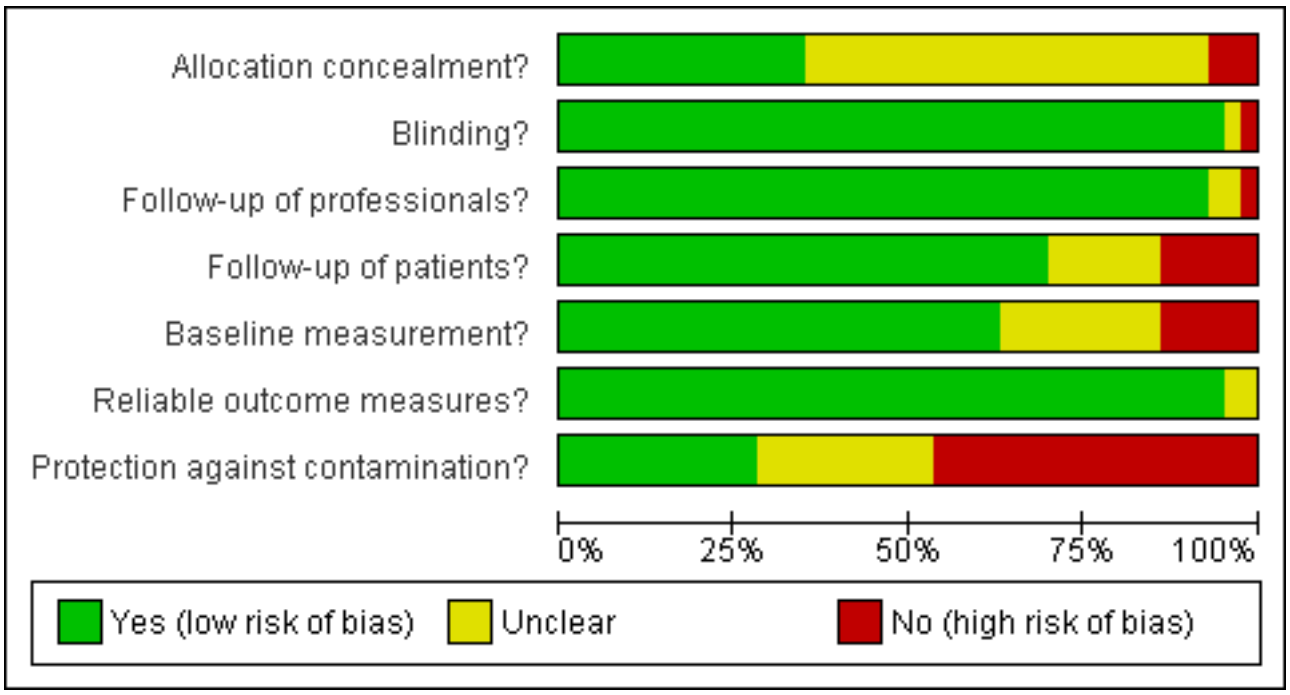


Figure 2. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

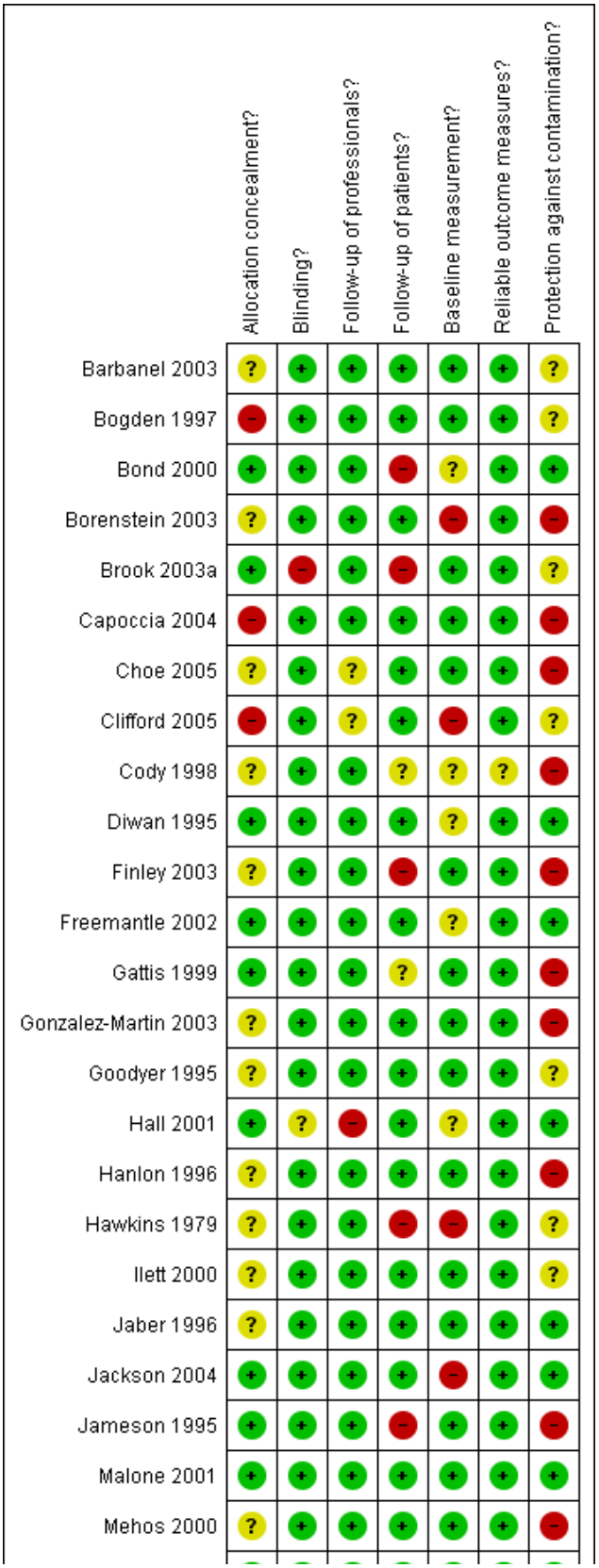
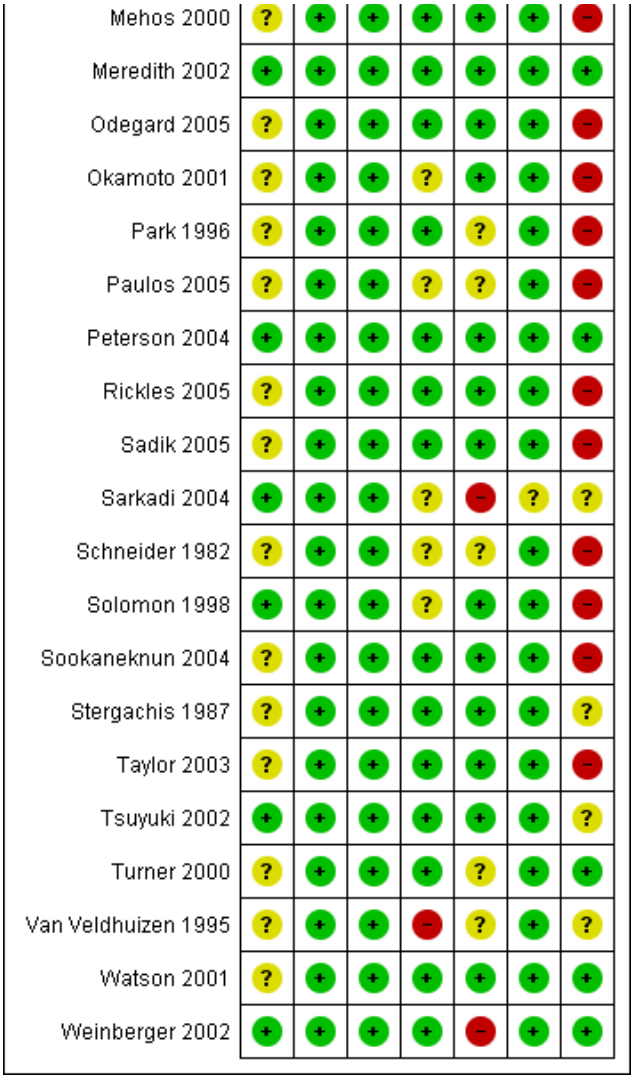


Figure 2. (Continued)



There were no major differences in the risk of bias of studies targeted at patients versus studies targeted at health professionals. Three of 43 studies had no risk of bias (Malone 2001; Meredith 2002; Peterson 2004). Only 15 of 43 studies adequately concealed allocation. Adequate follow-up of patients or health professionals (depending on target subject of study) was done in 27 of 43 studies. Baseline measures of primary outcomes were performed and were similar between intervention versus control groups in 27 of 43 studies, and protection against contamination was adequate in 12 of 43 studies. Because we only included objective primary outcomes in our review, most studies (41) were coded as having reliable outcomes and blinded assessment of outcomes.

Four studies had a unit of analysis mismatch. Of the four studies, three did not correct for clustering in the study analyses (Freemantle 2002; Turner 2000; Weinberger 2002). In two of these studies, the unit of allocation was practice while the unit of analysis was patient (Turner 2000; Weinberger 2002) and in the third study, unit of allocation was health authority while unit of analysis was practice (Freemantle 2002). One study corrected for clustering in the analysis (Bond 2000).

Effects of interventions

All included outcomes are listed under the Characteristics of included studies and Data and analyses sections.

Comparison 1. Pharmacist services targeted at patients versus services delivered by other health professionals

For detailed descriptions of outcomes see Analysis 1.1.

One study evaluating the effect of pharmacist directed medication management versus physician medication management showed a small, but statistically significant increase in systolic blood pressure in the intervention group (-2mmHg in intervention group versus 2mmHg in control group). No statistically significant difference was noted in diastolic blood pressure and blood glucose levels (Hawkins 1979).

Comparison 2. Pharmacist services targeted at patients versus the delivery of no comparable service

For detailed descriptions of outcomes see Analysis 2.1, Analysis 2.2, Analysis 2.3, Analysis 2.4.

Five of the 36 studies targeting patients reported process of care outcomes (Bond 2000; Jameson 1995; Meredith 2002; Taylor 2003; Tsuyuki 2002). These studies measured the effect of pharmacist interventions on prescribing, with one study showing improvement in eliminating therapeutic duplication (Meredith 2002), three studies showing a decrease in the total number of medications prescribed (Bond 2000; Jameson 1995; Taylor 2003), and one study showing an improvement in testing and statin prescribing for patients with hyperlipidemia (Tsuyuki 2002). Despite showing improvement in therapeutic duplication, Meredith et al were unable to demonstrate improvement for overall, cardiovascular, NSAID and psychotropic medication use.

Twenty-nine of the 36 studies targeting patients reported clinical and humanistic patient outcomes (including one study which reported process of care outcomes mentioned above (Taylor 2003)). Pharmacist interventions resulted in improvement in most clinical outcomes, although these improvements were not always statistically significant. A meta-analysis was performed on studies with similar disease state, outcome, type of pharmacist intervention, duration of intervention, and length of follow-up. Hypertension and diabetes were the only disease states with a sufficient number of studies of comparable design; thus meta-analyses were performed only on studies evaluating these disease states.

Seven studies demonstrated improvement in systolic blood pressure ranging from 3.8 mmHg to 12.3 mmHg (Borenstein 2003; Mehos 2000; Okamoto 2001; Park 1996; Schneider 1982; Solomon 1998; Sookaneknun 2004), with two of these studies showing an increase in the proportion of patients controlled for blood pressure (Borenstein 2003; Sookaneknun 2004). Four of the seven hypertension studies (Mehos 2000; Okamoto 2001; Solomon 1998; Sookaneknun 2004) were included in a meta-analysis; these studies yielded an effect size of -6.32 mmHg (95% confidence interval (CI) -8.8 to -3.83) for systolic blood pressure and -3.12 (95% CI -4.57 to -1.67) for diastolic blood pressure ($P < 0.001$ for both measures).

Seven studies targeted diabetic patients (Choe 2005; Clifford 2005; Hawkins 1979; Jaber 1996; Odegard 2005; Sarkadi 2004; Van Veldhuizen 1995). Three of the five studies that assessed HbA1c demonstrated significant improvements in HbA1C between 0.5% and 2.1% (Choe 2005; Clifford 2005; Jaber 1996). Two of the three studies that assessed blood glucose levels demonstrated improvements in blood glucose between 7 mg/dL and 15 mg/dL compared to control (Jaber 1996; Van Veldhuizen 1995). Two comparable studies were included in a meta-analysis (Choe 2005; Clifford 2005); these studies yielded an effect size of -0.75% for HbA1c ($P = 0.03$; 95% CI -1.41 to -0.09) .

Three trials (Bogden 1997; Paulos 2005; Peterson 2004) targeting patients with hyperlipidemia demonstrated reductions in total cholesterol (-15.47 mg/dl to -37 mg/dl), triglyceride levels (-50.5 mg/dl), and the proportion of patients with decreased cholesterol and triglyceride levels. It was not clear, however, whether these findings were statistically significant in two of the three studies (Paulos 2005; Peterson 2004). The improvement in total cholesterol was significant in women in one study (Bogden 1997). In three studies evaluating heart failure patients, pharmacist interventions were effective in decreasing all-cause mortality (odds ratio = 0.22, $P < 0.05$) (Gattis 1999), increasing mean distance walked in a two-minute test (16.1 meters in intervention group versus -3.6 meters in control group) (Sadik 2005), and increasing mean distance walked in 6 min/distance till breathless (21 meters in intervention group versus -22 meters in control group) (Goodyer 1995). In patients with asthma, pharmacist interventions significantly improved asthma symptom score on the North of England asthma scale (-6.0 in intervention group versus 0.3 in control group) (Barbanel 2003), but did not significantly improve forced expiratory volume in one second (FEV1) (0.07 in intervention group versus 0.17 in control group) and forced vital capacity (FVC) (0.07 in intervention group versus 0.19 in control group) spirometry testing (Gonzalez-Martin 2003). One study examined anticoagulation, diabetes, dyslipidemia, and hypertension control in patients with a high risk of medication related problems and found a significant increase in the proportion of patients at goal for these conditions as a result of the pharmacist intervention (Taylor 2003). In one study targeting patients on warfarin therapy, the pharmacist intervention resulted in a decreased incidence of total bleeding and improved anticoagulation control (67% of intervention group versus 41% of control group with a therapeutic international normalized ratio (INR)) although the median INR was not shown to be significantly different between the intervention and control groups (Jackson 2004). Pharmacist interventions did not result in significant improvements in clinical outcomes for patients with COPD (Solomon 1998; Weinberger 2002) and depression (Brook 2003a; Capoccia 2004; Finley 2003; Rickles 2005).

Eight of the 36 studies that reported patient outcomes collected data on quality of life outcomes using SF-36 and other questionnaires (Cody 1998; Gonzalez-Martin 2003; Hanlon 1996; Malone 2001; Okamoto 2001; Sadik 2005; Solomon 1998; Taylor 2003). Three studies showed improvement in three or more quality of life subdomains in patients with asthma (Gonzalez-Martin 2003), heart failure (Sadik 2005) and high risk of medication related problems (Malone 2001).

Comparison 3: Pharmacist services targeted at health professionals versus services delivered by other health professionals

None included.

Comparison 4: Pharmacist services targeted at health professionals versus delivery of no comparable service

For detailed descriptions of outcomes see Analysis 3.1.

In all seven studies targeting health professionals, the effect of the intervention was measured by changes in prescribing of specific medications for specific disease states. In one study, educational outreach visits by a pharmacist to promote guideline-based prescribing for two of four disease states (aspirin as antiplatelet therapy, angiotensin converting enzyme inhibitors (ACEIs) in heart failure, NSAIDs in osteoarthritis pain, antidepressants for depression) resulted in a statistically significant 5.2% increase in overall guideline adherence (Freemantle 2002). In one study, the number of total antibiotic prescriptions decreased as a result of the pharmacist intervention, although the significance for this outcome was not reported (Ilett 2000). Another study showed that pharmacist-provided academic detailing related to cholesterol treatment significantly increased the number of lipid-treatment prescriptions in females (Diwan 1995). In three studies evaluating prescribing of appropriate medications for *H. pylori* infection (Hall 2001), ACEIs for heart failure (Turner 2000), and NSAIDs (Watson

2001), educational outreach visits by pharmacists failed to produce statistically significant changes in prescribing. Only one of three measured outcomes showed a significant increase in an additional study evaluating the effect of educational outreach visits by pharmacists prescribing NSAIDs (Stergachis 1987).

DISCUSSION

Overall, pharmacist interventions are beneficial in improving patient and health professional outcomes. Study design and intervention heterogeneity make it challenging to summarize overall benefit. Heterogeneity was noted in the type of pharmacist interventions delivered in individual studies as well as outcome variables measured. Interventions differed by site of delivery (for example, primary care clinic, community pharmacy, specialized clinic setting), length of each intervention session (for example, one hour long session with pharmacist, 15 minute session with pharmacist), and frequency of intervention (for example, three sessions per year, monthly session). The most common interventions provided involved: a) oral or written recommendations to physicians regarding therapy modifications or resolution of medication-related problems and b) multiple follow-up visits with patients spanning several months; these interventions showed mostly positive outcomes.

An attempt was made to summarize data by therapeutic area, but variability in the type of intervention provided, length of intervention, frequency of intervention, type of outcome measures collected, and time of collection precluded our ability to pool data for each area. Meta-analyses were performed on hypertension and glycemic control studies with similar study characteristics. The meta-analyses performed for systolic blood pressure, diastolic blood pressure, and HbA1c showed a beneficial effect of -6.32 (95% CI -8.8 to -3.83), -3.12 (95% CI -4.57 to -1.67), and -0.75% (95% CI -1.41 to -0.09) for each outcome respectively.

Of the studies reviewed, pharmacist interventions showed the largest effect in blood pressure measures and the smallest effect in improving COPD and depression outcomes. Several reasons may explain the lack of effect of pharmacist interventions treating depression and COPD outcomes. It is possible that the studies did not have enough participants to detect the true impact of the intervention. All studies targeting depression recruited fewer than 150 patients. Two studies performed power calculations for medication adherence outcomes only, so it is possible that these studies were not adequately powered to detect differences in clinical outcomes (Finley 2003; Rickles 2005). Two studies failed to recruit the number of patients needed to detect the specified effect size (13% to 28% difference in depression outcomes between intervention and control groups) at the 0.05 significance level (Brook 2003a; Capoccia 2004). It is unlikely that the study period was too short to detect the clinical benefit of the pharmacist interventions as study duration ranged from 3 months to 12 months for all depression studies. Similarly, two of the COPD studies had fewer than 100 patients, which may not have yielded an adequate sample size to detect the effect of the pharmacist intervention. Although one COPD study recruited more than 200 patients, the intervention was performed in a community pharmacy setting and may not have been as rigorous as interventions performed in outpatient clinics and, as a result, failed to produce a significant improvement in COPD disease control (Weinberger 2002).

The impact of pharmacist interventions on healthcare practice measures is mixed. Few studies (12) in this review evaluated the effect of pharmacist interventions on healthcare practice measures, with prescribing practices being the most common primary outcome reported. The studies yielded conflicting results, with six studies showing a beneficial effect (Diwan 1995; Freemantle 2002; Jameson 1995; Meredith 2002; Taylor 2003; Tsuyuki 2002), another study not reporting statistical significance (Ilett 2000), and the other four studies failing to show a statistically significant difference between study groups (Hall 2001; Stergachis 1987; Turner 2000; Watson 2001).

Study quality could have impacted study results. Although most studies were blinded, many did not explicitly report methods to conceal allocation of subjects to intervention or control groups. Given the nature of practice-based interventions, it is not always possible to blind patients or conceal allocation to an intervention group. The impact of concealment of allocation on study results was likely minimal as outcome variables included in this review were objective (for example, validated clinical scales, labs). Patient or health professional follow-up was done in 27 of 43 studies; follow-up was inadequate in seven studies and unclear or not reported in nine studies. This could have impacted individual study outcomes. For example, poor patient follow-up could reflect patient satisfaction or dissatisfaction with the intervention. Follow-up rate may also reflect typical attrition shown in healthcare practice settings (for example, patient transfer to new health professionals). Only objective primary outcomes were included in this review and as such, most studies were coded as having reliable outcomes and blinded assessment of outcomes. Few studies (12 of 43) met protection against contamination criteria. This is challenging to accomplish in studies of this nature; most studies occur within one clinic setting or one healthcare practice group (with multiple health professionals). Bidirectional communication (for example, verbal, written, medical charts) between clinic staff (for example, health professionals, other staff), changing practice environments, and staff/patient transfers make it possible for health professionals to improve upon the level of care provided or incorporate new knowledge acquired through informal consultation and educational sessions into practice. Given continuous improvement in the delivery of care, contamination would have likely reduced the difference in effect seen between interventions.

To simplify intervention delivery and minimize contamination between intervention groups, it is often easier for study investigators to randomize clinics/institutions based on location. This does, however, introduce the possibility of unit of analysis errors associated with cluster randomization. It is important to ensure that the appropriate unit of analysis is used in cluster randomization studies. There were few unit of analysis errors in this review. Of the four unit of analysis errors noted, two were in studies targeting health professionals. No studies with unit of analysis errors were included in meta-analyses.

A limitation of Phase I of this update is that it included only studies in the EPOC Specialised Register. The EPOC Specialised Register includes studies identified from MEDLINE back to 1966, HealthSTAR back to 1975, EMBASE back to 1980, and CINAHL back to 1982, for studies that meet the EPOC inclusion criteria. The CENTRAL database in *The Cochrane Library* is also searched on a regular basis.

For more information see EPOC Specialised Register. Phase II will include both MEDLINE and EMBASE (January 1966 to March 2008).

Overall, this review indicates that pharmacist interventions can lead to improved patient outcomes for multiple disease states, although effect size may not always be substantial or statistically significant. Pooling data from multiple studies to perform a meta-analysis could help to better determine the true effect and magnitude of pharmacist interventions. However, the ability to perform meta-analyses is limited by heterogeneity in comparison groups, clinical conditions, outcomes variables, and type of pharmacist intervention studied. In addition, poor reporting of variance in outcome variables further complicates the ability to perform accurate meta-analyses. Practice-based interventions are challenging to evaluate and are often limited by available data in the practice setting or the ability to collect data without impeding care or both. Standardization of outcome variables assessed could facilitate comparisons of pharmacist interventions across multiple studies. Standardizing outcome variables for specific disease states and outcome data reporting in study manuscripts to include measures of variance (for example, standard deviation) would facilitate comparison of pharmacist interventions across multiple studies.

AUTHORS' CONCLUSIONS

Implications for practice

1. Does the delivery of patient-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of the same services by other health professionals?

There is not enough quality evidence available to make a conclusion in this area. The study included in this review that evaluated this comparison was of low quality (Hawkins 1979).

2. Does the delivery of patient-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of no comparable services?

The majority of included studies supported the roles of pharmacists in medication/therapeutic management and patient counseling.

3. Does the delivery of health professional-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of the same services by other health professionals?

There is not enough evidence available to make a conclusion in this area. None of the studies that met the review inclusion criteria evaluated this comparison.

4. Does the delivery of health professional-targeted services by pharmacists improve patient or health professional outcomes compared to the delivery of no comparable services?

Prescribing practice was the most common outcome reported in these studies. These studies showed mixed results, with three of the studies showing improvement and the other four showing no significant difference between groups. This is consistent with the results found in the Cochrane Review evaluating the effects of educational outreach visits (O'Brien 2007). The clinical relevance of these effects is unknown and should be further studied.

The evidence supports continued integration of pharmacists providing medication/therapeutic management of patients independent of or in collaboration with other health professionals and delivering patient counseling regarding drug therapy and other public health issues. There may be some benefit in providing educational outreach visits to health professionals as well.

Implications for research

Recommendations should be made on a standardized approach to measuring and reporting clinical, humanistic, and process outcomes for future randomized controlled trials evaluating the impact of outpatient pharmacists. Heterogeneity in study design, outcomes, and measures make it challenging to make generalized statements regarding the impact of pharmacists in specific settings, disease states, and patient populations. Future studies should continue to use a randomized controlled trial design with explicit reporting on factors that impact study quality (for example, concealment of allocation, blinding, follow-up) in the study manuscript. Steps should be taken to minimize risk of bias in studies; to accomplish this, investigators can measure objective outcome variables, collect baseline measurements, and minimize contamination. In study reports/manuscripts, authors should address both internal and external threats to study validity.

As expected in this type of research, the type of interventions will differ across studies. This is typically unavoidable as many of the interventions tested in this review are innovative practices or modifications of previously studied practices or both. Investigators should explicitly describe the type of intervention, format/content of intervention, individuals delivering/receiving the intervention, the length of intervention, and the frequency of sessions/visits within the intervention in the study manuscript. Thorough reporting of details related to the study intervention allows other individuals or organizations to replicate beneficial models and make health care decisions based on comparing the best available evidence.

One of the challenges in summarizing the evidence in this area is the large degree of heterogeneity between studies. To facilitate the ability to make comparisons between studies, investigators should attempt to model the design of new studies after other well-designed studies (for example, selected outcome variables, time points to collect outcome variables). Studies should include clinically relevant outcome measures and strive, when possible, to measure clinical endpoints. This is often challenging in RCTs of shorter duration as it often takes years to see the effect of interventions on some outcomes (for example, stroke, myocardial infarction). Studies assessing the effect of educational outreach visits should include clinically relevant outcomes as opposed to surrogate markers such as physician prescribing habits. Few studies that assess the effects of pharmacists on patient outcomes include measures of the intervention's impact on preventing adverse drug events and medication errors. More studies should be performed in this area.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barbanel 2003

Methods	RCT (randomized by patient)
Participants	community pharmacy in Tower Hamlets, east London (United Kingdom) patients with asthma patients - 24 (12 intervention group, 12 control group) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacists reviewed inhaler technique, provided personal education on a variety of asthma-related topics and followed up with patients with weekly telephone calls vs usual care length of intervention - 45 to 60 min initial education session and weekly telephone calls number of interventions - 12 during 3 months
Outcomes	PROCESS not measured PATIENT improvement in asthma symptoms based on North of England asthma symptom scale
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Patients were randomized using sealed envelopes to intervention or control groups
Blinding? All outcomes	Low risk	Outcome variables are objective
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	There were follow-up data on all 12 in the intervention group and 11 in the control group (1 person moved away).
Baseline measurement?	Low risk	"baseline scores were similar in the intervention and control groups"

Barbanel 2003 *(Continued)*

Reliable outcome measures?	Low risk	objective validated instrument - North of England asthma symptom scale
Protection against contamination?	Unclear risk	Did not explicitly mention

Bogden 1997

Methods	RCT (randomized by patient)
Participants	university affiliated teaching clinic outpatient clinic in Hawaii (United States) patients with hypercholesterolemia patients - 100 health professional (delivering intervention) - 1 practice -1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist advising and interacting with patients and physicians on the best course of pharmacologic therapy vs usual care length of the intervention - 30 min number of interventions - 1 or more during 6 months
Outcomes	PROCESS not measured PATIENT Total Cholesterol (men and women)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	Authors report randomization by last digit of social security number (even vs odd)
Blinding? All outcomes	Low risk	Objective outcomes assessed-total cholesterol
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	50 patients were randomized; at time of study completion "there were 47 patients able to be evaluated in the intervention and control groups"
Baseline measurement?	Low risk	Primary outcome based on absolute change "from the baseline enrolment value"
Reliable outcome measures?	Low risk	Objective outcomes assessed - total cholesterol

Bogden 1997 *(Continued)*

Protection against contamination?	Unclear risk	Not explicitly described; subjects recruited from same clinic

Bond 2000

Methods	RCT (by medical practice)
Participants	university affiliated setting medical practices in Grampian, United Kingdom patients on repeat medications patients - 3074 (1614 intervention, 1460 control) health professional (delivering intervention) - 62 practice - 19 unit of analysis mismatch corrected (randomized by practice, analyzed by patient---analysis accounted for clustering effect)
Interventions	targeted towards PATIENTS pharmacist dispensed repeat prescriptions following a protocol to check whether items were required, or patients were experiencing side-effects or drug interactions vs usual care length of the intervention - not clear number of interventions - 12 during 12 months
Outcomes	PROCESS prescribing costs (excluded) PATIENT death rate adverse drug reactions hospital admissions
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	Random number tables were used
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	High risk	Of 1614 patients recruited to intervention group, complete data were available for 905 patients
Baseline measurement?	Unclear risk	Baseline measures not reported
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Allocation was by practice

Borenstein 2003

Methods	RCT (randomized by patient)
Participants	outpatient hypertension clinic run by clinical pharmacists (patients recruited from two main offices of a group medical practice of general internists and internal medicine subspecialists affiliated with a large community hospital) patients with uncontrolled hypertension patients - 1272 (635 intervention, 637 control) health professional (delivering intervention) - not clear practice - 2 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist assessed patients' blood pressure, medication regimen, medication adherence, adverse drug effects and lifestyle habits and provided individualized patient education regarding dietary and life-style modifications during initial and follow-up visits vs usual care targeted towards HEALTH PROFESSIONALS pharmacist reported findings and treatment recommendations to patients' physicians vs usual care length of the intervention - not clear number of interventions - not clear; follow-up visits scheduled every 2 to 4 weeks at the discretion of the pharmacist over 12 months
Outcomes	PATIENT achievement of blood pressure control based on Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure (JNC V)
Notes	Total professional visits (pharmacist and physician) in the intervention vs control (8.0 vs 6.6, P = 0.06)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Not explicitly mentioned
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	Based on reported data-of the 197 patients included in the study, data was reported on all 197 patients
Baseline measurement?	High risk	Collected, but statistically significant difference in systolic blood pressure and number of African-American patients between groups
Reliable outcome measures?	Low risk	Objective outcomes assessed
Protection against contamination?	High risk	Patients recruited from same medical group

Brook 2003a

Methods	RCT (randomized by patient)
Participants	community pharmacy in the Netherlands patients with depression patients - 135 (intervention 64, control 71) health professional (delivering intervention) - 19 practice - not clear no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist coaching patients and take-home video vs usual care length of the intervention - not clear number of interventions - 3 during 6 months
Outcomes	PROCESS not measured PATIENT disease control assessed by self-rating 90-item (Hopkins) Symptom Checklist (SCL-90)
Notes	required 75 patients per arm to detect 13% difference in depression at significance level of 0.05

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	Randomization used "block randomization"
Blinding? All outcomes	High risk	"Neither patients nor pharmacists were blinded for group assignment; could potentially impact patient self-rating.
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	High risk	"the attrition rate at 3- and 6-month follow-up was 21% and 27%."
Baseline measurement?	Low risk	"At baseline there were no significant differences" between groups
Reliable outcome measures?	Low risk	Validated objective tool used-90-item Hopkins Symptom checklist
Protection against contamination?	Unclear risk	All participants received care from same pharmacy. To minimize "all pharmacists attended a pre-trial meeting at which they were instructed how to approach eligible patients, how to randomise them, and how to use different protocols for patients"

Capoccia 2004

Methods	RCT (randomized by patient)
Participants	university affiliated teaching clinic outpatient clinic in United States patients with depression patients - 74 (41 intervention, 33 control) health professional (delivering intervention) - 2

Capoccia 2004 *(Continued)*

	practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist collaborating with primary care physicians (PCPs) to provide patient education, antidepressant therapy adjustment, monitoring of adherence and adverse drug reactions and prevention of relapse vs usual care length of the intervention - 15 min number of interventions - 13 during 12 months
Outcomes	PATIENT disease control using 20-item Hopkins Symptom Checklist (SCL-20)
Notes	-not all patients completed 13 sessions -required 55 patients per arm to detect a difference of 28% in clinical improvement rates at 0.05 significance level -Boudreau is the design paper for this study; no results reported in Boudreau

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	Not explicitly mentioned in paper
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	93% of patients completed the 12-month follow-up
Baseline measurement?	Low risk	"no significant differences on any demographic or clinical variables between the two groups"
Reliable outcome measures?	Low risk	Objective validated instrument used to assess outcome
Protection against contamination?	High risk	Patients received care from same medical center and potentially same group of professionals. "We cannot rule out the possibility of spillover effect" between groups

Choe 2005

Methods	RCT (randomized by patient)
Participants	university affiliated internal medicine clinic patients - 80 (41 intervention, 39 control) professional (delivering intervention) - unclear practices -1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist evaluated/modified therapy, educated on diabetes management and complications, performed screening processes and telephone follow-ups vs usual care

Choe 2005 *(Continued)*

	targeted towards HEALTH PROFESSIONALS pharmacist discussed therapeutic recommendations with the primary care physicians vs usual care length of intervention - 1 hour number of interventions - unclear number in 12 months with another 12 months of follow-up
Outcomes	PATIENT HbA1c
Notes	Follow-up for HbA1c measurement was 13.6 months for intervention group and 14.9 months for control group

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Unit of randomization by patient; drew numbers (0 or 1) from a container
Blinding? All outcomes	Low risk	Objective outcome measure
Follow-up of professionals?	Unclear risk	Not explicitly reported
Follow-up of patients?	Low risk	Outcome measures were obtained for 81% of subjects
Baseline measurement?	Low risk	no statistically significant differences in demographic variables between groups
Reliable outcome measures?	Low risk	Objective outcome measure
Protection against contamination?	High risk	Patients received care from same medical center

Clifford 2005

Methods	RCT (randomized by patient)
Participants	university affiliated internal medicine clinic patients - 180 (92 intervention, 88 control) professional (delivering intervention) - unclear practices -1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist assessed patients' drug regimen and clinical parameters, developed therapeutic plan, provided patient education regarding diet, exercise, compliance and home-glucose monitoring and forwarded patient information (medication lists, labs results, goals) to PCPs vs usual care length of intervention - 5 to 30 minutes (average 15 minutes) number of interventions - 8 in 12 months (face-to-face meetings at baseline, 6, and 12 months; 6-weekly intervals by phone)
Outcomes	PATIENT HbA1c (primary) Fasting plasma glucose, blood pressure, serum lipids, urinary albumin-to-creatinine ratio

Clifford 2005 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	High risk	"randomised...by consecutive allocation"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Unclear risk	Not explicitly reported
Follow-up of patients?	Low risk	91% of recruited subjects completed the study
Baseline measurement?	High risk	Intervention patients had a longer duration of diabetes, higher HbA1c, and were taking a greater number of medications
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	All participants received care from same clinic entity. Did not explicitly mention method to protect against contamination.

Cody 1998

Methods	RCT (by patient) + CBA (by geographic area) Similar control site: NOT CLEAR
Participants	community pharmacies of the Kaiser Permanente patients - 6000 in the RCT / 4600 in the CBA pharmacies - 9 in the RCT / 101 in the CBA no unit of analysis error for the RCT unit of analysis error for the CBA
Interventions	targeted toward PATIENTS comparison of three models Control model: usual care before 1992 in California California state model (1992) which requires outpatient pharmacist to counsel all patients who receive new or changed prescription about direction for use, the importance of compliance, proper storage, and relevant precautions and warnings. Kaiser Permanente (KP) model that focuses on a more comprehensive pharmacist consultation and other elements of pharmaceutical care on selected high-risk patients. length of study - 23 months
Outcomes	PROCESS not measured PATIENT Quality of life (SF 36)
Notes	see McCombs 1998 for design

Risk of bias

Cody 1998 *(Continued)*

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described; appears to have been performed via a central randomized scheme/computer system
Blinding? All outcomes	Low risk	Objective outcome assessed; nature of study design appears to have ensured blinding - patients were randomly assigned to separate pharmacies with a more comprehensive consultation model
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Not explicitly described
Baseline measurement?	Unclear risk	Not explicitly described
Reliable outcome measures?	Unclear risk	Patients self-completed and mailed in quality of life surveys
Protection against contamination?	High risk	NOT DONE for the RCT / DONE FOR the CBA

Diwan 1995

Methods	RCT (randomized by health center)
Participants	primary care health centers in Sweden, excluding health centers in counties with a university hospital, department of general medicine, or extensive activities for the prevention of cardiovascular disease or both. education provided by pharmacists focused on treating patients with cardiovascular disease. patients - 1308 practices - 134 health centers professional - 1 no unit of analysis error (the unit of analysis was the health center)
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist vs. no intervention pharmacist conducted academic group detailing sessions at health centers length of intervention - four 30 minute detailing sessions over a 5 month period product related
Outcomes	PROCESS number of prescriptions of lipid-lowering drugs/month PATIENT not measured
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	Coin toss
Blinding?	Low risk	Objective outcome assessed

Diwan 1995 *(Continued)*
All outcomes

Follow-up of professionals?	Low risk	Data collected from 87% of health centers
Follow-up of patients?	Low risk	Data were missing on 17 of 1308 patients
Baseline measurement?	Unclear risk	Not explicitly described; some differences existed in the number of baseline prescriptions between control and intervention groups. May not affect outcome
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Detailing occurred in specific health center

Finley 2003

Methods	RCT (randomized by patient)
Participants	outpatient clinic in Kaiser Permanente Medical Center, San Rafael, United States patients with depression patients - 125 (75 intervention, 50 control) professional (delivering intervention) - 2 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist managed medication regimens, conducted in-clinic and telephone follow-ups and educated patients regarding medications and disease state vs usual care length of the intervention - 30 min initial clinic visit, "brief" second and third clinic visits, 5 to 10 min telephone calls number of interventions - 3 clinic visits + 5 telephone follow-ups during 6 months
Outcomes	Brief Inventory for Depressive Symptoms (BIDS) score % patients with ≥ 50% reduction in BIDS score % patient achieving remission (BIDS score < 9) % patients with reduction in Work and Social Disability Scale (WSDS) score
Notes	-pharmacists met weekly with a psychiatrist ("psychiatric mentor") to present new patients and provide updates on other patients; the psychiatrist was also available for consultations as needed -study was powered to detect compliance outcomes only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	used "sealed envelopes", no mention of whether envelopes were opaque
Blinding? All outcomes	Low risk	objective primary outcomes
Follow-up of professionals?	Low risk	Not applicable

Finley 2003 *(Continued)*

Follow-up of patients?	High risk	data analyzed for < 80% of randomized patients
Baseline measurement?	Low risk	objective outcome assessed
Reliable outcome measures?	Low risk	objective primary outcomes
Protection against contamination?	High risk	patients randomized within 1 practice

Freemantle 2002

Methods	RCT (randomized by health authority)
Participants	outpatient general practices in United Kingdom National Health Service health authorities professional (delivering intervention) - 12 practice - 75 unit of analysis error (randomized by health authority, analyzed by practice)
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist performed educational outreach visits on two of four practice guideline topics ((1) use of aspirin as antiplatelet therapy, (2) use of ACEIs in heart failure, (3) use of NSAIDs in pain due to osteoarthritis, (4) choice of antidepressant for depression) vs non-targeted guideline control length of the intervention - not clear number of interventions - 2; 12 months pre-intervention and 12 months post-intervention periods
Outcomes	PROCESS # of patients treated in accordance with guideline recommendations
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	health authorities allocated in pairs through a central random process
Blinding? All outcomes	Low risk	objective measures
Follow-up of professionals?	Low risk	6 out of 69 practices refused follow-up
Follow-up of patients?	Low risk	not applicable
Baseline measurement?	Unclear risk	baseline adherence to recommendations not reported for intervention vs control groups
Reliable outcome measures?	Low risk	objective outcome measure
Protection against contamination?	Low risk	randomized by health authority

Gattis 1999

Methods	RCT (randomized by patient)
Participants	university affiliated teaching clinic outpatient cardiology clinic in United States patients with heart failure patients - 181 (90 intervention, 91 control) professional (delivering intervention) - not clear practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist educated patients regarding therapy modification and provided telephone follow-up vs usual care with telephone follow-up targeted towards HEALTH PROFESSIONALS pharmacist made recommendation to physicians regarding therapy optimization length of the intervention - not clear number of interventions - 4 during 6 months
Outcomes	PATIENT all-cause mortality and heart failure events at 6 months
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"computer generated randomization scheme"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Not explicitly described
Baseline measurement?	Low risk	Baseline characteristics were similar between groups
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients received care from same medical center

Gonzalez-Martin 2003

Methods	RCT (randomized by patient)
Participants	outpatient pediatric clinic affiliated with Catholic University, Chile patients with asthma patients - 21 (11 intervention, 10 control) professional (delivering intervention) - not clear practice - 1

Gonzalez-Martin 2003 *(Continued)*

	no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist educated patients on medication therapy and inhaler use using asthma explanatory booklet and prescribed medications brochure vs usual care length of the intervention - 30 min number of interventions - 3 during 9 weeks
Outcomes	PATIENT Pediatric asthma quality of life questionnaire (PAQLQ) score: emotions, activities, symptoms domains Spirometry testing: FVC, FEV1
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	not applicable
Follow-up of patients?	Low risk	"All 21 recruited children completed the study"
Baseline measurement?	Low risk	There were no statistically significant differences between groups
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	randomized by patient within 1 practice

Goodyer 1995

Methods	RCT (randomized by patient)
Participants	outpatient clinics of the Medicine for Elderly Department at Charing Cross Hospital (United Kingdom) patients over the age of 70 years - 100 no unit of analysis error
Interventions	targeted towards PATIENTS verbal counseling on the correct use of medication + medication calendar and information leaflets length of intervention - 3 domiciliary visits over a 6 to 12 week period
Outcomes	PROCESS not measured PATIENT compliance (pill count) defined as the percentage of the number that should have been consumed patient knowledge exercise test (distance in 6 min and distance till breathless) clinical assessment

Goodyer 1995 *(Continued)*

	Nottingham Health Profile breathlessness when performing different activities.
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Physician performing clinical assessment was blinded; outcome collected for the purpose of this review is objective
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	18 out of 100 patients dropped out by the end of the study
Baseline measurement?	Low risk	There were no significant differences between groups. The only concern was a non-significant difference between groups in baseline edema
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Two people from same family could have been assigned to different groups

Hall 2001

Methods	RCT (randomized by practice) - before and after pragmatic randomized controlled trial
Participants	outpatient general practice clinics in a single health authority district, Enlgand professional (delivering intervention) - 1 practice -79 (38 intervention, 38 control) no unit of analysis error (general practices the unit of analysis)
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist conducted educational outreach visits to promote undertaking of *H. pylori* eradication using mailed consensus guidelines vs mailed consensus guidelines alone length of the intervention - not clear number of interventions - 1 between 12 months pre-intervention and 12 months post-intervention periods
Outcomes	PROCESS increase in omeprazole prescribing in accordance with consensus guidelines increase in metronidazole prescribing in accordance with consensus guidelines
Notes	21 practices from randomized 38 received intervention

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"computer generated random number list"

Hall 2001 *(Continued)*

Blinding? All outcomes	Unclear risk	Objective outcome assessed
Follow-up of professionals?	High risk	3 of 19 intervention practices (that allowed a visit) allowed an audit
Follow-up of patients?	Low risk	Not applicable
Baseline measurement?	Unclear risk	Not explicitly described
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	General practices unit of randomization

Hanlon 1996

Methods	RCT (randomized by patient)
Participants	general medicine clinic at the Durham Veteran Affairs Medical Center North Carolina (United States) patients over 64 years with 5 or more regularly scheduled medications - 208 professional (delivering intervention) - 1 practices -1 no unit of analysis error
Interventions	targeted towards PATIENTS education regarding any drug related problem + reinforcement of physician instructions targeted towards HEALTH PROFESSIONALS thorough medication history review; recommendation and their rationale presented orally and in writing to the patients' physicians length of intervention - not clear number of interventions - multiple during 12 months
Outcomes	PROCESS Medication Appropriateness Index (MAI) PATIENT SF 36 (Health Related Quality of Life) Adverse Drug Events (ADE) Compliance Satisfaction
Notes	ADE and Compliance were self reported by the patients and are therefore not reported in this review

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Randomised using a computer generated scheme
Blinding? All outcomes	Low risk	Objective outcome assessed

Hanlon 1996 *(Continued)*

Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	169 out of 208 patients followed up
Baseline measurement?	Low risk	Control patients were more likely to have been married, to take more medications, and to have more medications for which the clinical pharmacist developed recommendations. Analyses controlled for these baseline differences.
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients received care in the same clinic

Hawkins 1979

Methods	RCT (randomized by patient)
Participants	outpatient primary care clinic in United States (Texas) diabetic or hypertensive patients or both episodes of care - 12,918 patients - 1148 professionals (delivering intervention) - 2 practices - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist management of drug therapy (physician not involved) vs usual care (physician only) pharmacists prescribed drugs and modified drug therapy as needed length of intervention - 29 months product related
Outcomes	PROCESS kept appointment rate follow-up clinic visits hospital admissions emergency department visits PATIENT compliance mean blood pressure blood sugar level percent of patients with decreased blood pressure percent of patients with decreased blood sugar levels
Notes	Intervention was delivered by pharmacists who were assisted by trainees

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Objective outcome assessed

Hawkins 1979 *(Continued)*

Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	High risk	Total attrition was 39.2% and 51.2% in experimental and control group, respectively
Baseline measurement?	High risk	Control group contained a higher percentage of patients with hypertension as an only diagnosis; a higher percentage of experimental patients had both hypertension and diabetes
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Possible physician influence on intervention group

Ilett 2000

Methods	RCT (randomized by health professional)
Participants	outpatient clinics in Australia patients with antibiotic prescriptions physicians (receiving intervention) - 112 (56 intervention, 56 control) health professional (delivering intervention) - not clear practice - unclear (multiple practices in Osborne Division of General Practice in the Perth Western Australia) no unit of analysis error
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist provided academic detailing, consisting of in-person visit and paper chart, to physicians on best practice guidelines for antibiotic use vs no intervention length of the intervention - 10 to 15 min number of interventions - 1 during 3 months
Outcomes	PROCESS Number of prescriptions for all antibiotics PATIENT none measured
Notes	Guidelines for antibiotic prescribing were developed by an expert panel and were in line with published Australian therapeutic guidelines for antibiotics

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Outcome data were available for all 112 physicians included in the study

Ilett 2000 *(Continued)*

Follow-up of patients?	Low risk	Not applicable
Baseline measurement?	Low risk	"had similar demographic profile"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Communication between physicians was possible

Jaber 1996

Methods	RCT (randomized by patient)
Participants	university-affiliated general medicine outpatient clinic in United States (Michigan) urban African-American patients with diabetes patients - 45 health professionals - 1 practices - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist provided diabetes education, medication counseling, instructions on dietary regulation, exercise and home glucose monitoring, and evaluation and adjustment of drug regimen vs usual care length of intervention - 4 months non-product related
Outcomes	PROCESS not measured PATIENT glucose levels quality of life
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	39 out of 45 patients completed the study
Baseline measurement?	Low risk	Objective outcome assessed
Reliable outcome measures?	Low risk	Objective outcome assessed

Jaber 1996 *(Continued)*

Protection against contamination?	Low risk	Unlikely that the control group received the intervention

Jackson 2004

Methods	open-label RCT (randomized by patient)
Participants	home-based follow-up of patients discharged from Royal Hobart acute care teaching hospital in southern Tasmania, Australia patients - 128 (60 intervention, 68 control) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist conducted home-visit to test INR and educate patients regarding anticoagulant therapy using printed educational materials targeted towards HEALTH PROFESSIONALS pharmacist informed physicians regarding patients' INR, recommended dosage adjustments and implemented therapy changes vs usual care length of the intervention - 24 min number of interventions - 4 during 90 days
Outcomes	PATIENT therapeutic INR as defined by ACCP on day 8 after-discharge total, major, and minor bleeding complications within 90 days of discharge
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	Patients were home-based; allocation was likely adequately concealed
Blinding? All outcomes	Low risk	Objective outcomes assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	127 of the 131 patients completed the study
Baseline measurement?	High risk	"The two groups were well matched with regard to baseline demographics. There was a significantly higher incidence of previous myocardial infarction in the intervention group compared to the control group"
Reliable outcome measures?	Low risk	Objective outcomes assessed
Protection against contamination?	Low risk	Patients were home-based, contamination unlikely

Jameson 1995

Methods	RCT (randomized by patient)
Participants	primary care practice in United States (Michigan) patients at high risk for adverse consequences of drug therapy patients - 64 health professionals - 1 practices - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist conducted a single pharmacotherapy consultation with patient, met with physician to discuss findings, conducted educational session with patient vs usual care length of intervention - brief (a few hours total) product related
Outcomes	PROCESS number of drugs doses of drugs costs of drugs PATIENT compliance side effects
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Randomised by a simple coin toss"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	High risk	268 of 340 patients completed the study
Baseline measurement?	Low risk	"There were no differences in demographics between patients"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients received care in the same clinic; communication between the pharmacist and physician could have influenced usual care

Malone 2001

Methods	RCT (randomized by patient)
Participants	ambulatory care clinics in Veterans Affairs Medical Centers across continental United States patients with high risk for medication related problems (≥ 3 of following criteria: (1) more than 5 medications, (2) more than 12 doses per day, (3) more than 3 chronic medical conditions, (4) more than 4

Malone 2001 *(Continued)*

	changes to medication regimen over past year, (5) taking < 80% of medications based on pharmacy refill records, (6) taking medication requiring therapeutic monitoring patients - 1054 (intervention 523, control 531) health professional (delivering intervention) - 78 practice - 9 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist reviewed medical records, performed physical assessment and laboratory tests to assess appropriateness of medication therapy, modified therapy as necessary, educated patients, and made referrals to other health professionals vs usual care length of the intervention - > 15 minutes for > 73% of patient contacts number of interventions - mean of 3.5 during 12 months
Outcomes	PATIENT health-related quality of life using SF-36 questionnaire
Notes	*Ellis 2000 is a subgroup analysis of Improve Study (Malone 2001)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Were randomised by a central coordinating centre"
Blinding? All outcomes	Low risk	Objective outcomes assessed
Follow-up of professionals?	Low risk	not applicable
Follow-up of patients?	Low risk	931 of 1054 patients completed the study
Baseline measurement?	Low risk	"The two groups were similar in demographics and medical conditions at study enrolment. The scores for intervention group were lower for all domains compared with the control group, but differences were not statistically significant at the P = 0.01 level"
Reliable outcome measures?	Low risk	Objective outcomes assessed
Protection against contamination?	Low risk	Multi-site study

Mehos 2000

Methods	RCT (randomized by patient)
Participants	family medicine residency training clinic in Colorado, United States patients with stage 1 or 2 hypertension patients - 41 (intervention 20, control 21) health professionals (delivering intervention) - not clear practices - 1 no unit of analysis error
Interventions	targeted towards PATIENTS

Mehos 2000 *(Continued)*

	patients received blood pressure monitors, blood pressure diaries and telephone contacts by pharmacist to evaluate blood pressure and response to therapy vs usual care without blood pressure self-monitoring targeted towards HEALTH PROFESSIONALS pharmacist informed primary care health professionals of patients' blood pressure results and provided therapy recommendations vs usual care length of intervention - 30 minutes (initial visit) number of interventions - initial visits and phone call follow-ups during 6 months product and non-product related
Outcomes	PATIENT systolic, diastolic, and mean arterial blood pressure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	"randomized using a deck of cards". Unclear how this concealed allocation
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	36 out of 41 patients completed the study
Baseline measurement?	Low risk	"No statistically significant differences in baseline characteristics between" groups
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients received care in the same clinic; communication between the pharmacist and physician could have influenced usual care

Meredith 2002

Methods	RCT (randomized by patient)
Participants	home care agencies in United States (New York City and Los Angeles) patients with home care services patients - 317 (160 intervention group, 157 control group) health professional (delivering intervention) - 2 practice -2 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist, assisted by a patient's nurse, reviewed patient profiles, identified medication problems (related to inappropriate use of H2 blockers, cardiovascular medication, psychotropic medication and NSAIDs); the nurse assisted the patient with the medication changes and monitored the effect. Clinical pharmacists provided nurses with educational materials that explained the background of each of the problems and suggested ways to resolve them. targeted towards HEALTH PROFESSIONALS pharmacist developed a plan to address therapeutic problems to the patient's physician vs usual care

Meredith 2002 *(Continued)*

	length of the intervention - 30 min number of interventions - 1 during 6 weeks to 90 days
Outcomes	PROCESS improvement in prescribing for any medication use therapeutic duplication cardiovascular medication use psychotropic medication use NSAIDs use as % of patients
Notes	nurse presented the plan to physicians for uncomplicated cases and assisted patients with medication changes and monitored their effect

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Coordinating centre randomised eligible patients using balanced block randomisation"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	259 of 317 patients completed the study
Baseline measurement?	Low risk	There were no demographic differences between the intervention and control groups
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Intervention took place in patients' home

Odegard 2005

Methods	RCT (randomized by patient)
Participants	university affiliated teaching clinic outpatient clinic in University of Washington Medicine Neighborhood Clinics, United States patients with Type II diabetes patients - 77 (43 intervention group, 34 control group) health professional (delivering intervention) - not clear practice - 8 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist developed a diabetes care plan and communicated with patients and physicians regarding diabetes care progress vs usual care length of the intervention - 10 min per telephone call and 30 min per in-person visit

Odegard 2005 *(Continued)*

	number of interventions - average of 4.5 telephone contacts and 2.1 in-person visits during 6 months followed by 6 month usual care follow-up
Outcomes	PROCESS not measured PATIENT HbA1C at 6 months (end of intervention) and 12 months (6 months of usual care follow-up)
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome measure
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	66 out of 77 subjects completed the study
Baseline measurement?	Low risk	Groups were similar, with the exception of the intervention group being less likely to have a high school education.
Reliable outcome measures?	Low risk	Objective outcome measure
Protection against contamination?	High risk	Patients received care within the same clinic system (unit of allocation by the patient). Communication between the pharmacist and physician could have influenced usual care.

Okamoto 2001

Methods	RCT (randomized by patient)
Participants	hypertension and general medicine clinics within a managed care facility in United States patients with hypertension patients - 330 (164 intervention group, 166 control group) health professional (delivering intervention) - 1 practice - not clear no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist managed treatment of patients with hypertension and obtained consent from physicians for therapy changes vs usual care length of the intervention - not clear number of interventions - 5 during 6 months
Outcomes	PATIENT Blood pressure Health-related quality of life using short-form health survey (SF-36)

Okamoto 2001 *(Continued)*

Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Specific data not provided on number of patients lost to follow-up
Baseline measurement?	Low risk	330 of 381 patients completed the study
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients received care within the same facility. Communication between the pharmacist and physician could have influenced usual care.

Park 1996

Methods	RCT (randomized by patient)
Participants	two sites of a chain pharmacy in Chicago Ill, United States patients with hypertension - 64 health professionals (delivering intervention) - 2 pharmacy residents practices -2 (not studied at the same time) no unit of analysis error
Interventions	targeted towards PATIENTS oral and written education about hypertension, its treatments and risk factors to the patients + recommendation to the physician if necessary length of the intervention - 15 to 30 min approximately frequency of the intervention - 4 in 4 months
Outcomes	PROCESS not measured PATIENT blood pressure compliance (pill count) Health Status Questionnaire (HSQ) Hypertension/Lipid Form (HTN)
Notes	the intervention group and control group were different at baseline (for their systolic blood pressure) but the authors did not provide the significance level of this difference

Risk of bias

Bias	Authors' judgement	Support for judgement

Park 1996 *(Continued)*

Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	not applicable
Follow-up of patients?	Low risk	53 out of 64 patients completed the study
Baseline measurement?	Unclear risk	The intervention group and control group were different at baseline (for their systolic blood pressure) but the authors did not provide the significance level of this difference
Reliable outcome measures?	Low risk	Resident performed blood pressure measurement, which were not blinded from patients; these are objective outcomes
Protection against contamination?	High risk	All subjects were recruited from the same community pharmacy; there was the possibility of communication between subjects within the same household or family

Paulos 2005

Methods	RCT (randomized by patient)
Participants	community pharmacy in Chile patients with hyperlipidemia patients - 42 (23 in intervention group, 19 in control group) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist measured total blood cholesterol and triglyceride levels and educated patients on cardiovascular disease and risk factors and appropriate medication use vs usual care length of the intervention - 20 to 25 min number of interventions - 5 during 4 months
Outcomes	PROCESS not measured PATIENT Total cholesterol levels Triglyceride levels % of patients with decrease in total cholesterol levels % of patients with decrease in triglyceride levels
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Randomization and allocation process was not described
Blinding?	Low risk	Objective outcome measure

Paulos 2005 *(Continued)*

All outcomes		
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Specific data not provided
Baseline measurement?	Unclear risk	Significance for differences in baseline measurements for primary outcomes was not reported
Reliable outcome measures?	Low risk	Objective outcome measure
Protection against contamination?	High risk	All subjects were recruited from the same community pharmacy; there was the possibility of communication between subjects within the same household or family

Peterson 2004

Methods	RCT (randomized by patient)
Participants	acute care teaching hospital (Royal Hobart Hospital) in southern Tasmania, Australia patients with cardiovascular disease discharged from the hospital on statin therapy patients - 94 (46 intervention, 48 control) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist conducted home-visits to perform cholesterol measurements, assess medication regimen and educate patients regarding lipid-lowering drug therapy and dietary and life-style modifications vs usual care length of the intervention - not clear number of interventions - 6 during 6 months
Outcomes	PATIENT cholesterol level at follow-up (6 months)
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Low risk	"Computer-generated list of random numbers"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	81 out of 94 subjects completed the study
Baseline measurement?	Low risk	There were no statistically significant differences between groups

Peterson 2004 *(Continued)*

Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Patients randomized within 1 hospital but intervention performed at home

Rickles 2005

Methods	RCT (randomized by patient) - randomized, controlled, unblinded, mixed experimental design
Participants	community pharmacies within a large managed care organization in Wisconsin, United States patients presenting with new antidepressant prescriptions patients - 63 (31 intervention, 32 control) health professional (delivering intervention) - 14 practice - 8 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist provided monthly telephone-based education on antidepressant use and goal of therapy and monitoring of adverse effects and adherence vs usual care length of the intervention - 19, 12, and 11 min for first, second, and third phone call, respectively number of interventions - 3 during 3 months
Outcomes	PATIENT greater than 50% improvement in depression symptoms measured with Beck Depression Inventory-II (BDI-II) instrument
Notes	-past use of psychiatric medications was different between groups at baseline -study was powered to detect compliance outcomes only

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	assignment sealed in an envelope; envelope not reported as "opaque"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	not applicable
Follow-up of patients?	Low risk	60 out of 63 patients completed the study
Baseline measurement?	Low risk	Intervention group was more likely to have a history of psychotropic medication use
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. There was the possibility of communication between subjects within the same household or family

Sadik 2005

Methods	RCT (randomized by patient)
Participants	outpatient clinic in Al-Ain Hospital, Al-Ain, UAE patients with heart failure (HF) patients - 221 (intervention 109, control 112) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist providing patient education regarding HF medications and disease management during clinic follow-up visits, printed booklet on HF, symptom monitoring diary card targeted towards HEALTH PROFESSIONALS pharmacist discussed drug therapy with patients' physicians vs usual care length of the intervention - not clear number of interventions - 5 during 12 months
Outcomes	PATIENT mean distance walked in 2 min test QOL (quality of life) using SF-36 questionnaire
Notes	Patients were recruited from the hospital ward and hospital outpatient clinic; intervention took place in hospital outpatient clinic

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described. Manuscript cited a reference from 1981 for randomization method (minimization methods)
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	not applicable
Follow-up of patients?	Low risk	208 of 221 patients completed the study
Baseline measurement?	Low risk	No difference was mentioned between the groups
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. Communication between the pharmacist and physician could have influenced usual care.

Sarkadi 2004

Methods	RCT (randomized by patient)
Participants	community pharmacies in Sweden patients with diabetes mellitus Type II patients - 64 (intervention 33, control 31) health professional (delivering intervention) - unclear practice - unclear

Sarkadi 2004 *(Continued)*

	no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist led an educational program using a video, a dice game and a booklet on diabetes management to promote dietary modifications, exercise and blood glucose control and referred patients to health professionals in cases of unsatisfactory glucose control vs no intervention length of the intervention - unclear number of interventions - 3 during 1 year; 1 year follow-up after intervention completion
Outcomes	PATIENT HbA1c at 12 months (end of study) HbA1c at 24 months (follow-up)
Notes	Pharmacist led educational group had assistance from a diabetes nurse specialist on the first two occasions; patients were self-referred to the program

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"An assistant mixed envelopes in a box, took them out one at a time, and randomly placed them into 2 piles. A third person, acting as a witness, pointed out which pile should be allocated to the intervention group and which pile to the control group"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Not explicitly described
Baseline measurement?	High risk	Intervention group had longer diabetes duration compare with control group
Reliable outcome measures?	Unclear risk	Reliability of measurements unclear (patients brought in glycosylated hemoglobin measures)
Protection against contamination?	Unclear risk	Settings of intervention and control groups not explicitly described

Schneider 1982

Methods	RCT (randomized by patient)
Participants	outpatient medicine clinic at the University Hospital Clinic, University Hospital, Ohio State University patients with essential hypertension and congestive heart failure patients - 40 (intervention 20, control 20) health professional (delivering intervention) - 1 practice - 1 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist examined and evaluated patients during a clinic visit targeted towards HEALTH PROFESSIONALS pharmacist communicated findings and suggestions to physician vs usual care

Schneider 1982 *(Continued)*

	length of intervention - 12 months
Outcomes	PATIENT systolic and diastolic blood pressure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Not explicitly described
Baseline measurement?	Unclear risk	Not explicitly described
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. Communication between the pharmacist and physician could have influenced usual care

Solomon 1998

Methods	RCT (randomized by patient)
Participants	outpatient clinics at 10 Veterans Administration Medical Centers and 1 university hospital in United States patients with hypertension and/or COPD patients - hypertension arm 133 (intervention 63, control 70); COPD arm 98 (intervention 43, control 55) health professionals - not clear practices - 11 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist provided clinical pharmaceutical care services vs usual care length of intervention - approximately 60 minutes for initial visits, 30 minutes for follow-up visits number of interventions - monthly visits over 6 months no unit of analysis error
Outcomes	PATIENT blood pressure (hypertension arm) Borg Scale (COPD arm)
Notes	-pharmaceutical care services included clinical management of hypertension and COPD via standardized patient assessment activities, pharmacists' involvement with the health care team, collaboration with physicians to develop patient-specific plan, patient education on hypertension and COPD, counseling to address patients' questions or concerns, and regular patient assessments and care

Solomon 1998 *(Continued)*

	-intention-to-treat analysis not done (number of patients reported is number of patients analyzed; number of patients randomized not clear)

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Table of random numbers"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Unclear risk	Not explicitly described
Baseline measurement?	Low risk	"No significant differences in group characteristics were found"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. Communication between the pharmacist and physician could have influenced usual care. "Seven sites participated in both study arms."

Sookaneknun 2004

Methods	RCT (randomized by patient)
Participants	university-affiliated community pharmacy and 2 primary care units in Thailand (Mahasarakham, Takonyarng village, Kharmrieng village) patients with hypertension patients -235 (intervention 118, control 117) health professionals - not clear practices - 3 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist provided monthly consultation and blood pressure monitoring vs usual care targeted towards HEALTH PROFESSIONALS pharmacist made medication regimen change recommendations to physicians after identifying drug-related problems length of the intervention - 30 to 50 minutes number of interventions - 6 (monthly) during 6 months
Outcomes	PATIENT blood pressure
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Sookaneknun 2004 *(Continued)*

Allocation concealment?	Unclear risk	Not explicitly described (Per study - "Simple randomization technique was used")
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	227 of 235 patients completed the study
Baseline measurement?	Low risk	"The two groups were equal in all variables"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. Communication between the pharmacist and physician could have influenced usual care.

Stergachis 1987

Methods	RCT (randomized by clinic)
Participants	outpatient primary care clinic that is part of a managed care organization in the United States (Washington) patients receiving NSAIDS and salicylates patients - not clear health professionals - 2 pharmacists, 17 physicians practices - 2 no unit of analysis error
Interventions	targeted towards PATIENTS (minimal) AND HEALTH PROFESSIONALS (primary intervention) pharmacist in family practice clinic provided educational/drug monitoring services to physicians and counseling to patients vs usual care length of intervention - 6 months product related
Outcomes	PROCESS number of prescriptions drug ingredient costs operating cost of clinical pharmacy program PATIENT not measured
Notes	This was one of few studies that included an assessment of the cost of the intervention

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Allocation procedure not described explicitly
Blinding? All outcomes	Low risk	Objective outcome assessed

Stergachis 1987 *(Continued)*

Follow-up of professionals?	Low risk	Data were included for all 17 physicians
Follow-up of patients?	Low risk	Not applicable
Baseline measurement?	Low risk	"There were no significant differences among" demographic characteristics
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Intervention part of broader education campaign affecting cases and controls

Taylor 2003

Methods	RCT (randomized by patient)
Participants	University of Alabama School of Medicine affiliated outpatient clinics in Alabama, United States patients with high risk for medication-related adverse effects (≥ 3 of the following: 5 or more medications, 12 or more doses/day, 4 or more medication changes in previous year, 3 or more concurrent diseases, history of medication noncompliance, drugs requiring therapeutic monitoring) patients - 81 patients enrolled (12 lost to follow-up); Study analyses based on 69 (33 intervention, 36 control) health professional (delivering intervention) - 4 practice - 3 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist performed pharmaceutical care including chart and medication review, patient education and therapeutic monitoring vs usual care length of the intervention - 20 min number of interventions - multiple during 12 months
Outcomes	PROCESS Number of prescribed medications at 12 months Number of inappropriate prescriptions for various MAI domains PATIENT patients at goal for hypertension patients at goal for diabetes patients at goal for dyslipidemia patients at goal for anticoagulation QOL using SF-36 questionnaire
Notes	Number of patients randomized not explicitly mentioned (appears to be 81) - not intention-to-treat analysis. Analysis based on number of patients who completed the study

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed

Taylor 2003 *(Continued)*

Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	69 out of 81 patients completed the intervention
Baseline measurement?	Low risk	"The intervention and control groups were not significantly different with respect to demographic characteristics and medication use, compliance, and knowledge"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	High risk	Patients were randomized. Communication between the pharmacist and physician could have influenced usual care.

Tsuyuki 2002

Methods	RCT (randomized by patient)
Participants	community pharmacies in 2 provinces of Canada: Alberta and Saskatchewan patients at high risk for cardiovascular disease: previous acute myocardial infarction, stable or unstable angina, coronary revascularization, cerebral or peripheral vascular disease, diabetes mellitus with at least 1 other cardiovascular risk factor (cigarette smoking, hypertension, positive family history of premature cardiovascular disease, obesity, sedentary lifestyle, hypercholesterolemia, male > 45 years old, female > 55 years old) patients - 675 (344 intervention, 331 control) health professional (delivering intervention) - unclear practice - 54 no unit of analysis error
Interventions	targeted towards PATIENTS pharmacist provided regular follow-ups to perform point-of-care cholesterol testing and educate patients regarding cardiovascular risk factors using patient brochure developed by Alberta Medical Association and the Clinical Quality Improvement Network targeted towards HEALTH PROFESSIONALS pharmacists faxed recommendations to patients' primary physician regarding disease management and testing length of intervention - not clear number of interventions - 5 episodes during 12 months
Outcomes	PROCESS # of new prescribed cholesterol-lowering medications # of modified pre-existing cholesterol-lowering medications PATIENT patients at goal for hyperlipidemia
Notes	-Tsuyuki 1999 is a companion paper for this study; Simpson 2001; Simpson 2004 are planned subgroup analyses of this paper.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Computer generated sequence using block randomization (block size of 4) with stratification by study centre (pharmacy)"

Tsuyuki 2002 *(Continued)*

Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	657 out of 675 patients completed the study
Baseline measurement?	Low risk	"Randomisation resulted in a balance of patient demographics"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Multi-center study could have minimized contamination. Patients were randomized. There was the possibility of communication between subjects within the same household or family

Turner 2000

Methods	RCT (randomized by practice)
Participants	outpatient practices in Avalon Peninsula, Newfoundland, Canada all physicians in the region were invited to participate in the study; intervention focused on physicians treating CHF (congestive heart failure) patients patients - not clear health professional (delivering intervention) - not clear practice - 72 unit of analysis error (no correction)
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist provided academic detailing to physicians on use and dosage of ACEIs and ARBs for prevention and management of CHF using Canadian consensus guidelines on management of CHF vs no intervention length of the intervention - not clear number of interventions - 1 during 3 months
Outcomes	PROCESS utilization of ACEIs in patient receiving digoxin and furosemide for CHF targeted daily dose of ACEIs
Notes	Number of patients allocated to each group not reported Statistical analysis of results did not account for clustering and unit of analysis error

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	"First and second interviews were successfully completed with 25 and 23 physicians, respectively, in the control group and 32 and 31 physicians in the intervention group"

Turner 2000 *(Continued)*

Follow-up of patients?	Low risk	Not Applicable
Baseline measurement?	Unclear risk	Not explicitly described
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	"All members of a group practice were randomized to the same study group to minimize cross-contamination"

Van Veldhuizen 1995

Methods	RCT (by patient)
Participants	outpatient diabetes center in United States (Indiana) diabetic patients patients - 41 health professionals - 1 practices - 1 no unit of analysis error
Interventions	targeted towards PATIENTS 1-on-1 interaction with pharmacist plus follow-up vs group education from pharmacist vs standard education. length of intervention - 2 months product related
Outcomes	PROCESS not measured PATIENT knowledge of diabetes perception/attitudes towards diabetes, therapy, pharmacists blood glucose levels
Notes	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	High risk	Based on figures, 32 out of 41 patients completed the study (for blood glucose values)
Baseline measurement?	Unclear risk	Not explicitly described, but there appears to be differences in the numbers presented (statistical significance not reported); data not reflected in a table or figure.

Van Veldhuizen 1995 *(Continued)*

Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Unclear risk	Not explicitly described; subjects recruited from the same Regional Diabetes Center

Watson 2001

Methods	cluster RCT (randomized by practice)
Participants	university affiliated teaching clinic outpatient general practices in Avon, United Kingdom health professional (delivering intervention) - 3 practice - 20 no unit of analysis error
Interventions	targeted towards HEALTH PROFESSIONALS pharmacist performed educational outreach visits to promote mailed practice guideline on NSAID use vs mailed practice guideline alone vs no intervention length of the intervention - less than 10 minutes number of interventions - 2 during 12 months
Outcomes	PROCESS change in volume of prescribing for ibuprofen, diclofenac and naproxen as % of total NSAID prescribing
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Unclear risk	Not explicitly described
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Data are presented for all practices included in the study
Follow-up of patients?	Low risk	not applicable
Baseline measurement?	Low risk	"There were only slight differences in NSAID prescribing between the three groups at baseline"
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Randomised by practice

Weinberger 2002

Methods	RCT (by practice - 36 drugstores divided into 12 clusters of 3 geographically proximal drugstores)
Participants	CVS community pharmacies in Indianapolis, United States patients with COPD and asthma patients - 1113 asthma - 660 (pharmaceutical care program 262, peak flow monitoring control 233, usual care control 165) COPD - 453 (pharmaceutical care program 185, peak flow monitoring control 130, usual care control 138) health professional (delivering intervention) - not clear practice - 36 unit of analysis error (randomized by practice, analyzed by patient)
Interventions	targeted towards PATIENTS pharmaceutical care (patients received peak flow monitor + instructions for use, written educational materials, and monthly telephone calls from research personnel to collect PEFR results; pharmacist assessed PEFR results and other relevant medical information (medications, refill history, emergency department visits and hospitalizations) and implemented pharmaceutical care activities) vs peak flow monitoring (patients received peak flow monitors and instructions for use and monthly telephone calls from research personnel to collect peak flow PEFR results (results were not seen by the pharmacist)) vs usual care (patients did not receive peak flow monitors but received monthly follow-up phone calls from research personnel) length of the intervention - not clear number of interventions - mean 19.4 in asthma, 22.4 in COPD patients during 12 months
Outcomes	PATIENT peak flow rate (PEFR) (combined for asthma and COPD patients) at 12 months HRQOL (health-related quality of life) for asthma patients at 12 months HRQOL for COPD patients at 12 months
Notes	No statistical analysis done to adjust for unit of analysis error

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	"Used a randomized number chart"
Blinding? All outcomes	Low risk	Objective outcome assessed
Follow-up of professionals?	Low risk	Not applicable
Follow-up of patients?	Low risk	"Completed interviews with 947 patients (85.1%) at 6 months and 898 patients (80.7%) at 12 months. Completion rates did not differ significantly by disease or study group."
Baseline measurement?	High risk	DONE for asthma patients, NOT DONE for COPD patients; "study groups were comparable at baseline, except for race (asthma/COPD) and PEFR (COPD only)...we controlled for race in all analyses and for baseline PEFR among COPD patients only."
Reliable outcome measures?	Low risk	Objective outcome assessed
Protection against contamination?	Low risk	Sites were randomized in clusters.

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
Abramowitz 1982	Hospital-based intervention
Bogden 1998	Not RCT
Bolas 2004	Hospital-based intervention
Bouvy 2003	Subjective primary outcome
Bozovich 2000	Not RCT
Brook 2003b	Subjective primary outcomes
Brook 2005	Subjective primary outcome
Bucci 2003	Intervention not performed solely by pharmacist - patients followed by a multidisciplinary team including a pharmacist
Charrois 2004	Design paper - no results reported. A search was performed for the completed manuscript. The completed manuscript was found by searching for studies that referenced the original design paper. The completed manuscript is not indexed in PubMed; it is in the Studies awaiting classification section and will be coded in Phase II.
Chisholm 2001	Relevant and interpretable data are not presented
Cowper 1998	Economic data only reported as primary outcomes
Davidson 2000	Not RCT (experimental gp-not prospectively assigned)
de Maat 2004	Sequential study design
De Tullio 1987a	Subjective primary outcome
De Tullio 1987b	Not RCT
Erickson 1997	Not RCT
Fischer 2002	Resource utilization and costs only reported as primary outcomes
Fornos 2004	Design paper - no results reported. Manuscript for completed study is in Studies awaiting classification section
Forstrom 1990	Costs only reported as primary outcomes
Garnett 1981	Patient self-reported data
Gourley 1998	Subgroup analysis of Solomon 1998; focused on humanistic outcomes only
Helling 1979	RCT Subjective outcome measure - patient satisfaction only was measured
Holland 2005	Subjective primary outcomes

Study	Reason for exclusion
Ibrahim 1990	No control group
Jameson 2001	Subjective primary outcome - adverse effect and symptom score self reported by patients
Johnson 1998	Patient self-reported data
Jones 1991	Costs only reported as primary outcomes
Karki 1988	Hospital-based intervention
Knoell 1998	Not RCT
Krska 2001	Subjective primary outcome - pharmaceutical care issues identified by pharmacist
Lai 1998	Not RCT
Law 2003	Cost-savings only reported as primary outcome
Lim 2004	Relevant and interpretable data not reported for primary outcome
Malone 2000	Economic analysis only reported as primary outcome
Malone 2003	Not RCT
McKenney 1973	Not RCT
Murray 2004	Intervention not primarily performed by a pharmacist
Murray 2004a	Design paper - no results presented; Manuscript for completed study is in Studies awaiting classification section.
Peterson 1995	Not RCT
Peterson 1996	Not RCT
Peterson 1997	Not RCT
Powers 1983	Not RCT
Raisch 1990	All three comparison groups included a pharmacist intervention, therefore there was no relevant control group for this review
Rathbun 2005	Subjective primary outcome (medication compliance)
Rodgers 1999	Not RCT
Rogers 1998	Cost-savings only reported as primary outcomes
Schaffner 1983	Not RCT
Sczupak 1977	Results not interpretable
Sellors 2001	Results not interpretable - no baseline data
Sellors 2003	Results not interpretable - no baseline data

Study	Reason for exclusion
Shaw 2000	Hospital-based intervention
Shibley 1997	Patients served as their own control
Sidel 1990	Subjective primary outcome
Simpson 2001	Subgroup analysis
Simpson 2004	Subgroup analysis
Smith 1999	Cost-savings only reported as primary outcome
Soumerai 1986	Cost-savings only reported as primary outcome
Steele 1989	Cost-savings only reported as primary outcome
Tamai 1987	Not RCT
Varma 1999	Hospital-based intervention
Vrijens 2006	Subjective primary outcome (medication compliance)
Wandless 1981	Subjective primary outcome (medication compliance)
Yamada 2005	Not RCT
Zermansky 2001	Primary outcome not relevant - number of changes to prescriptions over one year

DATA AND ANALYSES

Comparison 1. Pharmacist services targeted at patients versus services delivered by other health professionals

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Outcomes Table: 2009 Review			Other data	No numeric data

Analysis 1.1. Comparison 1 Pharmacist services targeted at patients versus services delivered by other health professionals, Outcome 1 Outcomes Table: 2009 Review.

		Outcomes Table: 2009 Review					
Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
Hawkins 1979	PATIENT OUTCOMES 1. Mean systolic blood pressure (mmHg)	1. 145 vs 143 2. 86 vs 86 3. 192 vs 182	1. 147 vs 141 2. 84 vs 84 3. 184 vs 189	1. 2 vs -2 2. -2 vs -2 3. -8 vs 7	1. 4 2. 0 3. 15	1. p</= 0.001 2. not sig 3. not sig	

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
	2. Mean diastolic blood pressure (mmHg) 3. Mean fasting blood sugar (mg/dl)						

Comparison 2. Pharmacist services targeted at patients versus the delivery of no comparable service

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Outcomes Table: 2009 Review			Other data	No numeric data
2 Systolic Blood Pressure (mmHg)	4	734	Mean Difference (IV, Random, 95% CI)	-6.32 [-8.80, -3.83]
3 Diastolic Blood Pressure (mmHg)	4	734	Mean Difference (IV, Random, 95% CI)	-3.12 [-4.57, -1.67]
4 Decrease in HbA1C (%)	2	260	Mean Difference (IV, Random, 95% CI)	-0.75 [-1.41, -0.09]

Analysis 2.1. Comparison 2 Pharmacist services targeted at patients versus the delivery of no comparable service, Outcome 1 Outcomes Table: 2009 Review.

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
Barbanel 2003	PATIENT Asthma symptom score - North of England asthma scale	26.3+/-4.8 vs 27.8+/-3.7	20.3+/-4.2 vs 28.1+/-3.6	-6.0 vs 0.3	7	p-value < 0.001 95% CI 4.40-9.50	
Bogden 1997	PATIENT 1. Total cholesterol--Men (mg/dl) 2. Total cholesterol-Women (mg/dl)	n/a	n/a	1. -57 vs -26 2. -37 vs -9	1. 31 2. 28	1. not significant 2. p<0.05	
Bond 2000	PROCESS # items prescribed (median quartile) PATIENT 1. Death rate (% patients) 2. Adverse drug reactions (% patients)	PROCESS not reported PATIENT 1. n/a 2. n/a	PROCESS 2 vs 3 PATIENT 1. 3.6 vs 3.8 2. 8.3 vs 6.7	PROCESS n/a PATIENT 1. n/a 2. n/a	PROCESS n/a PATIENT 1. n/a 2. n/a	PROCESS p-value 0.0001 PATIENT 1. p-value NS* 2. p-value 0.259	*exact value not reported
Borenstein 2003	PATIENT 1. Systolic blood pressure (mmHg) 2. Diastolic blood pressure (mmHg)	1. 162 vs 156 2. 92 vs 90 3. n/a	1. 140 vs 145 2. 85 vs 82 3. 60 vs 43 %	1. -22 vs -11 2. -7 vs -8 3. n/a	1. 11 † 2. 1 † 3. 17%†	1. p-value <0.01 2. p-value <0.01 3. p-value 0.02	†calculated from reported data

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
	3. % pts achieving blood pressure control						
Brook 2003a	PATIENT SCL - general anxiety subscale*	3.1 vs 2.8	1.8 vs 1.8	-1.3 vs -1.0†	0.3†	p-value 0.4	*intention-to-treat analysis, group mean imputation (GMI) †calculated from reported data
Capoccia 2004	PATIENT SCL-20 score at 12 mo (mean(SD))	1.83(0.10) vs 1.75(0.10)	0.75 vs 0.6*	-1.08 vs -1.15†	-0.07†	p-value 0.92	*data estimated from graph †calculated from reported data
Choe 2005	PATIENT Hemoglobin A1c (%) (mean(SD))	10.1(1.8) vs. 10.2(1.7)*	8.0(1.4) vs. 9.3(2.1)	-2.1(2.5) vs -0.9(2)	1.2†	p-value 0.03	†calculated from reported data *SIG lower in control group at baseline (p-value 0.046)
Clifford 2005	PATIENT Hemoglobin A1c (%)	7.5 vs. 7.1	7 vs. 7.1†	-0.5 vs 0	0.5†	p-value 0.002*	†calculated from reported data
Cody 1998	PATIENT OUTCOME Quality of Life SF36	n/a	n/a	n/a	n/a	change not statistically significant	
Finley 2003	PATIENT 1. BIDS score (mean(SD)) 2. % pts with ≥50% reduction in BIDS score 3. % pts with remission (BIDS score < 9) 4. % patients with reduction in WSDS score	1. 18.7(5.8) vs 18.3(5.8) 2. n/a 3. n/a 4. n/a	1. 12.1 vs 9.4† 2. 40.7 vs 54.1 3. 55.6 vs 58.3 4. 56 vs 67	1. -6.6(7.3) vs -8.9(8.3) 2. n/a 3. n/a 4. n/a	1. -2.3† 2. n/a 3. n/a 4. n/a	1. p-value 0.23 2. p-value 0.27 3. p-value 0.36 4. p-value 0.36	†calculated from reported data
Gattis 1999	PATIENT All cause mortality and heart failure events at 6 mo (# of events)	n/a	4 vs 16 (OR 0.22)	n/a		p-value 0.005 (OR 95% CI 0.06, 0.63)	
Gonzalez-Martin 2003	PATIENT 1. PAQLQ score (mean(SD)): a) emotions domain b) activities domain c) symptoms domain 2. Spirometry testing (mean(SD)): a) FVC b) FEV1	1. a) 5.2(0.4) vs 5.2(0.4)‡ b) 3.8(0.3) vs 4.0(0.3)‡ c) 4.1(0.5) vs 4.6(0.4)‡ 2. a) 3.08(0.97) vs 2.66(0.19) b) 2.41(0.76) vs 2.34(0.22)	1. a) 6.5 vs 5.3 b) 6 vs 4.1 c) 6 vs 4.8 2. a) 3.13(1.14) vs 2.85(0.29) b) 2.48(0.89) vs 2.51(0.27)	1. a) 1.3 vs 0.1 b) 2.2 vs 0.1 c) 1.9 vs 0.2 2. a) 0.07 vs 0.19† b) 0.07 vs 0.17†	1. a) 1.2 b) 2.1 c) 1.7 2. a) -0.12† b) -0.1†	1. a) p-value < 0.001 b) p-value < 0.001 c) p-value < 0.002 2. a) p-value NS* b) p-value NS*	*exact p-value not provided †calculated from reported data ‡ data extrapolated from a graph
Goodyer 1995	PATIENT OUTCOMES Exercise test (1. distance in 6 min and 2. distance till breathless)	1. 138 vs 145 2. 85 vs 91	1. 159 vs 123 2. 111 vs 71	1. 21 vs -22 † 2. 26 vs -20†	1. 43† 2. 46†	p<0.001 (unclear for which outcome)	†calculated from reported data
Hanlon 1996	PATIENT SF 36 (Health Related Quality of Life) SF-36 domains: physical function-	1. n/a	1. n/a	1. n/a	1. n/a	1. p=0.99 (NS all domains)	

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
	ing, social functioning, physical role function, emotional role function, mental health, energy, pain, general health perception						
Jaber 1996	PATIENT 1. Fasting plasma glucose (mmol/L) 2. Glycated hemoglobin (%) 3.Quality of life	1. 11.1 (4.0) vs 12.7 (4.7) 2. 11.5 (2.9) vs 12.2 (3.5) 3. n/a	1. 8.5 (2.3) vs 11 (3.9) 2. 9.2 (2.1) vs 12.1 (3.7) 3. n/a	1. -2.6 vs -1.8 2. -2.2 vs -0.1 3. n/a	1. 0.8† 2. 2.1† 3. n/a	1. p<0.05 (in final fasting plasma glucose) 2. p<0.05 (mean ablsolute change in glycated hemoglobin) 3. no stat sig differences*	*p-value not reported †calculated from reported data
Jackson 2004	PATIENT 1. % pts with therapeutic INR 2. median INR 3. total bleeding up to 90 days after discharge (% pts)	1. 42 vs 45 2. 2.0 vs 2.2 3. n/a	1. 67 vs 41 2. 2.4 vs 2.1 3. 15 vs 36	1. 25 vs -4 2. 0.4 vs -0.1 3. n/a	1. 29 2. 0.5 3. n/a	1. p-value 0.01* 2. p-value 0.84* 3. p-value 0.009	*p-value for I vs C at day 8
Jameson 1995	PROCESS OUTCOMES 1. # of drugs 2. doses of drugs/day	1. 5.6 vs 5.7 2. 9.5 vs 9.9	1. 5.0 vs 6.2 2. 7.9 vs 10.5	1. -0.6 vs 0.5 2. -1.6 vs 0.6	1. 1.1 2. 2.15	1. p=0.004 2. p=0.007	
Malone 2001	PATIENT HRQOL change over 12 mo - SF-36 domains: physical functioning, role physical, bodily pain*, general health perceptions, vitality*, social functioning, role emotional, mental health*, change in health*	n/a	n/a	n/a	n/a	*p-value < 0.05	bodily pain and change in health domains were significantly higher in control group at baseline
Mehos 2000	PATIENT 1. Systolic blood pressure (mmHg) (mean(SD)) 2. Diastolic blood pressure (mmHg) (mean(SD)) 3. Mean arterial blood pressure (mmHg) (mean(SD))	1. 157.9(16.4) vs 153.9(14.6) 2. 91.1(10.8) vs 89.6(9.8) 3. 113.4(8.0) vs 111.0(6.4)	1. 140.8 vs 146.9 2. 80.6 vs 85.8 3. 100.7 vs 106.1	1. -17.1 vs -7 2. -10.5 vs -3.8 3. -12.7 vs -4.9	1. 10.1 † 2. 6.7 † 3. 7.8 †	1.p-value 0.069 2. p-value 0.022 3. p-value 0.01	†calculated from reported data
Meredith 2002	PROCESS - improvement in prescribing 1. any medication use (% pts) 2. therapeutic duplication (% pts) 3. cardiovascular medication use (% pts) 4. psychotropic medication use (% pts) 5. NSAID use (% pts)	1. n/a 2. n/a 3. n/a 4. n/a 5. n/a	1. n/a 2. n/a 3. n/a 4. n/a 5. n/a	1. 50 vs 38 2. 70.8 vs 23.5 3. 55 vs 17.6 4. 40.3 vs 31.6 5. 42.2 vs 52.1	1. 12 2. 47.3 3. 37.4 4. 8.8 5. -10	1. p-value 0.05, 95% CI 0-24 2. p-value 0.003, 95% CI 20.2-74.5 3. p-value 0.02, 95% CI 9-65.7 4. p-value > 0.2, 95% CI -9.7-27.4 5. p-value > 0.2, 95% CI -30.4-10.5	calculated from reported values

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
Odegard 2005	PATIENT 1. HbA1C at 6 mo (end of intervention) (%) (mean(SD)) 2. HbA1C at 12 mo (6 mo usual care follow-up) (%)(mean(SD))	1. 10.2(0.8) vs 10.6(1.4) 2. 10.2(0.8) vs 10.6(1.4)	1. 8.7 vs 8.8‡ 2. 8.2 vs 8.3‡	1. -1.5 vs -1.8† 2. -2 vs -2.3†	1. 0.3† 2. 0.3†	p-value 0.61	†calculated from reported data ‡ data extrapolated from a graph
Okamoto 2001	PATIENT *Note-authors did not define units for all outcomes; based on other data reported in study, it is assumed that data is reported as (mean(SD)).* 1. Systolic blood pressure (mmHg) 2. Diastolic blood pressure (mmHg) 3. QOL - SF-36 domains: physical functioning, role-physical*, bodily pain, general health, vitality, social functioning, role-emotional, mental health	1. 144.23(18.4) vs 142.91(18) 2. 82.79(11.2) vs 82.13(11.4) 3. n/a	1. 135.10(15.3) vs 141.66(17.90) 2. 77.65(11.2) vs 80.67(10.2) 3. n/a	1. -9.13(17.1) vs -1.32(15.7) 2. -5.14(9.2) vs -1.46(10.1) 3. n/a	1. 7.81 † 2. 3.68 † 3. n/a	1. p-value < 0.001 2. p-value < 0.001 3. *p-value SIG	†calculated from reported data
Park 1996	PATIENT OUTCOMES 1. Systolic Blood Pressure (mmHg) 2. Diastolic Blood Pressure (mmHg) 3. Health Status Questionnaire (HSQ)	1. 155 (21.1) vs 147.9 (18.6) 2. 87.9 (9.9) vs 83.3 (8.5) 3. n/a	1. 143.2 (11.5) vs 148.6 (20.1) 2. 83.2 (8) vs 83.7 (10.9) 3. n/a	1. -11.8 vs 0.7 2. -4.7 vs 0.4 3. n/a	1. 12.5 2. 5.1 3. n/a	1. no p-value reported 2. no p-value reported 3. p<0.05 only in energy/fatigue category (no sig in other 7 categories)	
Paulos 2005	PATIENT 1. Total cholesterol (mg/dL) 2. Triglycerides (mg/dL) 3. % pts with decrease in total cholesterol 4. % pts with decrease in triglycerides	1. 205.1(44.7) vs 203.2(40.6) 2. 190.7(88.7) vs 163.6(116.4) 3. n/a 4. n/a	1. 178(31.1) vs 199.1(37.6) 2. 140.3(47.6) vs 193.2(108.0) 3. 72.8 vs 33.3 4. 77.3 vs 27.8	1. -27.1(41.1) vs -1.4(37.2) 2. -50.5(80.3) vs 29.6(118.5) 3. n/a 4. n/a	1. 25.7 2. 80.0 3. n/a 4. n/a	1. p-value 0.0266* 2. p-value 0.0169* 3. p-value n/a 4. p-value n/a	*p-value for change in intervention group over study period
Peterson 2004	PATIENT cholesterol levels - mmol/L (mean(SD))	4.8(0.70) vs 4.8(0.9)	4.4(0.6) vs 4.6(0.8)	-0.4 VS -0.2†	0.2†	p-value 0.24*	*p-value for I vs C at follow-up †calculated from reported data
Rickles 2005	PATIENT ≥50% improvement in BDI-II score (# (%) pts)	n/a	21 (75) vs 21 (65.6)	n/a	n/a	p-value NS*	*exact value not reported
Sadik 2005	PATIENT 1. mean distance walked in two min test @ 12 mo (meters) 2. QOL - SF-36 domains: physical functioning, role-physical*, bodily pain*, gen-	1. 124 vs 120.8 2. n/a	1. 140.2 vs 117.2 2. n/a	1. 16.2 vs -3.6 † 2. n/a	1. 19.8 † 2. n/a	1. p-value 0.001‡ 2. *p-value SIG	†calculated from reported data ‡p-value for I vs C at 12 months

Outcomes Table: 2009 Review

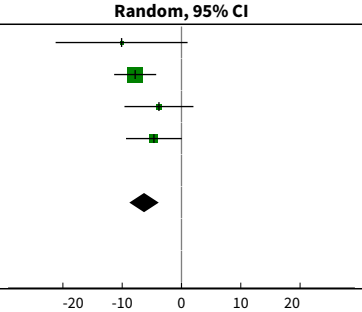
Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
	eral health, vitality*, social functioning*, role-emotional*, mental health*						
Sarkadi 2004	PATIENT 1. Hemoglobin A1c at 12 months (end of study) (%) 2. Hemoglobin A1c at 24 months (follow-up) (%)	1. 6.5 vs. 6.5† 2. 6.5 vs. 6.5†	1. 6.3 vs. 6.4† 2. 6.2 vs. 6.6†	1. -0.2 vs. -0.1† 2. -0.3 vs. 0.15†	1. 0.1† 2. 0.4†	1. p-value NS*‡ 2. p-value 0.023‡	*actual value not provided †values extrapolated from graph ‡p-value for I vs C at the end of study period
Schneider 1982	PATIENT 1. Systolic blood pressure (mmHg) 2. Diastolic blood pressure (mmHg)	1. 169 vs 162 2. 98 vs 97	1. 139 vs 153 2. 89 vs 92	1. -20 vs -9 † 2. -9 vs -5 †	1. 11 † 2. 4 †	1. p-value <0.05* 2. p-value <0.05*	*p-value for I vs C at 12 mo †calculated from reported data
Solomon 1998	PATIENT 1. Systolic Blood Pressure - 1st measurement (mmHg) (mean(SD)) 2. Systolic Blood Pressure - 2nd measurement (mmHg) (mean(SD)) 3. Diastolic Blood Pressure - 1st measurement (mmHg) (mean(SD)) 4. Diastolic Blood Pressure - 2nd measurement (mmHg) (mean(SD)) 5. BORG Scale - pre-challenge score 6. BORG Scale - post-challenge score	1. 146.7(16.8) vs 146.2(17.0) 2. 144.4(17.2) vs 146.4(16.3) 3. 84.6(13.2) vs 87.0(10.9) 4. 85.0(13.0) vs 86.0(10.4) 5. 2.63(2.33) vs 2.03(1.71) 6. 0.7(0.092) vs 0.68(0.94)	1. 138.5(13.9) vs 144.9(21.3) 2. 138.2(12.9) vs 144.0(20.1) 3. 80.2(9.6) vs 83.2(11.5) 4. 80.6(8.7) vs 83.3(11.5) 5. 2.24(2.46) vs 2.44(2.26) 6. 0.87(1.10) vs 1.24(1.48)	1. -8.2 vs -1.3 2. -6.2 vs -2.4 3. -4.4 vs -3.8 4. -4.4 vs -2.7 5. -0.39 vs 0.41† 6. 0.17 vs 0.56†	1. 6.9 † 2. 3.8 † 3. 0.6 † 4. 1.7 † 5. 0.8† 6. 0.39†	1. p-value 0.044‡ 2. p-value NS** 3. p-value NS** 4. p-value NS** 5. p-value NS** 6. p-value NS**	†calculated from reported data ‡p-value for I vs C at the end of intervetion *p-value for I vs C at end of intervention ** actual p-values not reported
Sookaneknun 2004	PATIENT 1. Systolic blood pressure (mmHg) (mean(SD)) 2. Diastolic blood pressure (mmHg) (mean(SD)) 3. % patients controlled for systolic blood pressure and diastolic blood pressure	1. 144.76(19.69) vs 142.41(19.81) 2. 85.72(13.56) vs 85.86(12.94) 3. 22.9 vs 17.9	1. 121.47(14.90) vs 124.77(17.97) 2.71.55(10.80) vs 74.23(11.87) 3. 66.1 vs 57.3	1. -23.29(19.10) vs -18.64(17.67) 2. -14.18(11.20) vs -11.73(10.08) 3. 43.2 vs 39.4	1. 4.65 † 2. 2.45 † 3. 3.8%	1. p-value <0.001 2. p-value <0.001 3. p-value 0.061	†calculated from reported data
Taylor 2003	PROCESS 1. # of medications at 12 mo (mean(SD)) 2. #of inappropriate prescriptions for all MAI domains PATIENT 1. # (%) pts at goal for hypertension 2. # (%) pts at goal for diabetes	PROCESS 1. 6.3(2.2) vs 5.7(1.7) 2. 831 vs 895 PATIENT 1. 3 (12.5) vs 9 (31) 2. 3 (23.1) vs 9 (56.3) 3. 2 (10.5) vs 3 (15.8) 4. 1 (25) vs 3 (50) 5. n/a	PROCESS 1. 4.7(2.0) vs 6.2(2.0) 2. 264 vs 978 PATIENT 1. 22 (91.7) vs 8 (27.6) 2. 13 (100) vs 5 (26.7) 3. 14 (77.8) vs 1 (5.9) 4. 4 (100) vs 1 (16.7) 5. n/a	PROCESS 1. -1.6 vs 0.5† 2. -567 vs 83† PATIENT 1. 19 (79.2) vs -1 (-3.4)† 2. 10 (76.9) vs -4 (-29.6)† 3. 12 (67.3) vs -2 (-9.9)† 4. 3 (75) vs -2 (-33.3)† 5.n/a	PROCESS 1. 2.1† 2. 650† PATIENT 1. 20 (82.6)† 2. 14 (106.5)† 3. 14 (77.2)† 4. 5 (108.3)† 5. n/a	PROCESS 1. p-value 0.002* 2. not reported PATIENT 1. p-value 0.001* 2. p-value 0.001* 3. p-value 0.001* 4. p-value 0.048* 5. p-value NS (all domains)	†calculated from reported data *p-value for I vs C at 12 mo

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (intervention vs control group)	Post-intervention (intervention vs control group)	Change due to intervention (intervention vs control group)	Result interval (ΔI - ΔC)	Significance	Notes
	3. # (%) pts at goal for dyslipidemia 4. # (%) pts at goal for anticoagulation 5. QOL - SF-36 domains: physical functioning, social functioning, physical role function, emotional role function, mental health, energy, pain, general health perception						
Tsuyuki 2002	HEALTH PROFESSIONAL % patients reaching a composite outcome†	n/a	57 vs. 31% (odds ratio 3.0)	n/a	n/a	p-value <0.001 95% CI 2.2-4.1	†composite score of complete cholesterol panel done by PCP OR new prescription for cholesterol lowering medication OR increase in dosage of cholesterol lowering medication
Van Veldhuizen 1995	PATIENT OUTCOMES Mean Blood glucose levels (mg/dl) (Group II=1st; Group III=2nd; Control=3rd)	164† vs 168† vs 189†	140† vs 152† vs 158†	-24† vs -16† vs -31†	Gp II vs C = 7* GpIII vs C =15*	Pts in intervention groups achieved lower average weekly blood glucose values than control group (p<0.05)	†values extrapolated from graph *calculated
Weinberger 2002	PATIENT (PC vs PFM vs UC)* 1. unadjusted PERFs at 12 mo (% predicted) (mean(SD)) 2. overall HRQOL with asthma, COPD	1. 63.8(21.6) vs 61.2(22) vs 60.4(22) 2. n/a	1. 65.5(19.5) vs 64.2(21.5) vs 61.6(22.6) 2. n/a	1. -1.7 vs -3 vs -1.2† 2. n/a	1. 1.3 (PC vs PFM), 0.5 (PC vs UC)† 2. n/a	1. p-value 0.006 across all groups, 0.28 for PC vs PFM at 12 mo 2. p-value NS	*PC = pharmaceutical care program PFM = peak flow meter monitoring program UC = usual care program †calculated from reported data

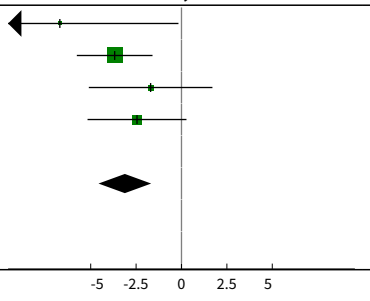
Analysis 2.2. Comparison 2 Pharmacist services targeted at patients versus the delivery of no comparable service, Outcome 2 Systolic Blood Pressure (mmHg).

Study or subgroup	Intervention group N	Intervention group Mean(SD)	Control group N	Control group Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Mehos 2000	18	-17.1 (18)	18	-7 (16)		4.97%	-10.1[-21.23,1.03]
Okamoto 2001	164	-9.1 (17.1)	166	-1.3 (15.7)		49.02%	-7.81[-11.35,-4.27]
Solomon 1998	63	-6.2 (18)	70	-2.4 (16)		18.2%	-3.8[-9.61,2.01]
Sookaneknun 2004	118	-23.3 (19.1)	117	-18.6 (17.7)		27.81%	-4.65[-9.35,0.05]
Total * **	**363**		**371**			**100%**	**-6.32[-8.8,-3.83]**
Heterogeneity: Tau²=0; Chi²=2.33, df=3(P=0.51); I²=0%							
Test for overall effect: Z=4.99(P<0.0001)							



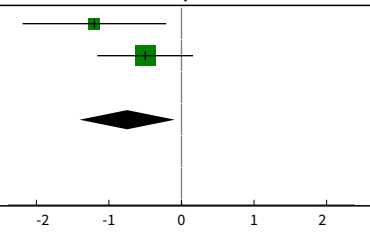
Analysis 2.3. Comparison 2 Pharmacist services targeted at patients versus the delivery of no comparable service, Outcome 3 Diastolic Blood Pressure (mmHg).

Study or subgroup	Intervention group N	Mean(SD)	Control group N	Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Mehos 2000	18	-10.5 (10)	18	-3.8 (10)		4.93%	-6.7[-13.23,-0.17]
Okamoto 2001	164	-5.1 (9.2)	166	-1.5 (10.1)		48.5%	-3.68[-5.76,-1.6]
Solomon 1998	63	-4.4 (10)	70	-2.7 (10)		18.18%	-1.7[-5.1,1.7]
Sookaneknun 2004	118	-14.2 (11.2)	117	-11.7 (10.1)		28.39%	-2.45[-5.17,0.27]
Total ***	**363**		**371**			**100%**	**-3.12[-4.57,-1.67]**
Heterogeneity: Tau^2=0; Chi^2=2.33, df=3(P=0.51); I^2=0%							
Test for overall effect: Z=4.21(P<0.0001)							



Analysis 2.4. Comparison 2 Pharmacist services targeted at patients versus the delivery of no comparable service, Outcome 4 Decrease in HbA1C (%).

Study or subgroup	Intervention group N	Mean(SD)	Control group N	Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
Choe 2005	41	-2.1 (2.5)	39	-0.9 (2)		35.55%	-1.2[-2.19,-0.21]
Clifford 2005	92	-0.5 (2.5)	88	0 (2)		64.45%	-0.5[-1.16,0.16]
Total ***	**133**		**127**			**100%**	**-0.75[-1.41,-0.09]**
Heterogeneity: Tau^2=0.06; Chi^2=1.33, df=1(P=0.25); I^2=24.82%							
Test for overall effect: Z=2.23(P=0.03)							



Comparison 3. Pharmacist services targeted at health professionals versus the delivery of no comparable service

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Outcomes Table: 2009 Review			Other data	No numeric data

Analysis 3.1. Comparison 3 Pharmacist services targeted at health professionals versus the delivery of no comparable service, Outcome 1 Outcomes Table: 2009 Review.

	Outcomes Table: 2009 Review						
Study	Primary outcomes	Pre-intervention (I vs C)	Post-intervention (I vs C)	Change due to intervention (I vs C)	Result interval (I - C)	Significance Measure	Notes
Diwan 1995	PROCESS number of Rx of lipid-lowering drugs/month	Women: 25.6 vs 22 Men: 20 vs 17	Women: 35.5 vs 21 Men: 28 vs 20.6	Women: 9.9 vs -1† Men: 8 vs 3.6†	Women: 10.9† Men: 4.4†	n/a* Stat sig change in # of Rxs among women	*exact value not reported †calculated from reported data
Freemantle 2002	PROCESS increase in # of pts treated ac-	n/a	n/a	n/a	5.2% (OR = 1.24)	95% CI 1.7, 8.7 (OR 95% CI 1.07-1.42)	

Outcomes Table: 2009 Review

Study	Primary outcomes	Pre-intervention (I vs C)	Post-intervention (I vs C)	Change due to intervention (I vs C)	Result interval (I - C)	Significance Measure	Notes
	cording to practice guidelines						
Hall 2001	PROCESS 1. change in omeprazole use due to intervention 2. change in metronidazole use due to intervention	1. n/a 2. n/a	1. n/a 2. n/a	1. n/a 2. n/a	1. -0.02 dose units per year 2. -0.005 dose units per year	1. 95% CI -0.12, 0.08 2. 95% CI -0.025, 0.015	
Ilett 2000	PROCESS Antibiotic prescribing (# all ABX RXs)	5182 vs 6666	7262 vs 9654	-2080 vs -2988	908	p-value n/a*	*not reported
Stergachis 1987	PROCESS number of Rx per 1000 enrollees per physician (1. piroxicam, 2. ibuprofen, 3. salicylates)	1. 58 vs 27 2. 167 vs 194 3. 142 vs 114	1. 55 vs 40 2. 183 vs 202 3. 213 vs 125	1. -3 vs 13† 2. 16 vs 8† 3. 71 vs 11†	1. -16† 2. 8† 3. 60†	1. ns* (p-value n/a) 2. ns* (p-value n/a) 3. sig* (p-value n/a)	*exact value not reported †calculated from reported data
Turner 2000	PROCESS 1. utilization of ACEIs in patient receiving digoxin and furosemide for CHF (# of patients) 2. targeted daily dose of ACEIs (# of patients)	1. 71 vs 40 2. 52 vs 29	1. 72 vs 38 2. 59 vs 28	1. 1 vs -2† 2. 7 vs -1†	1. 3† 2. 8†	1. p-value NS* 2. p-value 0.14	*exact value not reported †calculated from reported data
Watson 2001	prescribing of ibuprofen, diclofenac and naproxen as % of total NSAID prescribing (mean %(SD)) (intervention vs mailed guideline vs no intervention)	78.1(2.6) vs 79.0(4.9) vs 77.0(7.6)	82.7(2.6) vs 81.2(3.7) vs 80.3(7.2)	4.6 vs 2.2 vs 3.3†	1. 2.1 (intervention vs no intervention) 2. 1.6 (intervention vs mailed guideline)	1. 95% CI -0.8, 5.0 2. 95% CI -1.4, 4.7	†calculated from reported data

APPENDICES

Appendix 1. EPOC search strategy (Phase I of review)

20 March 2007

(pharmacy or pharmacies)

(pharmacist*)

(limit to yr=1999-2007)

Appendix 2. MEDLINE/EMBASE search strategy (Phase II of review)

Database: Ovid MEDLINE(R) <1950 to March Week 4 2008>
Search Strategy:

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1 Pharmacy/ (7133)
2 Pharmacists/ (7094)
3 Community Pharmacy Services/ (1561)

4 (pharmacy or pharmacies or pharmacist?).tw. (26558)
5 or/1-4 (33073)
6 Outpatients/ (4996)
7 Ambulatory Care/ (29634)
8 (outpatient? or clinic? or ambulatory).tw. (232669)
9 or/6-8 (244132)
10 5 and 9 (2527)
11 randomised controlled trial.pt. (252479)
12 random$.tw. (403476)
13 control$.tw. (1640371)
14 intervention$.tw. (283147)
15 evaluat$.tw. (1307567)
16 or/11-15 (3081343)
17 10 and 16 (1269)
18 animal/ (4234665)
19 human/ (10283089)
20 18 not (18 and 19) (3195568)
21 17 not 20 (1268)
22 limit 21 to yr="1999 - 2008" (810)

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Appendix 3. EMBASE search strategy (Phase II of review)

Database: EMBASE <1980 to 2008 Week 13>
Search Strategy:
---
1 Pharmacy/ (20653)
2 Pharmacist/ (20352)
3 Clinical Pharmacy/ (2338)
4 (pharmacy or pharmacies or pharmacist?).tw. (28822)
5 or/1-4 (47390)
6 Outpatient/ (18861)
7 Outpatient Care/ (11815)
8 Ambulatory Care/ (6629)
9 (outpatient? or clinic? or ambulatory).tw. (178841)
10 or/6-9 (188274)
11 5 and "12".mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer name] (1831)
12 Randomized controlled trial/ (155932)
13 random$.tw. (365568)
14 experiment$.tw. (710140)
15 (time adj series).tw. (6431)
16 (pre test or pretest or posttest or post test).tw. (6933)
17 impact.tw. (205541)
18 intervention$.tw. (250052)
19 chang$.tw. (1151986)
20 evaluat$.tw. (1119409)
21 effect$.tw. (2558556)
22 compar$.tw. (1897202)
23 control$.tw. (1399426)
24 or/12-23 (5527329)
25 11 and 24 (1338)
26 Nonhuman/ (3042239)
27 25 not 26 (1255)
28 limit 27 to yr="1999 - 2008" (944)

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FEEDBACK

Pharmacist interventions

Summary

Where and how pharmacist can intervent in e-prescribing to reduce or prevent doctor's errors?

I certify that I have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of my criticisms.

Reply

Reply from Dr. Lisa Bero,

E-prescribing is not within the scope of our review as not all e-prescribing interventions involve pharmacists and, in fact, none of the studies in our review involved e-prescribing. However, we will mention in the discussion update that pharmacists have a potential role in e-prescribing and cite some work that Helene Lipton has done in this regard. This has been published in abstract; a full paper is being prepared.
I certify that I have no affiliations with or involvement in any organisation or entity with a direct financial interest in the subject matter of my criticisms.

Contributors

Lay Hook Kam, pharmacist

WHAT'S NEW

Date	Event	Description
1 December 2010	Amended	Conflict of interest modified.

HISTORY

Protocol first published: Issue 2, 1995
Review first published: Issue 4, 1997

Date	Event	Description
16 June 2010	New citation required but conclusions have not changed	New search, criteria for included studies changed to only include RCTs, new authors
16 June 2010	New search has been performed	Reconciled old and new studies
21 August 2008	Amended	Converted to new review format.
18 January 2000	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

LB conceived of the idea for the review.
For the first version of this review (1997), LB, NM (see Acknowledgements) and CB developed the search strategy, decided which studies should be included, extracted data from the studies, and developed the tables. KB (see Acknowledgements) conducted hand searches and extracted data. LB drafted the paper and all authors commented on the manuscript. LB is guarantor for the review.

For the last update of this review (2000), JB and LB, decided which studies should be included. JB, LB, and CB extracted data from the studies. JB drafted the review and all authors commented on the draft. LB is guarantor for the review.

For this update (2010), OM, NN, and LB reviewed studies for inclusion. OM, NN, TC, CY, and JB extracted data from the studies. NN and OM wrote the review, with contributions from TC, CY, and LB. NN is the guarantor for the review.

DECLARATIONS OF INTEREST

Christine Bond is involved in a study that could be eligible for inclusion in a future update to this review.

SOURCES OF SUPPORT

Internal sources

- University of California, San Francisco, USA.
- University of Aberdeen, UK.
- Institut Central des Hôpitaux Valaisans, Sion, Switzerland.

External sources

- No sources of support supplied

NOTES

This is Phase I of a two-part review. Phase I includes results from the EPOC search. Phase II will include results from the MEDLINE/EMBASE searches.

INDEX TERMS

Medical Subject Headings (MeSH)

*Ambulatory Care; *Community Pharmacy Services; *Delivery of Health Care; *Outcome Assessment, Health Care; *Professional Role; Hypertension [drug therapy]; Patient Education as Topic; Pharmacists; Practice Patterns, Physicians'; Prescription Drugs [supply & distribution] [therapeutic use]; Randomized Controlled Trials as Topic

MeSH check words

Humans