SUBJECT REVIEW

A Systematic Review of the Clinical and Economic Effectiveness of Clinical Pharmacist Intervention in Secondary Prevention of Cardiovascular Disease

Abdulaziz Altowaijri, MSc; Ceri J. Phillips, PhD; and Deborah Fitzsimmons, PhD

ABSTRACT

BACKGROUND: Cardiovascular disease (CVD) is considered to be the main cause of death and one of the most common diseases affecting health care systems worldwide. Many methods have been used to improve CVD outcomes, one of which is to involve clinical pharmacists in the direct care of patients with CVD.

OBJECTIVE: To perform a systematic review assessing the effectiveness of clinical pharmacist interventions within a multidisciplinary team in the secondary prevention of CVD, using studies conducted on patients with heart failure, coronary heart disease, or those with CVD risk factors.

METHODS: Extensive searches of 13 databases were performed—with no time limitation—to identify randomized controlled trials (RCT) in English that evaluated clinical pharmacist intervention in patients with CVD or with CVD risk factors. Two independent reviewers evaluated 203 citations that were the result of this search. Studies were included if they reported direct care from a clinical pharmacist in CVD or CVD-related therapeutic areas such as disease-led management or in collaboration with other health care workers; if they were RCTs; if they were inpatients, outpatients, or in the community setting; and if they included the following outcomes: CVD control or mortality, CVD risk factor control, patient-related outcomes (knowledge, adherence, or quality of life), and cost related to health care systems.

RESULTS: A total of 59 studies were identified: 45 RCT, 6 non-RCT, and 8 economic studies. 68% of the outcomes reported showed that clinical pharmacy services were associated with better improvement in patients' outcomes compared with the control group.

CONCLUSION: The involvement of a pharmacist demonstrated an ability to improve CVD outcomes through providing educational intervention, medicine management intervention, or a combination of both. These interventions resulted in improved CVD risk factors, improved patient outcomes, and reduced number of drug-related problems with a direct effect on CVD control. These improvements may lead to an improvement in patient quality of life, better use of health care resources, and a reduced rate of mortality.

J Manag Care Pharm. 2013;19(5):408-16

What is already known about this subject

- Cardiovascular disease (CVD) is one of the main causes of death worldwide and is associated with high cost impact on national economies through direct health costs, productivity losses, and informal health care costs.
- The quality of care of CVD patients has been reported to be suboptimal.
- Clinical pharmacist interventions in the care of patients with CVD or in the care of those with high risks have been evaluated in several studies. Koshman et al. (2008) conducted a systematic review to measure the clinical benefit of adding a clinical pharmacist to the care of patients with heart failure in both inpatient and outpatient settings worldwide. This review demonstrated an improvement for many outcomes, including mortality and hospitalization.

What this study adds

- The current study is the first systematic review to evaluate pharmacist interventions in coronary heart disease (CHD) and heart failure and to evaluate the effect of pharmacist intervention in the prevention of CVD risk factors whether as part of primary prevention or secondary prevention.
- Pharmacist intervention resulted in greater improvements in many outcomes than using usual care only.
- This review highlights the need for further studies to evaluate pharmacist intervention in secondary prevention of CHD in inpatient settings and for a full economic evaluation investigating the cost-effectiveness of health care services in this setting.

Cardiovascular disease (CVD) is considered to be the main cause of death worldwide.[1] In 2008, CVD was responsible for about 48% of the 36 million deaths worldwide.[1] Similar percentages were also found in countries with advanced health care systems. CVD accounted for 33.4% of deaths in the United States, 34% in the United Kingdom (UK), and in Europe, the percentage increased to close to half of all deaths (48%).[2,3] CVD is also considered the main cause of premature death in people under 70 worldwide, being responsible for about 39% of those reported deaths.[1] The main forms of CVD are coronary heart disease (CHD) and heart failure (HF). The National Institute for Health and Clinical Excellence (NICE) defined CHD as "a narrowing (stenosis) of the coronary arteries as a result of deposition of atherosclerotic plaque, which results in an insufficient supply of oxygen to the heart muscle.[4] NICE also defined HF as "a complex clinical syndrome of symptoms and signs that suggest the efficiency of the heart as a pump is impaired. It is caused by structural or functional abnormalities of the heart."[5] CHD by itself is

responsible for about 12.7% of all deaths, while it is considered to be the main cause of death in the UK, where 46% of all CVD deaths were due to CHD. On the other hand, HF is responsible for about 5% of all hospital admissions in Europe, with 40% of these admissions dying or being re-admitted within 1 year,[6] and represents a large proportion of treatment costs. For example, a U.S. report showed that HF admissions constitute about 60% of the total treatment costs.[7] CVD also has a significant economic impact through direct health care costs, productivity losses, and informal health care costs. It has been estimated that in the UK CVD costs the health care system approximately £8.7 billion and that 23% of this cost was due to medication prescribing.[8] In the United States, CVD was estimated to cost the health care system around $167 billion.[3]

Newly developed medications are designed to be more potent with precise mechanism of action. These require more attention to avoid potential inappropriate prescribing that can lead to an increase in the CVD treatment cost. The traditional method of prescribing and dispensing has proved insufficient to prevent costly consequences from improper medication use.[9] Furthermore, despite efforts made to optimize therapies through published CVD treatment guidelines, the adherence to guideline recommendations is relatively low, and the quality of care provided to patients is documented to be below the target level.[10,11] The presence of a clinical pharmacist can help decrease these problems and optimize patient therapy so as to achieve greater benefits.[12] The European Society of Clinical Pharmacy defines the role of a clinical pharmacist as one that "develop[s] and promote[s] safe and appropriate drug use with the goal of optimizing patient care."[13] The American College of Clinical Pharmacy defines clinical pharmacy as a "health science discipline in which pharmacists provide patient care that optimizes medication therapy and promotes health, wellness, and disease prevention."[14] The addition of a clinical pharmacist to the care of patients with CVD can lead to an improvement in CVD patients in many areas, including a reduction in CVD risk rates, optimizing CVD medications, improving patient knowledge and satisfaction, improving patient adherence, and preventing potential drug-related problems (DRPs). These improvements can lead to increased quality of life for CVD patients, reduced mortality rates, and decreased number of hospitalizations or emergency room (ER)/clinic visits. This, in turn, results in a decrease in total health care costs.[15,16] Clinical pharmacists may participate in such services as patient education, medicine management, or both.[14]

Previous systematic reviews conducted to measure the effect of clinical pharmacists on the direct care of patients with CVD have shown a positive impact on patient outcomes.[17-19] However, it is unknown if this impact would be seen in patients with established CHD or if it would result in a decrease or increase in health care costs. In this review, we aimed to evaluate the effectiveness of including clinical pharmacists in the treatment of patients with CVD. The scope of our review focused on the 2 main forms of CVD: CHD and HF. A comprehensive, systematic review was conducted of studies that evaluate the effects of clinical pharmacist intervention within a multidisciplinary team in the secondary prevention of CVD. Since the secondary prevention of CHD requires modification of risk factors in addition to secondary prevention medication, this review will consider the impact of clinical pharmacists in both areas, as well as their role in HF treatment. Since the intervention provided by clinical pharmacists to help control CVD risk factors is the same in primary and secondary prevention of CVD, we included studies evaluating the pharmacist effect in controlling CVD risk factors in both primary and secondary prevention. We included CVD risk factors that necessitate medication prescription in order to control them, such as hypertension, high cholesterol, diabetes mellitus (DM), and cigarette smoking.

Methods

We searched the following databases in February 2011 (with no time limitation included): Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effectiveness (DARE), Health Technology Assessment Database (HTA), MEDLINE/PubMed, Web of Knowledge, HMIC (Ovid), Cumulative Index to Nursing and Allied Health Literature (CINAHL) plus search engine, National Health Service (NHS) Evidence, Science Direct, Pharmacy Abstract, National Institute for Health's Clinical Trials.gov database, Trip database, and Current Controlled Trials (CCT; Appendix A, available online). Systematic reviews and meta-analyses were excluded because their inclusion and exclusion criteria may not have been in accord with our criteria, although their bibliographies and references were searched for additional articles that may not have been captured in our electronic database search. The results were limited to published studies in English.

Inclusion and Exclusion Criteria

We included studies if they (a) involved participants who received direct care from a clinical pharmacist in the CVD therapeutic area or for CVD risk factors; (b) described pharmacist intervention as a part of a multidisciplinary team, in collaboration with other health care workers or in disease-led management in direct patient care; (c) reported 1 of the following outcomes: CVD control or mortality, CVD risk factor control, patient-related outcomes (knowledge, adherence, or quality of life), or cost related to health care systems; (d) were randomized controlled trials (RCT); and (e) conducted in inpatient, outpatient, or community settings. Nonrandomized controlled trials (non-RCT) reporting costs and patient quality of life were described but not included in the synthesis. The description of these non-RCTs helped explain differences found in the cost or quality of life. We excluded studies that had no pharmacist involvement in service or intervention and that were

nonanalytical or interventional studies, studies with no comparison group present, studies not conducted in the CVD therapeutic area, and systematic reviews or meta-analyses.

Study Selection

We screened the electronic search results and excluded irrelevant studies based on the exclusion criteria. The screening process was implemented to select potential studies included for the evaluation. This process was performed by 1 reviewer and checked for accuracy by another. The results of the screening step were then assessed by 2 reviewers who independently evaluated the studies' titles and abstracts. Full copies of studies accepted in the abstract assessment process were then retrieved and assessed independently by 2 reviewers. Any discrepancies were resolved by discussion, or if needed, a third reviewer was consulted.

Data Extraction and Study Quality Assessment

We extracted the studies included in this review by using a standardized data extraction form. The extraction process was performed by one of our reviewers and checked for accuracy by another. Quality assessment tools used in Jadad et al. (1996)[20] were used to assess RCTs, while the technique from Drummond et al. (2005)[21] was used to assess economic studies.

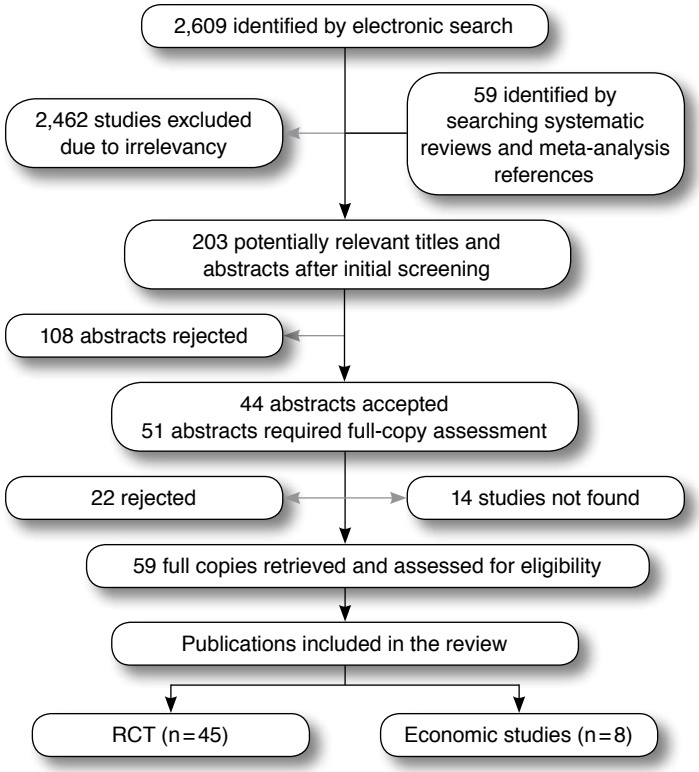
Data Analysis

Qualitative analyses were conducted to characterize the type of pharmacist services provided to patients and their effects on patient outcomes. Study outcomes were categorized into 4 groups: the CVD outcomes and mortality group (mortality, CHD risk, and HF); the CVD risk factor control group (controlling DM, hypertension, lipids, or cigarette smoking cessation); the patient outcomes group (patient adherence, knowledge, satisfaction, or quality of life); and the health care systems cost outcomes group (DRPs, hospitalization, length of hospital stay, ER/clinic visit, or direct). These outcomes were measured in each type of pharmacist-provided service, whether it was medicine management, educational intervention, or a combination of both.

Results

Our search resulted in 2,665 studies after removing any duplication, from which 2,609 studies were found from the electronic search and 56 studies from searching other systematic reviews and meta-analyses' bibliographies and references. The initial screening excluded 2,462 studies, leaving a total of 203 studies. Title and abstract assessment of the remaining 203 studies resulted in the further exclusion of 108 studies. In the process of retrieving full copies of the studies, 14 studies were not obtainable and therefore not included. The full-copy assessment process resulted in the inclusion of 59 studies, of which 51 described clinical and cost outcomes, and 8 were full economic evaluations. Figure 1 illustrates the study selection process.

FIGURE 1 Study Selection Process



RCT=randomized controlled trial.

Clinical Studies

The majority of clinical studies measured pharmacist impact on CVD risk factor control. Fifteen studies were conducted to measure the impact of a clinical pharmacist in improving patients' DM, 12 in hypertension patients, 10 in hyperlipidemia patients, and 1 RCT in helping smoking patients to quit. One RCT and 1 cohort study were included in this review because they concerned the benefit of clinical pharmacists in improving DRPs associated with CVD risk factor control. The CVD risk factor control and DRP studies were conducted in inpatient, outpatient, and community settings. (Appendix B, available online)

RCTs included in this review reported 116 different outcomes, which included mortality, CHD outcomes, HF outcomes, DM control, hypertension control, lipid control, smoking cessation, patient adherence, patient knowledge, patient satisfaction, quality of life, DRPs, hospitalization, length of hospital stay (LOS), ER/clinic visits, and direct costs. The 116 outcomes found in this review were measured as result of pharmacists providing medicine management intervention only (14), providing educational interventions only (44), or providing both types of intervention (58). When the outcomes

TABLE 1 Positive Reported Outcomes: Clinical Pharmacist Services Categorized According to Service Types

		Medicine Management (%)	Educational Intervention (%)	Educational and Medicine Management (%)	Total (%)	Total Studies
CVD	Mortality	1 (100)[24]	1 (33)[22,23,25]	-	2 (50)	6 (75%)
	CHD control	-	-	2 (100)[24,34]	2 (100)	
	HF control	1 (100)[24]	-	1 (100)[26]	2 (100)	
CVD risk factors	DM control	1 (33)[63-65]	1 (50)[29,30,50,59]	7 (100)[27,31-36]	10 (71.5)	44 (74.6%)
	Smoking cessation	-	1 (100)[37]	0 (0)[31]	1 (50)	
	BP control	1 (50)[38,63]	6 (86)[29,30,39-42,66]	13 (93)[26,27,31,34-36,43-49,67]	20 (86.9)	
	Lipid control	1 (50)[51,63]	7 (78)[29,30,41,42,50,52-55]	5 (56)[27,31,34-36,49,56-58]	13 (65)	
Patient outcomes	Adherence	1 (100)[63]	3 (100)[22,25,42]	2 (66.6)[44,48,61]	6 (85.7)	22 (70%)
	Knowledge	-	3 (100)[29,50,59]	1 (50)[48,57]	4 (80)	
	Satisfaction	-	2 (100)[25,59]	3 (75)[43,48,49,60]	5 (83.3)	
	Quality of life	0 (0)[62]	2 (33.3)[22,23,25,30,55,59]	5 (83.3)[26,43,44,48,58,61]	7 (53.8)	
Health care systems costs	DRPs	1 (100)[24]	1 (100)[29]	0 (0)[36,60]	2 (50)	8 (61.5%)
	Hospitalization	-	1 (33)[22,23,25]	-	1 (33)	
	LOS	-	1 (100)[25]	-	1 (100)	
	ER/clinic visit	-	-	1 (33)[36,48,56]	1 (33)	
	Cost	0 (0)[51,62]	1 (100)[40]	3 (75)[47,49,56,61]	4 (57.1)	
Total (%)		7 (50)	30 (68.2)	43 (74.1)	69%	

BP = blood pressure; CHD = coronary heart disease; CVD = cardiovascular disease; DM = diabetes mellitus; DRPs = drug-related problems; ER = emergency room; HF = heart failure; LOS = length of stay.

were categorized according to the setting, 62 outcomes were measured in outpatients settings, 51 in community settings, and 3 in inpatient settings. Table 1 summarizes the different types of outcomes and types of services provided by the pharmacists. Table 2 categorizes the reported outcomes according to the settings.

CVD and Mortality. Eight RCTs reported improvement in CVD or mortality as 1 of their outcomes. Five out of 7 studies showed that clinical pharmacists have a statistical significant effect, while 2 studies showed no significant differences. The 2 studies that reported no significant differences in patient mortality were performed by providing educational intervention only.[22,23] The other 5 studies reported statistical significant differences: 1 study measuring improvements in mortality and HF through medicine management only,[24] 1 study measuring mortality after educational intervention only,[25] and 3 studies measuring improvement in CHD and HF by providing both types of service.[23,26,27] All the studies reporting outcomes related to CHD or HF control showed statistical significant improvement.

Risk Factor Control. Thirty-six RCT were found to report changes in CVD risk factors as 1 of their outcomes. In terms of DM control, 10 studies out of 14 reported statistically significant improvements with clinical pharmacist interventions. Of the studies demonstrating a significant difference, 1 intervention was medicine management only;[28] 2 studies were educational interventions only;[29,30] and 7 studies consisted of both types of services.[27,31-36] In terms of measuring the effect of pharmacist intervention on smoking cessation, only 2 studies were found that reported smoking cessation as one of their outcomes. One study of educational intervention found that there was a significant effect, while another study of both types of interventions reported no significant differences.[31,37] In terms of controlling blood pressure, 20 studies out of 23 (86.9%) showed statistical significant effects of clinical pharmacist intervention. Of these studies, 1 performed medicine management (50%);[38] 6 studies provided educational interventions (86%);[29,30,39-42] and 13 studies provided both types of intervention (93%).[26,27,31,34-36,43-49] In terms of controlling patients' lipid levels, 13 studies out of 20 (65%) showed a significant positive effect with the inclusion of a clinical pharmacist.[27,29,34,42,50-58]

Patient Outcomes. We found 20 different studies that reported outcomes relating to patient knowledge, satisfaction, adherence, or quality of life. Twenty-two outcomes out of 31 (71%) were found to have statistical significant differences with clinical pharmacist intervention, while 9 of the outcomes showed no statistical significant difference. In terms of patient knowledge, 4 studies (80%) showed positive effects for clinical pharmacist intervention,[29,50,57,59] while 1 study showed no significant differences.[48] Educational intervention was performed in 3 different studies, and all of them reported significant positive differences for clinical pharmacist intervention. One study in which both types of services were provided showed statistical significant differences, while another study showed no significant effect. In terms of patient satisfaction, 5 out of 6 studies (83.3%) reported statistical significant positive outcomes with clinical pharmacist services. In 2 of the studies, pharmacists provided educational

TABLE 2 *Clinical Pharmacist Intervention Outcomes Categorized According to Setting and Type of Outcomes Measured*

		Inpatients	Outpatients	Community
CVD	Mortality	-	2[24,25]	2[22,23]
	CHD control	-	1[27]	1[23]
	HF control	-	2[24,26]	-
CVD risk factors	DM control	-	7[27,28,31,32,36,59,65]	7[29,30,33-35,50,63]
	Smoking cessation	-	1[31]	1[37]
	BP control	-	14[26,27,31,36,38,40-42,45-48,66,67]	9[29,30,34,35,39,43,44,49,63]
	Lipid control	-	9[27,31,36,41,42,51,54-56]	11[29,30,34,35,49,50,52,53,57,58,63]
Patient outcomes	Adherence	1[61]	3[25,42,48]	3[22,44,63]
	Knowledge	-	2[48,59]	3[29,50,57]
	Satisfaction	-	4[25,48,59,60]	2[43,49]
	Quality of life	1[61]	5[25,26,48,55,59]	7[22,23,30,43,44,58,62]
Health care systems costs	DRPs	-	3[24,36,60]	1[29]
	Hospitalization	-	1[25]	2[22,23]
	LOS	-	1[25]	-
	ER/clinic visit	-	3[36,48,56]	-
	Cost	1[61]	4[40,47,51,56]	2[49,62]

BP = blood pressure; CHD = coronary heart disease; CVD = cardiovascular disease; DM = diabetes mellitus; DRPs = drug-related problems; HF = heart failure; LOS = length of stay; ER = emergency room.

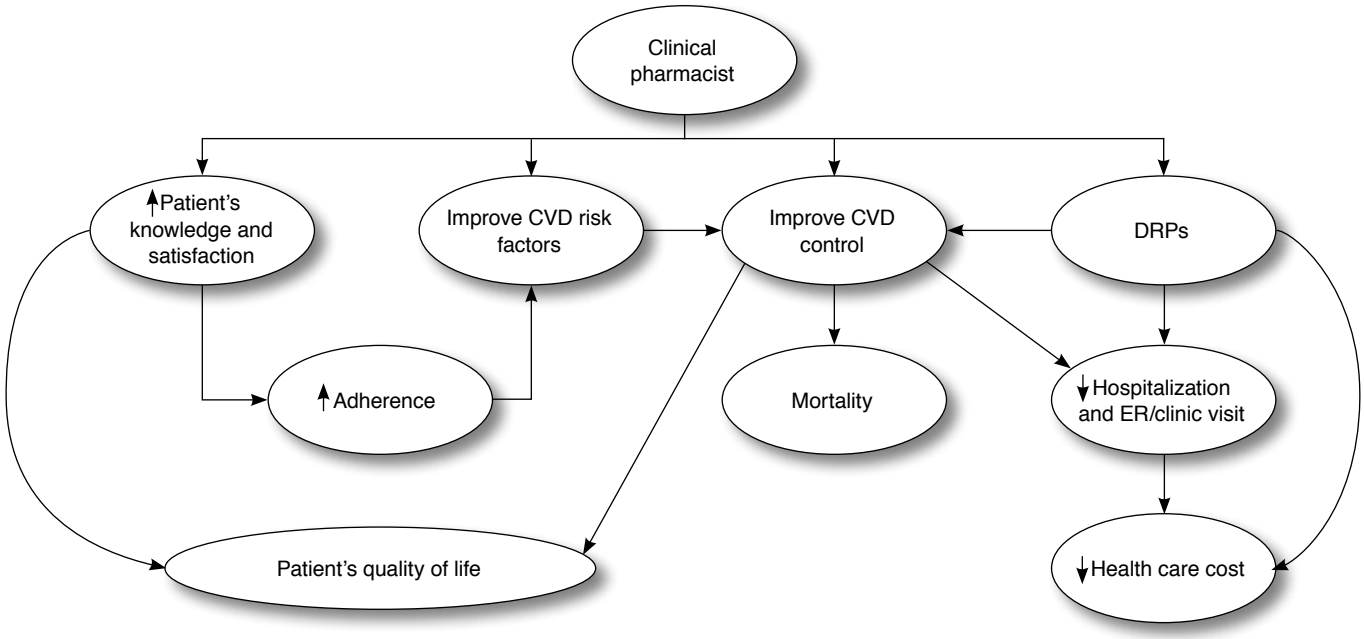
intervention, and in the other 3, they provided both medicine management and educational intervention.[25,43,48,49,59,60] One of the studies in which both services were provided showed no significant differences. In terms of patient quality of life, 7 out of 13 (53.8%) studies showed statistical significant effects for pharmacist intervention.[22,23,25,26,30,43,44,48,55,58,59,61,62] Two studies used educational intervention, and 5 studies provided medicine management and educational intervention. There was only 1 study in which just medicine management intervention was used, and it showed no significant differences.

Health Care Systems Cost. In our review, we found 16 studies that reported a total of 18 outcomes related to health care cost. These outcomes included DRPs, hospitalization, LOS, ER/clinic visits, and direct costs. DRPs were reported in 4 studies, of which 1 study used medicine management intervention and 1 provided educational intervention; these showed statistical significant effects for clinical pharmacist intervention.[24,29] Two studies using both types of intervention showed no significant improvement.[36,60] In terms of patient hospitalization, 1 study out of 3 that used educational intervention (33.3%) showed a statistical significant improvement.[22,23,25] No studies were conducted using medicine management or both types of intervention. In terms of LOS, we found only 1 study that used educational intervention and showed significant improvement.[25] In terms of the number of ER/clinic visits, 3 studies were carried out by providing both types of intervention.[36,48,56] One study showed positive effects in the clinical pharmacist group; another showed no significant differences; and 1 study showed significant differences in the control group. In studies reporting direct costs as one of their outcomes, there were 4 studies found to have significant effect with clinical pharmacist intervention (1 educational and 3 with both types of interventions provided).[40,47,56,61] Three studies were conducted in outpatient settings and 1 in inpatient settings. Two studies reported lower costs in the intervention group through savings in medication costs, while 2 studies reported lower costs through savings in the total health care costs. Two studies using medicine management intervention failed to show any significant differences, while 1 study that performed both types of interventions showed statistical significant differences in the control group.[49,51,62]

Economic Studies

We identified and included 8 economic studies in our review (Appendix C, available online). All of the economic studies were conducted as pharmacist-led interventions in community settings, except 1 that was conducted in an outpatient clinic. Three studies measured the economic impact of pharmacists in helping patients quit smoking; 2 studies involved patients with DM; and 1 study each addressed CHD, hyperlipidemia, and hypertension patients. Four economic studies were found to be cost-effectiveness analyses, while there was 1 each that addressed cost-benefit analysis, cost-utility analysis, cost-minimization analysis, and cost analysis. Three studies used an economic evaluation model, while 5 studies did not. In terms of helping patients quit smoking, 2 cost-effectiveness studies[68,69] and 1 cost-utility analysis[70] found that using pharmacists to provide smoking cessation services resulted in a better use of health care resources. The same results were found with pharmacists providing interventions to improve DM control,[71]

FIGURE 2 *Pharmacist Effect in Improving Clinical Outcomes and Decreasing Costs*



CVD = cardiovascular disease; DRPs = drug-related problems; ER = emergency room.

hypertension,[72] and lipid control.[73] Only 1 study reported an increase in the use of health care resources, with no change in patient outcomes.[74] This study was a cost-minimization study conducted to measure improvement in CHD outcomes. Five studies looked at the health care system, while 2 studies used a societal approach,[68,72] and 1 study took a government perspective.[73] Four studies reported pharmacist services providing educational intervention; 1 study examined medicine management; and 3 studies reported on educational and medicine management interventions. None of the studies considered longer-term effects through using an economic model. Figure 2 describes the process relationships of interventions by which clinical pharmacists can help improve clinical and economic outcomes of CVD patient care. It shows that medicine management interventions have an influence in CVD management and CVD risk factor control and in reducing the number of DRPs. This may lead to better quality of life and less mortality and reduce the number of hospitalizations or ER/clinic visits, which will contribute to reducing health care costs. Further improvements were gained through educational interventions affecting patient knowledge, satisfaction, and adherence to medications.

Discussion

The majority of outcomes reported in our review (68.6%) found that clinical pharmacy services were associated with better improvement in patient clinical outcomes compared with health care services that did not involve pharmacists in direct patient care. Clinical pharmacists have an impact on improving CVD control, improving patient quality of life, and in decreasing health care costs.

A high percentage (86.8%) of the studies measuring pharmacist impact on CVD risk factors reported significant positive outcomes, while only 2 studies evaluated the correlation with CVD control.[26,35] Clifford et al. (2005) reported that pharmacists were able to improve blood pressure and DM control, which was reflected in a significant decrease in the total CHD risk.[35] Similar results were found by Varma et al. (1999), who found that pharmacist intervention helped to decrease blood pressure, which was associated with an improvement in HF control, leading to a better score in patient quality of life measures.[26] The relationship between decreasing CVD risk factors and the improvement in CVD outcomes has been well established, and published clinical guidelines recommend an aggressive reduction in these risks.

Pharmacist intervention to improve patient outcomes such as patient satisfaction, adherence, and knowledge were found to lead to an improvement in CVD and patient quality of life. These results were found in 6 RCTs that showed improved patient outcomes were associated with an improvement in such CVD risk factors as blood pressure and lipid control.[42-44,50,61] Four RCTs found that this effect also extended to an

improvement in patient quality of life.[43,44,50,61] In 1 study, the effect of pharmacist intervention did not achieve significant changes in patient outcomes, and it was also associated with nonsignificant improvement in patient quality of life.

Pharmacist interventions to improve DRPs were associated with an improvement in CVD control and CVD risk factors. Gattis et al. (1999)[24] found that decreasing the number of DRPs in HF patients was associated with a decrease in HF events and mortality. Fornos et al. (2006)[29] found that a reduction in the number of DRPs was associated with an improvement in CVD risk factors. Both sets of results demonstrate the relationship between DRPs and improved care of patients with CVD, regardless of whether this benefit is realized through direct effects on CVD control and mortality or through better control of CVD risk factors. Patient quality of life was found to be affected by clinical pharmacist intervention through improving patient outcomes, CVD risk factor control, or both.

Studies evaluating the relationship between pharmacist intervention and health care costs showed that pharmacists can decrease total health care costs through improving CVD risk factor controls and patient outcomes. This may indicate that a reduction in health care costs by using pharmacist interventions is achieved from the positive impact they have in improving CVD or CVD risk factor outcomes. It also highlighted that pharmacist services that improve CVD or CVD risk factors may use fewer health care resources.

Considering the potential positive CVD outcomes and health care system savings associated with pharmacist interventions, it seems reasonable to conduct a full economic study to evaluate the cost-effectiveness of involving clinical pharmacists in the direct care of patients with CVD.

Limitations

This systematic review provided evidence of pharmacist benefits in the care of patients with CVD, although there are several limitations that affect the robustness of its conclusion. The review only includes published studies that are more likely to exist if positive outcomes emerge. It also included data from different settings and provided by different types of interventions, which may increase the level of heterogeneity of the results. The review only included 1 clinical study conducted in an inpatient setting, which makes the estimation of pharmacist effect in this setting less reliable. Furthermore, the economic studies found in this review that intended to measure the cost-effectiveness of clinical pharmacist interventions with CVD patients had a number of limitations, including not providing a detailed explanation of pharmacist effect nor considering longer-term effects using economic modeling.

Conclusion

Clinical pharmacist intervention can result in a significant improvement in CVD patient outcomes. This can be achieved by improving various aspects of the process, including patient outcomes (knowledge, satisfaction, and adherence), CVD risk factor control, reducing the number of DRPs, and direct improvement in CVD control. These improvements may lead to an improvement in patient quality of life and mortality thus decreasing health care resources used. The quantity of this effect and its relation to the expected funds required to run such services is unknown. Because of deficiencies in current economic studies, further economic evaluations are required to assess the cost-effectiveness of clinical pharmacist intervention in patients with CVD.

Authors

ABDULAZIZ ALTOWAIJRI, MSc, is Researcher; CERI J. PHILLIPS, PhD, is Professor and Deputy Head; and DEBORAH FITZSIMMONS, PhD, is Reader and Director of Studies–Postgraduate Research, College of Human and Health Sciences, Swansea University, Swansea, Wales, United Kingdom.

AUTHOR CORRESPONDENCE: Abdulaziz Altowaijri, MSc, College of Human and Health Sciences, Vivian Tower, 2nd Fl., Swansea University, Swansea, SA2 8PP Wales, United Kingdom. Tel.: +44 (0) 1792.295729; Fax: +44 (0) 1792.295643; E-mail: Abdulaziz.altowaijri@gmail.com.

DISCLOSURES

The authors report no conflicts of interest regarding this study.

Concept and design were performed by Altowaijri, Phillips, and Fitzsimmons. Data were collected by Altowaijri and interpretated by Altowaijri, Fitzsimmons, and Phillips. Altowaijri wrote the manuscript with the help of Phillips and Fitzsimmons, and the manuscript was revised by Altowaijri, Phillips, and Fitzsimmons.

REFERENCES

1. World Health Organization. Noncommunicable diseases country profiles 2011. September 2011. Available at: http://www.who.int/nmh/publications/ncd_profiles2011/en/index.html. Accessed April 23, 2013.

2. Lloyd-Jones D, Adams R, Carnethon M, et al. Heart disease and stroke statistics—2009 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation*. 2009;119(3):e182.

3. Roger VL, Go AS, Lloyd-Jones DM, et al. Heart disease and stroke statistics—2011 update: a report from the American Heart Association. *Circulation*. 2011;123(4):e18-e209.

4. National Institute for Health and Clinical Excellence. Drug-eluting stents for the treatment of coronary artery disease (part review of NICE technology appraisal guidance 71). NICE technology appraisal guidance 152. July 2008. Available at: http://www.nice.org.uk/nicemedia/live/12013/41262/41262.pdf. Accessed April 23, 2013.

5. National Institute for Health and Clinical Excellence. CG108 Chronic heart failure: management of chronic heart failure in adults in primary and secondary care. NICE clinical guidelines. August 2010. Available at: http://publications.nice.org.uk/chronic-heart-failure-cg108. Accessed April 23, 2013.

6. Dickstein K, Cohen-Solal A, Filippatos G, et al. ESC guidelines for the diagnosis and treatment of acute and chronic heart failure 2008. *Eur Heart J.* 2008;29(19):2388-442.

7. Braunschweig F, Cowie MR, Auricchio A. What are the costs of heart failure? *Europace*. 2011;13(Suppl 2):ii13-ii17.

8. British Heart Foundation. Heart statistics. 2012. Available at: http://www.bhf.org.uk/research/heart-statistics.aspx. Accessed April 23, 2013.

9. Manasse H Jr. Medication use in an imperfect world: drug misadventuring as an issue of public policy, Part 2. *Am J Hosp Pharm*. 1989;46(6):1141-52.

10. Fonarow GC, Yancy CW, Heywood JT; ADHERE Scientific Advisory Committee, Study Group, and Investigators. Adherence to heart failure quality-of-care indicators in US hospitals: analysis of the ADHERE Registry. *Arch Intern Med*. 2005;165(13):1469-77.

11. Lewis SJ, Robinson JG, Fox KM, et al. Underutilisation of cardiovascular medications among at-risk individuals. *Int J Clin Pract*. 2010;64(5):604-10.

12. Kaboli PJ, Hoth AB, McClimon BJ, Schnipper JL. Clinical pharmacists and inpatient medical care: a systematic review. *Arch Intern Med*. 2006;166(9):955-64.

13. Beney J. What is clinical pharmacy? European Society of Clinical Pharmacy. December 11, 2010. Available at: http://www.escpweb.org/cms/Clinical_pharmacy. Accessed April 23, 2013.

14. American College of Clinical Pharmacy. The definition of clinical pharmacy. *Pharmacotherapy*. 2008;28(6):816-17.

15. Chisholm-Burns MA, Graff Zivin JS, Lee JK, et al. Economic effects of pharmacists on health outcomes in the United States: a systematic review. *Am J Health Syst Pharm*. 2010;67(19):1624-34.

16. Chisholm-Burns MA, Kim Lee J, Spivey CA, et al. US pharmacists' effect as team members on patient care: systematic review and meta-analyses. *Med Care*. 2010;48(10):923-33.

17. Koshman SL, Charrois TL, Simpson SH, et al. Pharmacist care of patients with heart failure: a systematic review of randomized trials. *Arch Intern Med*. 2008;168(7):687-94.

18. Ponniah A, Anderson B, Shakib S, et al. Pharmacists' role in the post-discharge management of patients with heart failure: a literature review. *J Clin Pharm Ther.* 2007;32(4):343-52.

19. Blenkinsopp A, Anderson C, Armstrong M. Systematic review of the effectiveness of community pharmacy based interventions to reduce risk behaviours and risk factors for coronary heart disease. *J Public Health Med*. 2003;25(2):144-53.

20. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? *Control Clin Trials*. 1996;17(1):1-12.

21. Drummond MF, Sculpher MJ, Torrence GW, O'Brien BJ, Stoddart GL. *Methods for the Economic Evaluation of Health Care Programmes*. 3rd ed. Oxford: Oxford University Press; 2005.

22. Bouvy ML, Heerdink ER, Urquhart J, et al. Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: a randomized controlled study. *J Card Fail.* 2003;9(5):404-11.

23. Holland R, Brooksby I, Lenaghan E, et al. Effectiveness of visits from community pharmacists for patients with heart failure: HeartMed randomised controlled trial. *BMJ*. 2007;334(7603):1098.

24. Gattis WA, Hasselblad V, Whellan DJ, O'Connor CM. Reduction in heart failure events by the addition of a clinical pharmacist to the heart failure management team: results of the Pharmacist in Heart Failure Assessment Recommendation and Monitoring (PHARM) Study. *Arch Intern Med*. 1999;159(16):1939-45.

25. López Cabezas C, Falces Salvador C, Cubí Quadrada D, et al. Randomized clinical trial of a postdischarge pharmaceutical care program vs. regular follow-up in patients with heart failure. *Farm Hosp*. 2006;30(6):328-42. [Article in English, Spanish]

26. Varma S, McElnay J, Hughes C, Passmore A, Varma M. Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. *Pharmacotherapy*. 1999;19(7):860-69.

27. Al Mazroui NR, Kamal MM, Ghabash NM, Yacout TA, Kole PL, McElnay JC. Influence of pharmaceutical care on health outcomes in patients with Type 2 diabetes mellitus. *Br J Clin Pharmacol*. 2009;67(5):547-57.

28. Choe HM, Mitrovich S, Dubay D, et al. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. *Am J Manag Care*. 2005;11(4):253-60.

29. Fornos JA, Andrés NF, Andrés JC, et al. A pharmacotherapy follow-up program in patients with type-2 diabetes in community pharmacies in Spain. *Pharm World Sci.* 2006;28(2):65-72.

30. Krass I, Armour CL, Mitchell B, et al. The Pharmacy Diabetes Care Program: assessment of a community pharmacy diabetes service model in Australia. *Diabet Med*. 2007;24(6):677-83.

31. Taveira TH, Friedmann PD, Cohen LB, et al. Pharmacist-led group medical appointment model in type 2 diabetes. *Diabetes Educ*. 2010;36(1):109-17.

32. Sarkadi A, Rosenqvist U. Experience-based group education in type 2 diabetes: a randomised controlled trial. *Patient Educ Couns*. 2004;53(3):291-98.

33. Jameson JP, Baty PJ. Pharmacist collaborative management of poorly controlled diabetes mellitus: a randomized controlled trial. *Am J Manag Care*. 2010;16(4):250-55.

34. Scott DM, Boyd ST, Stephan M, et al. Outcomes of pharmacist-managed diabetes care services in a community health center. *Am J Health Syst Pharm*. 2006;63(21):2116-22.

35. Clifford RM, Davis WA, Batty KT, Davis TME. Effect of a pharmaceutical care program on vascular risk factors in type 2 diabetes. *Diabetes Care*. 2005;28(4):771-76.

36. Rothman RL, Malone R, Bryant B, et al. A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes. *Am J Med*. 2005;118(3):276-84.

37. Maguire TA, McElnay JC, Drummond A. A randomized controlled trial of a smoking cessation intervention based in community pharmacies. *Addiction*. 2001;96(2):325-31.

38. Carter BL, Ardery G, Dawson JD, et al. Physician and pharmacist collaboration to improve blood pressure control. *Arch Intern Med*. 2009;169(21):1996-2002.

39. McLean DL, McAlister FA, Johnson JA, et al. A randomized trial of the effect of community pharmacist and nurse care on improving blood pressure management in patients with diabetes mellitus: study of cardiovascular risk intervention by pharmacists-hypertension (SCRIP-HTN). *Arch Intern Med*. 2008;168(21):2355-61.

40. Tobari H, Arimoto T, Shimojo N, et al. Physician-pharmacist cooperation program for blood pressure control in patients with hypertension: a randomized-controlled trial. *Am J Hypertens*. 2010;23(10):1144-52.

41. Olson KL, Delate T, Rasmussen J, et al. Outcomes of patients discharged from pharmacy-managed cardiovascular disease management. *Am J Manag Care*. 2009;15(8):497-503.

42. Lee JK, Grace KA, Taylor AJ. Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol. *JAMA*. 2006;296(21):2563-71.

43. Carter B, Barnette D, Chrischilles E, et al. Evaluation of hypertensive patients after care provided by community pharmacists in a rural setting. *Pharmacotherapy*. 1997;17(6):1274-85.

44. Park J, Kelly P, Carter B, Burgess P. Comprehensive pharmaceutical care in the chain setting: drug therapy monitoring and counseling by pharmacists contributed to improved blood pressure control in study patients. *J Am Pharm Assoc (Wash).* 1996;NS36(7):443-51.

45. Bogden P, Abbott R, Williamson P, et al. Comparing standard care with a physician and pharmacist team approach for uncontrolled hypertension. *J Gen Intern Med.* 1998;13(11):740-45.

46. Weber CA, Ernst ME, Sezate GS, et al. Pharmacist-physician comanagement of hypertension and reduction in 24-hour ambulatory blood pressures. *Arch Intern Med.* 2010;170(18):1634-39.

47. Borenstein JE, Graber G, Saltiel E, et al. Physician-pharmacist comanagement of hypertension: a randomized, comparative trial. *Pharmacotherapy.* 2003;23(2):209-16.

48. Hunt J, Siemienczuk J, Pape G, et al. A randomized controlled trial of team-based care: impact of physician-pharmacist collaboration on uncontrolled hypertension. *J Gen Intern Med.* 2008;23(12):1966-72.

49. Community Pharmacy Medicines Management Project Evaluation Team. The MEDMAN study: a randomized controlled trial of community pharmacy-led medicines management for patients with coronary heart disease. *Fam Pract.* 2007;24(2):189-200.

50. Phumipamorn S, Pongwecharak J, Soorapan S, Pattharachayakul S. Effects of the pharmacist's input on glycaemic control and cardiovascular risks in Muslim diabetes. *Prim Care Diabetes.* 2008;2(1):31-37.

51. Ellis SL, Billups SJ, Malone DC, et al. Types of interventions made by clinical pharmacists in the IMPROVE study. Impact of Managed Pharmaceutical Care on Resource Utilization and Outcomes in Veterans Affairs Medical Centers. *Pharmacotherapy.* 2000;20(4):429-35.

52. Tsuyuki RT, Johnson JA, Teo KK, et al. A randomized trial of the effect of community pharmacist intervention on cholesterol risk management: the Study of Cardiovascular Risk Intervention by Pharmacists (SCRIP). *Arch Intern Med.* 2002;162(10):1149-55.

53. Peterson GM, Fitzmaurice KD, Naunton M, et al. Impact of pharmacist-conducted home visits on the outcomes of lipid-lowering drug therapy. *J Clin Pharm Ther.* 2004;29(1):23-30.

54. Lee VWY, Fan CSY, Li AWM, Chau ACY. Clinical impact of a pharmacist–physician co-managed programme on hyperlipidaemia management in Hong Kong. *J Clin Pharm Ther.* 2009;34(4):407-14.

55. Villa LA, Von Chrismar A, Oyarzun C, Eujenin P, Fernandez M, Quezada M. Pharmaceutical care program for dyslipidemic patients at three primary health care centers: impacts and outcomes. *Lat Am J Pharm.* 2009;28(3):415-20.

56. Bogden PE, Koontz LM, Williamson P, Abbott RD. The physician and pharmacist team: an effective approach to cholesterol reduction. *J Gen Intern Med.* 1997;12(3):158-64.

57. Nola K, Gourley D, Portner T, et al. Clinical and humanistic outcomes of a lipid management program in the community pharmacy setting. *J Am Pharm Assoc (Wash).* 2000;40(2):166-73.

58. Paulos CP, Nygren CEA, Celedon C, Carcamo CA. Impact of a pharmaceutical care program in a community pharmacy on patients with dyslipidemia. *Ann Pharmacother.* 2005;39(5):939-43.

59. Clifford R, Batty K, Davis T, et al. A randomised controlled trial of a pharmaceutical care programme in high-risk diabetic patients in an outpatient clinic. *Int J Pharm Pract.* 2002;10(2):85-89.

60. Bucci C, Jackevicius C, McFarlane K, Liu P. Pharmacist's contribution in a heart function clinic: patient perception and medication appropriateness. *Can J Cardiol.* 2003;19(4):391-96.

61. Sadik A, Yousif M, McElnay JC. Pharmaceutical care of patients with heart failure. *Br J Clin Pharmacol.* 2005;60(2):183-93.

62. Bond CM, Fish A, Porteous TH, Reid JP, Scott A, Antonazzo E. A randomised controlled trial of the effects of note-based medication review by community pharmacists on prescribing of cardiovascular drugs in general practice. *Int J Pharm Pract.* 2007;15:39-46.

63. Doucette WR, Witry MJ, Farris KB, McDonough RP. Community pharmacist-provided extended diabetes care. *Ann Pharmacother.* 2009;43(5):882-89.

64. Choe HM, Mitrovich S, Dubay D, et al. Proactive case management of high-risk patients with type 2 diabetes mellitus by a clinical pharmacist: a randomized controlled trial. *Am J Manag Care.* 2005;11(4):253-60.

65. Kirwin JL, Cunningham RJ, Sequist TD. Pharmacist recommendations to improve the quality of diabetes care: a randomized controlled trial. *J Manag Care Pharm.* 2010;16(2):104-13. Available at: http://www.amcp.org/WorkArea/DownloadAsset.aspx?id=8300.

66. Hennessy S, Leonard C, Yang W, et al. Effectiveness of a two-part educational intervention to improve hypertension control: a cluster-randomized trial. *Pharmacotherapy.* 2006;26(9):1342-47.

67. Carter BL, Bergus GR, Dawson JD, et al. A cluster randomized trial to evaluate physician/pharmacist collaboration to improve blood pressure control. *J Clin Hypertens (Greenwich).* 2008;10(4):260-71.

68. Sinclair H, Silcock J, Bond C, et al. The cost-effectiveness of intensive pharmaceutical intervention in assisting people to stop smoking. *Int J Pharm Pract.* 1999;7(2):107-12.

69. Thavorn K, Chaiyakunapruk N. A cost-effectiveness analysis of a community pharmacist-based smoking cessation programme in Thailand. *Tob Control.* 2008;17(3):177-82.

70. Boyd KA, Briggs AH. Cost-effectiveness of pharmacy and group behavioural support smoking cessation services in Glasgow. *Addiction.* 2009;104(2):317-25.

71. Taylor SJ, Milanova T, Hourihan F, et al. A cost-effectiveness analysis of a community pharmacist-initiated disease state management service for type 2 diabetes mellitus. *Int J Pharm Pract.* 2005;13(1):33-40.

72. Cote I, Gregoire J, Moisan J, et al. A pharmacy-based health promotion programme in hypertension: cost-benefit analysis. *Pharmacoeconomics.* 2003;21(6):415-28.

73. Simpson SH, Johnson JA, Tsuyuki RT. Economic impact of community pharmacist intervention in cholesterol risk management: an evaluation of the Study of Cardiovascular Risk Intervention by Pharmacists. *Pharmacotherapy.* 2001;21(5):627-35.

74. Scott A, Tinelli M, Bond C. Costs of a community pharmacist-led medicines management service for patients with coronary heart disease in England: healthcare system and patient perspectives. *Pharmacoeconomics.* 2007;25(5):397-411.

75. Ellis SL, Carter BL, Malone DC, et al. Clinical and economic impact of ambulatory care clinical pharmacists in management of dyslipidemia in older adults: the IMPROVE study. *Pharmacotherapy.* 2000;20(12):1508-16.

76. Rothman RL, Malone R, Bryant B, et al. A randomized trial of a primary care-based disease management program to improve cardiovascular risk factors and glycated hemoglobin levels in patients with diabetes. *Am J Med.* 2005;118(3):276-84.

77. Anaya JP, Rivera JO, Lawson K, et al. Evaluation of pharmacist-managed diabetes mellitus under a collaborative drug therapy agreement. *Am J Health Syst Pharm.* 2008;65(19):1841-45.

78. Cranor C, Bunting B, Christensen D. The Asheville Project: long-term clinical and economic outcomes of a community pharmacy diabetes care program. *J Am Pharm Assoc (Wash).* 2003;43(2):173-84.

79. Erickson S, Slaughter R, Halapy H. Pharmacists' ability to influence outcomes of hypertension therapy. *Pharmacotherapy.* 1997;17(1):140-47.

80. Hilleman D, Faulkner M, Monaghan MA. Cost of a pharmacist-directed intervention to increase treatment of hypercholesterolemia. *Pharmacotherapy.* 2004;24(8):1077-83.

81. Gandhi PJ, Smith BS, Tataronis GR, Maas B. Impact of a pharmacist on drug costs in a coronary care unit. *Am J Health Syst Pharm.* 2001;58(6):497-503.

82. Munroe WP, Kunz K, Dalmady-Israel C, et al. Economic evaluation of pharmacist involvement in disease management in a community pharmacy setting. *Clin Ther.* 1997;19(1):113-23.

83. Lowey A, Moore S, Norris C, et al. The cost-effectiveness of pharmacist-led treatment of cardiac risk in patients with type 2 diabetes. *Pharm World Sci.* 2007;29(5):541-45.

APPENDIX A Search Strategy

1. Cochrane Database of Systematic Reviews (CDSR)	
Search terms	➢ **Step 1:** Entered the following terms in Search field (title): (Pharmacy OR pharmacist* OR "pharmaceutical service" OR "pharmaceutical care") ➢ **Step 2:** Entered the following terms in Search field (abstract): (Cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention OR outcomes OR mortality OR morbidity)
2. MEDLINE/PubMed	
Search terms	➢ **Step 1:** Entered the following terms in Search field (title and abstract): (Cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention* OR outcome* OR mortalit* OR morbidit*) The combination terms used were as follows: (((((((cost*[Title/Abstract]) OR economic*[Title/Abstract]) OR cost-effectiveness [Title/Abstract]) OR cost-benefits [Title/Abstract]) OR cost-saving[Title/Abstract]) OR intervention*[Title/Abstract]) OR outcome*[Title/Abstract]) OR mortalit*[Title/Abstract]) OR morbidit*[Title/Abstract] ➢ **Step 2:** Entered the following terms in Search field (title): (Pharmacy OR pharmacist* OR "pharmaceutical services" OR "pharmaceutical care") The combination terms used were as follows: (((pharmacy[Title]) OR pharmacist* [Title]) OR "pharmaceutical care"[Title]) OR "pharmaceutical service" [Title] ➢ **Step 3:** Entered the following terms in Search field, combining steps 1 and 2: (#1) AND (#2)
Limits	Publication type limits: Clinical Trial, Meta-Analysis, Practice Guideline, Randomized Controlled Trial, Review, Comparative Study, Controlled Clinical Trial, Guideline, Multicenter Study, English
3. Web of Knowledge	
Search terms	➢ **Step 1:** Entered the following terms in Search field (title): (Pharmacy OR pharmacist* OR pharmaceutical care OR pharmaceutical service) ➢ **Step 2:** Entered the following terms in Search field (topic): (Cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention OR outcomes OR mortality OR morbidity) ➢ **Step 3:** Entered the following term in Search field (topic): (Clinical trial) ➢ **Step 4:** combined search 1, 2 and 3
4. HMIC (Ovid)	
Search terms	(Pharmacy OR pharmacist* OR pharmaceutical care OR pharmaceutical service in the title field) AND (cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention OR outcomes OR mortality OR morbidity in the abstract field)
Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus Searching Engine	
Search terms	Entered the following terms in Search field: (Pharmacy OR pharmacist* OR pharmaceutical in the title AND cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention OR outcomes OR mortality OR morbidity in the abstract)

APPENDIX A Search Strategy *(continued)*

5. National Health Service (NHS) Evidence

Search terms

Entered the following terms in Search field:

(Pharmacy OR pharmacist*)

Due to the huge nature of databases included in this search, the following filters were used:

1-Area of interest
-Clinical
-Public health
-Social care
2-Type of information
-Evidence summaries
-Grey literature
-Ongoing trial
-Systematic reviews
3-Sources
-Agency for Health Research and Quality - AHRQ
-Association of Public Health Observatories - APHO
-Cardiovascular Diseases Specialist Collection (NHS Evidence)
-Centre for Reviews and Dissemination Health Technology Assessments - CRD HTA
-Database of Abstracts of Reviews of Effects - DARE
-Diabetes Specialist Collection (NHS Evidence)
-Emergency Care Specialist Collection (NHS Evidence)
-European Observatory on Health Systems and Policies
-Infections Specialist Collection (NHS Evidence)
-Later Life Specialist Collection (NHS Evidence)
-London Health Observatory
-National Library for Public Health
-NHS Economic Evaluation Database - NHS EED
-Patient and Public Involvement Specialist Collection (NHS Evidence)
-Respiratory Specialist Collection (NHS Evidence)
-Screening Specialist Collection (NHS Evidence)
-South West Public Health Observatory
-Stroke Specialist Collection (NHS Evidence)
-Theatres and Critical Care Collection
-Vascular Diseases Specialist Collection (NHS Evidence)
-WHO Health Evidence Network

6. Science Direct

Search terms

➢ **Step 1:** Entered the following terms in Search field (title):

(Pharmacy OR pharmacist* OR "pharmaceutical service" OR "pharmaceutical care")

➢ **Step 2:** Searched within the result of step 1 by using the following terms:

(Cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention* OR outcome* OR mortalit* OR morbidit*)

➢ **Step 3:** Limited the result of step 2 with the following topics:

"pharmaceutical care, health care ,medicare, ambulatory care, care service, patient satisfaction, pharmacy practice, pharmaceutical outcome, pharmaceutical service, pharmaceutical therapy"

7. Database of Abstracts of Reviews of Effectiveness (DARE)

➢ DARE database was searched by using the NHS searching engine. This search is discussed in further detail in step 5.

8. Health Technology Assessment Database (HTA)

➢ HTA database was searched by using the NHS searching engine. This search discussed in further detail in step 5.

9. Pharmacy Abstract (http://www.pharmacyabstracts.org/index.shtml)

Search terms

(pharmacist[TI]) AND (economic[AB] OR effectiveness[AB] OR mortality[AB] OR morbidity[AB])

APPENDIX A Search Strategy *(continued)*

The following trial registries were searched to identify any further completed and published trials:

1. National Institute for Health's Clinical Trials.gov database (http://www.clinicaltrials.gov)	
Search terms	Entered the following term in Search field: (pharmacist*)
2. Trip database (http://www.tripdatabase.com/)	
Search terms	1. Entered the following terms in Search field (title: All of these words): (pharmacist*) 2. Entered the following terms in Search field (anywhere in the document: Any of these words): (Cost* OR economic* OR cost-effectiveness OR cost-benefits OR cost-saving OR intervention* OR outcome* OR mortalit* OR morbidit*)
3. Current Controlled Trials (CCT) (http://controlled-trials.com/)	
Search terms	Entered the following terms in Search field: (pharmacist*)

APPENDIX B Clinical Studies Conducted to Measure the Pharmacist Impact in Treating Patients with CHD or CVD Risk Factors

TABLE B1 Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Diabetes Mellitus

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Al Mazroui, 2009[27]	United Arab Emirates	Pharmacist reviewed patient medical records and discussed with their physicians regarding drug therapy, patient awareness about their illness and their medication, including risk of diabetes complications, proper dosage, side effects and storage of medications, healthy lifestyle and management of diabetes mellitus signs and symptoms through self-monitoring. Printed leaflets about diabetes and other conditions such as hypertension and hyperlipidemia were given to the patients. (120 patients)	Patients received advice about self-monitoring of their blood glucose from medical and nursing staff. (120 patients)	A significant reduction was found in the intervention group compared to the control group. This includes body mass index ($P<0.001$), fasting blood glucose ($P<0.001$), HbA1c ($P<0.001$), systolic blood pressure ($P<0.001$), diastolic blood pressure ($P<0.001$), total cholesterol ($P<0.001$), HDL ($P<0.001$), LDL ($P<0.001$), and triglycerides ($P<0.001$). Framingham risk scores were also improved in the intervention group ($P<0.001$) and remained unchanged in the control group.	3	The study demonstrated that clinical pharmacists help to improve the health care of diabetic patients, but the sustainability of benefits over time need further assessment.
Choe, 2005[64]	United States	Pharmacist evaluated therapeutic regimens based on efficacy, safety, adverse effects, drug interactions, drug costs, and monitoring. Any changes required were discussed with primary care physicians before implementation. (41 patients)	Patients received the usual care without involvement in pharmacist services. (39 patients)	Patients in the intervention group achieved a greater decrease in HbA1c than those in the control group ($P=0.03$). Intervention group patients also had more frequent examinations than the control group. This included LDL ($P=0.02$), retinal examination ($P=0.004$), and foot examination ($P=0.002$).	3	Pharmacist improved both glycemic control and diabetic process of care in the primary setting.
Clifford, 2002[59]	Australia	Patients attended appointments with a clinical pharmacist at 6 weeks intervals for 6 months. A list of questions related to pharmacotherapy and diabetes including use of medication was covered in each visit. (48 patients)	Patients received the usual care with no intervention from a pharmacist. (25 patients)	No significant differences were found between the 2 groups in terms of changes in HbA1c measurements ($P>0.2$). Same results were found in terms of quality of life ($P>0.15$). In patient satisfaction survey, the intervention group had greater satisfaction with the service provided by the clinical pharmacist ($P=0.007$) and better drug information satisfaction ($P=0.036$).	3	The study concluded that the pharmacist had no impact on patients' glycemic control over short period of time.

HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

TABLE B2 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist-Led Intervention Model for Patients with Diabetes Mellitus*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Taveira, 2010[31]	United States	Patients attended 4 weekly, 2-hour support group sessions. The session was divided into 2 parts: education and pharmacological and behavioural intervention. The education element contained 4 learning objectives, and each objective was delivered by different health care staff. Acute complications by a clinical pharmacist, healthy eating by a nutritionist, physical activity by a physical therapist, and chronic complications delivered by a nurse. The clinical pharmacist delivered the second element. (64 patients)	Patients received usual care with no involvement in the support group session. (54 patients)	Intervention group had a significant improvement in HbA1c and systolic blood pressure compared with the control group ($P<0.05$). No significant changes were found between the 2 groups in terms of tobacco use and lipid reduction.	3	Pharmacist interventions improved CVD risk factor control. The highest benefit was achieved in controlling blood pressure and diabetes mellitus.
Sarkadi, 2004[32]	Sweden	A pharmacist measured patient blood glucose and provided educational intervention consisting of a patient interview, lifestyle advice, a video of how to live with diabetes, and diabetes education booklets. The pharmacist was assisted by a diabetes specialist or diabetes nurse during the first 2 interviews. (39 patients)	Patients received usual care without intervention from the pharmacist. (38 patients)	Significant reduction in HbA1c values were measured in the intervention group after 24 months ($P=0.05$), but not after 6 or 12 months.	3	The study provided information about the effect of educational program on glycemic control.
Kirwin, 2010[65]	United States	Clinical staff collected patient data by using data collection forms. A clinical pharmacist then reviewed the patient data and gave recommendations to the patient's physician in a letter. (171 patients)	Patients received usual care without intervention from the pharmacist. (175 patients)	There were no significant differences between the 2 groups in terms of HbA1c improvements, lipid profile, or pneumococcal vaccination. The only significant difference found was the annual eye exam ($P=0.017$) in favor of intervention group.	3	The study found that using a recommendation letter to provide pharmacist intervention had no effect in diabetic care.

CVD = cardiovascular disease; HbA1c = hemoglobin A1c.

TABLE B3 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist Collaborative Model for Patients with Diabetes Mellitus*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Fornos, 2006[29]	Spain	The pharmacist aimed to prevent, detect, and solve DRPs. The pharmacist provided verbal and written information about the correct use of each drug and its possible adverse reactions or interactions. The pharmacist also provided educational interventions aiming to improve lifestyles and to improve or maintain patient compliance. (58 patients)	Patients received usual care without any input from the pharmacist. (56 patients)	Patients in the intervention group had more improvement in many outcomes than those in the control group. These include DRP ($P<0.0001$), knowledge ($P<0.0001$), HbA1c ($P<0.0001$), fasting blood glucose ($P=0.0004$), total cholesterol ($P=0.0054$), and systolic blood pressure ($P=0.0006$).	3	Community pharmacist played an important role in improving diabetic care through increasing patient awareness to the disease and treatment.
Jameson, 2010[33]	United States	The pharmacist provided education regarding diabetes self-management, including diet, exercise, blood glucose level testing, medications, and insulin. The pharmacist also used guidelines for the management of hyperglycemia in type 2 diabetes. (52 patients)	Patients received usual care provided by their physicians without input from a clinical pharmacist. (52 patients)	The intervention group had a larger decrease in mean HbA1c compared with the control group ($P=0.06$). This improvement was found to be more significant in male ($P=0.3$) and white patients ($P=0.05$). For patients with a reduction of 1% or more in HbA1c, the intervention group had a significant number of patients compared with the control group ($P=0.02$).	3	The study concluded that using a clinical pharmacist can significantly improve patients' glycemic control in community setting.

DRP = drug-related problem; HbA1c = hemoglobin A1c.

TABLE B4 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Diabetes Mellitus*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Phumipamorn, 2008 [50]	Thailand	Patients met with a pharmacist at 2-month intervals, when the pharmacist refilled prescriptions, discussed the use of medication, checked pill counts, and gave education on diabetes, which included appropriate lifestyle and correct diet. (67 patients)	Patients received usual care from their physicians with no extra counseling from a pharmacist. (68 patients)	Results showed no significant differences between the 2 groups in terms of HbA1c ($P=0.56$). The intervention group had a significant improvement in total cholesterol reduction ($P<0.0001$), LDL reduction ($P=0.002$), HDL increase ($P=0.06$), and patient knowledge of diabetes ($P=0.002$).	3	This study showed that clinical pharmacist can improve patients' quality of life through increasing patient knowledge and satisfaction. The effect on CVD risk was only obtained from lipid control
Scott, 2006[34]	United States	A pharmacist provided education and pharmacotherapy management for diabetic patients. (76 patients)	Patients received usual care with no appointment to attend a pharmacist clinic. (73 patients)	The study showed that both groups had significant improvement in HbA1c ($P=0.003$) with more improvement in the intervention group ($P<0.05$). The intervention group also had more improvement in LDL level ($P=0.012$) and systolic blood pressure ($P=0.023$).	3	Pharmacist services had more effect on lipid, blood pressure, glycemic control, and patient quality of life, which help to reach the target treatment goal.
Clifford, 2005[35]	Australia	A pharmacist assessed patients at baseline then at 6-week intervals. This included developing a pharmacist-patient relationship; collecting, analyzing, and interpreting relevant information; listing and ranking drug-related problems; establishing pharmacotherapeutic outcomes with the patient; determining feasible pharmacotherapeutic alternatives; selecting the best pharmacotherapeutic solution; designing a therapeutic monitoring plan; implementing the individual regimen and monitoring plan; and follow-up. (99 patients)	Patients received usual care without any input from a pharmacist. (99 patients)	Patients in the intervention group had more improvement in fasting serum glucose ($P<0.001$), HbA1c ($P=0.002$), systolic blood pressure ($P=0.024$), and diastolic blood pressure ($P=0.043$). No significant differences were found in total cholesterol ($P=0.14$), HDL ($P=0.07$), or triglycerides ($P=0.09$). The estimated risk of first CHD events decreased more in the intervention group ($P=0.002$).	2	The study showed that clinical pharmacist had an effect on the glycemic control over 12 months.
Doucette, 2009[63]	United States	A pharmacist gathered and evaluated patient information then formulated and implemented a treatment plan. The pharmacist also followed up with patients and physicians to ensure better outcomes. (36 patients)	Patients received usual care. (42 patients)	There were no significant differences found between the intervention group and the control group in terms of changes in HbA1c, LDL, or blood pressure. The pharmacist helped patients to increase their engagement with diet ($P=0.001$) and diabetic self-activity ($P=0.027$).	2	Pharmacist had an effect in improving patient self-care, but this did not affect the clinical outcomes.
Krass, 2007[30]	Australia	Patients were provided with blood glucose measuring devices and asked to check their glucose levels on a daily basis. At each monthly visit, a pharmacist discussed with patients their blood glucose readings and identified interventions to support patient care. The discussion consisted of intervention related to adherence, medication, diabetes self-management, and lifestyle modification. (176 patients)	Patients in the control group had 2 visits with the pharmacist and did no more than the usual care service. (159 patients)	The intervention group had significant changes in HbA1c ($P<0.01$), systolic blood pressure (P=0.06), and quality of life (EQ-5D; utility score $P=0.07$, health state scale $P=0.02$). There were no significant differences in BMI, diastolic blood pressure, total cholesterol, and triglycerides.	3	This study provided evidence of the pharmacist effect on improving clinical outcomes of diabetic patients.

BMI = body mass index; CHD = coronary heart disease; HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

TABLE B5 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Hypertension*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Tobari, 2010[40]	Japan	Patients attended monthly sessions that included pharmacist counseling, questions about salt intake and lifestyle, setting individual goals, stressing the importance of achieving these goals, and providing education about drug therapy. (66 patients)	Patients received pharmacist counseling, questions about salt intake and lifestyle at baseline only. (66 patients)	The mean systolic blood pressure decrease in the intervention group was not significantly greater than in the control group for office and evening home measurements. The decrease in diastolic blood pressure was significant in the intervention group compared with the control group ($P=0.04$) for morning home measurements. Patients in the intervention group significantly reduced their use of antihypertensive medication ($P<0.0001$). More patients in the control group required additional medications to control blood pressure than in the intervention group ($P=0.003$).	3	The collaboration of physician and pharmacist showed an improvement in patients` blood pressure with less medication used.
Bogden, 1998[45]	United States	A pharmacist interacted with physicians to optimize hypertension medication therapy. Pharmacist met with each patient for 30 minutes before seeing the physician. Pharmacist obtained medication history, answered patient questions, and encouraged compliance. Resident or intern and pharmacist reviewed laboratory data together, and pharmacist gave advice with regard to drug costs and efficacy. Then resident or intern saw patients and formulated treatment plans and discussed it with a supervising physician and also discussed pharmacist recommendations, which were then accepted or rejected. The physician also considered current patient diseases, preferences, lifestyle, and circumstances. (50 patients)	Patients received same medical care as in the intervention group but without the input of a pharmacist. (50 patients)	Patients achieving target blood pressure level was more than double in the intervention group than in the control group (50% vs. 20%, $P<0.001$). The intervention group also showed better improvement in terms of diastolic blood pressure ($P< 0.001$) and systolic blood pressure ($P<0.01$).	2	Physician-pharmacist collaboration had an effect controlling patients` blood pressure even in those who were unable to reach the guidelines recommendations.

TABLE B5 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Hypertension (continued)*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Weber, 2010[46]	United States	A pharmacist interviewed patients to investigate patient factors that could affect target blood pressure and to compare current treatment with clinical guidelines. The pharmacist then discussed any changes required with the patient's physician who decided to accept or reject the recommendations. (101 patients)	Patient did not have an interview with the research pharmacist. (78 patients	Patients treated in the intervention group had more significant changes in their blood pressure than the control group. This included daytime systolic blood pressure ($P<0.001$), nighttime systolic blood pressure ($P=0.004$), overall 24-hour systolic blood pressure ($P<0.001$), at office systolic blood pressure ($P<0.001$), daytime systolic blood pressure ($P<0.001$), overall 24-hour diastolic blood pressure ($P<0.001$), at office diastolic blood pressure ($P<0.001$). No significant differences were found in nighttime diastolic blood pressure ($P=0.12$).	3	The study showed that the collaboration of pharmacist and physician resulted in more reduction in blood pressure and more patients with controlled blood pressure levels.
Hennessy, 2006[66]	United States	A pharmacist conducted an educational intervention for the selected health care provider describing recommendations for hypertension treatment and percentage of patients on target blood pressure. Based on approval from the provider, hypertensive patients were mailed motivational and educational material. (5,401 patients)	Patients and their providers did not receive educational intervention from a pharmacist. (5,295 patients)	The mean result was measured in terms of patients achieving their target levels for blood pressure, which showed no statistically significant differences between the 2 groups.	3	The authors of the study did not recommend implanting the program unless further evaluations were performed.
Borenstein, 2003[47]	United States	A pharmacist determined blood pressure, assessed patient adherence to medication, determined potential side effects, tobacco use, diet, and exercise. The pharmacist also provided patient education. Then the pharmacist contacted the patient's physician and recommended modifications. (635 patients)	Patients seen only by physician without any input from a pharmacist. (637 patients)	Both groups showed significant reduction in blood pressure with a greater decrease in the intervention group ($P<0.01$). More patients were found to achieve target blood pressure in the intervention group than in the control group ($P=0.02$). Patients in the intervention group had a lower average visit cost per patient than the control group ($P=0.02$) and lower average primary care visits ($P<0.01$).	2	The use of pharmacist-physician collaboration improved blood pressure control and decreased average clinic visits.

TABLE B5 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Hypertension (continued)*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Carter, 2009[38]	United States	A pharmacist assessed medications and blood pressure at baseline, and at 1 month, and by telephone at 3 months (more frequently if necessary) and made recommendations. (568 patients)	Clinical pharmacists did not provide care for study patients but continued to answer physician's general treatment questions. (674 patients)	Guideline adherence score increased in the intervention group more than in the control group ($P=0.09$). The mean blood pressure was also reduced in the intervention group more than in the control group ($P<0.05$) with the same effect found in 24-hour measurements. More patients achieved controlled blood pressure in the intervention group ($P<0.001$).	3	A better mean blood pressure was achieved by pharmacist-physician collaboration. The authors recommended to investigate team-based chronic disease management strategies.
Carter, 2008[67]	United States	The pharmacist assessed the patients, suggested a blood pressure goal, and recommended any changes required to improve blood pressure control. Also, a pharmacist was involved in patient education and encouraged adherence. (203 patients)	Patients did not receive any input from a pharmacist. (243 patients)	The percentage of hypertension patients who had controlled blood pressure were higher in the intervention group than in the control group ($P<0.001$). This included diabetic patients ($P=0.002$) and nondiabetic patients ($P<0.001$).	5	Pharmacist-physician collaboration improved blood pressure control and increased adherence to medications without increasing side effects.
Hunt, 2008[48]	United States	Pharmacists reviewed subject medication and lifestyle habits, assessed vital signs, screened for adverse drug reactions, identified barriers to adherence, provided education, optimized the antihypertensive regimen, and scheduled follow-up appointments as judged necessary. (230 patients)	Patients received the usual care without intervention from clinical pharmacists. (233 patients)	Patients in the intervention group had better reduction in both systolic ($P=0.007$) and diastolic blood pressure ($P=0.002$). This resulted in more patients achieving their target blood pressure in the intervention group than in the control group ($P=0.003$). In term of utilization, patients in the intervention group had a higher number of office visits ($P<0.0001$) and a lower number of physician visits ($P<0.0001$). There were no significant differences found between the 2 groups in terms of hypertension knowledge, medication adherence, quality of life, or patient satisfaction.	3	The involvement of pharmacists in the management of hypertension patients improved blood pressure control without increasing the cost, complexity of the drug regimen, or altering patients' quality of life.

TABLE B6 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist Collaborative Model for Patients with Hypertension*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
McLean, 2008[39]	Canada	Patients in the intervention group were assessed by a pharmacist-nurse team and received counseling. The counseling process included reviewing blood pressure as a risk factor, discussing the causes of high blood pressure, describing the importance and consequences of high blood pressure, explaining the effect of diabetes on high blood pressure, and focusing on the lifestyle strategies the patient could undertake to improve blood pressure. (115 patients)	Patients did not receive therapeutic advice from a pharmacist-nurse team. (112 patients)	The intervention group had a greater reduction in systolic blood pressure than the control group ($P=0.008$). In subgroup analysis of patients with blood pressure higher than 160 mmHg, clinical pharmacist intervention demonstrated an increased significant reduction by an adjusted mean 24.1 ± 1.9 ($P<0.001$).	3	Pharmacist and nurse collaboration resulted in improvement of blood pressure control in diabetic patients, especially in those with suboptimal blood pressure control.
Carter, 1997[43]	United States	Patients in the intervention group received education and monitoring of their blood pressure every 3-5 weeks. They also received advice about lifestyle modification and understanding of their current drugs. Information about each patient visit was recorded and sent to the physician for review. If immediate intervention was required, a pharmacist contacted the physician. (29 patients)	Patients received usual care with the traditional counseling from a community pharmacist. (26 patients)	Patients in the intervention group had a significant reduction in systolic blood pressure at 2, 3, 4, 5, and 6 months ($P<0.001$) compared with baseline. They also had significant reduction in diastolic blood pressure at 2, 4, and 5 months ($P<0.05$) and at end of study ($P=0.054$) from baseline. Patients in the control group did not show any significant changes. Patients in the intervention group also had significant improvements in quality of life scores and patient satisfaction after 6 months, whereas the control group did not have significant changes. In terms of total mean changes, the intervention group was higher than the control group ($P=0.006$).	3	Patients monitored by community pharmacist had more improvement in blood pressure control, quality of life, and patient satisfaction measured.

TABLE B7 *Randomized Controlled Trial Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Hypertension*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Park, 1996[44]	United States	Pharmacists assessed patient medical status and designed a health care plan. The patient's physician was contacted when there were any pharmacological changes required. Pharmacists also provided patient education and counseling. (32 patients)	Patients in control group continued to receive their usual care. (32 patients)	The study showed that pharmacist intervention significantly improved patient blood pressure (visit 3 & 4, $P<0.05$), medication compliance ($P=0.025$ and 0.037 in visit 2 & 3), and quality of life ($P<0.05$).	3	Pharmacist services in community improved patient compliance and blood pressure control.

TABLE B8 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Hypertension*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Bogden, 1997[56]	United States	Pharmacists routinely interacted with and gave advice to patients and physicians about drugs, dosage, drug selection, and provided monitoring. Intervention group patients were interviewed by a pharmacist for half an hour before meeting their physicians. The interview included taking patient medication history, answering any questions and encouraging compliance. Then a pharmacist reviewed laboratory measures with an intern or resident and gave recommendations. Then the intern or resident discussed recommendations with an attending physician and decided to accept or reject recommendations. (50 patients)	Patients received the same medical care as the intervention group but without the input of a pharmacist. (50 patients)	The rate of patients achieving target LDL level in the intervention group was double the rate of those in the control group (43% vs. 21%, $P<0.05$). In subgroup analysis, it was found that pharmacist intervention was more significant in patients with CHD ($P<0.01$) or with 2 or more risk factors ($P<0.05$) while no significances were detected in patients without CHD or with less than 2 risk factors. In the last month of the study, medication charges decreased by $11.40 per patient in the intervention group, while it increased by $3.82 in the control group, but the difference was not statistically significant. More clinic visits were found in the intervention group than in the control group ($P<0.05$).	3	Managing high risk patients by using pharmacist-physician collaboration had better outcomes than using standard care alone.
Lee, 2009[54]	China	Pharmacists provided patient counseling and an assessment of patient compliance and adverse drug reactions. Pharmacists also contacted the patients at 4-week intervals for a follow-up. (59 patients)	Patients received only routine medical care without additional pharmacist intervention. (60 patients)	Patients in the intervention group had a greater reduction in their LDL ($P<0.001$), total cholesterol ($P<0.001$), and triglycerides levels ($P=0.022$). They also had better improvement in their HDL levels ($P=0.03$).	3	Pharmacist-physician collaboration was an effective method to achieve target cholesterol level.

CHD = coronary heart disease; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

TABLE B9 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist-Led Intervention Model for Patients with Hyperlipidemia*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Olson, 2009[41]	United States	Pharmacists contacted patients by phone to review their annual full lipid profiles, blood pressure measurements, and medication adherence; provided counseling on diet and exercise regimens; and made medication adjustments to maintain treatment goals. A pharmacist also ordered follow-up laboratory tests, mailed patients their results, and scheduled lipid follow-ups. (214 patients)	Patients were discharged from the pharmacist service and continued to receive the usual care. (207 patients)	Study showed that individuals who were discharged from clinical pharmacist services continued to have controlled blood lipids and blood pressure with no significant differences between the 2 groups: LDL-C goal: < 100, $P = 0.46$, and < 70 mg/dL, $P = 0.23$; blood pressure goal: < 140/90 mmHg, $P = 0.03$ and <130/80 mmHg, $P = 0.71$.	3	Patients discharged from pharmacist services after controlling their lipids and blood pressure can continue under control with minimal follow-up.
Villa, 2009[55]	Chile	Pharmacists educated patients about their illnesses and provided them with information about pharmacological and nonpharmacological interventions. (85 patients)	Control group did not receive any intervention from pharmacists. (57 patients)	The intervention group had significant changes in many laboratory outcomes including total cholesterol ($P = 0.0001$), LDL (P = 0.0001), HDL ($P > 0.05$), and triglycerides ($P = 0.009$). The intervention group also had significant improvements in their quality of life compared with the control group ($P < 0.001$).	3	The study showed that pharmacist care program improved patients' lipid control, CVD risk, and quality of life.
Ellis, 2000[75]	United States	Pharmacists provided medication assessments and applied any changes when required. They also followed up with patients and monitored responses until desired goals were achieved. (208 patients)	Control group did not receive any intervention from a pharmacist. (229 patients)	Patients in the intervention group were found to have greater fasting lipid profiles than the control group ($P = 0.021$). They also showed more improvement in their total cholesterol ($P = 0.028$) and LDL ($P = 0.042$). No significant differences were found in terms of patients reaching goal lipid measurements or overall costs.	3	Pharmacist can improve LDL and total cholesterol significantly without increase of overall health care cost.

CVD = cardiovascular disease; HDL = high-density lipoprotein; LDL-C = low-density lipoprotein cholesterol; mg/dL = milligram per deciliter; mmHg = millimeter mercury.

TABLE B10 *Randomized Controlled Trial Conducted in a Community Setting Using a Pharmacist Collaborative Model for Patients with Hyperlipidemia*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Tsuyuki, 2002[52]	Canada	Pharmacists interviewed patients and obtained their medical histories, measured cholesterol levels, and educated them about CVD risk factors. Then, patients were encouraged to make appointments with their physicians for further assessment when required. Single page forms for each patient were faxed, containing information about patient risk factors, medication, cholesterol, and blood pressure measurements, along with any suggestions. (344 patients)	Patients received their usual care and were not involved in the community pharmacist care program. (331 patients)	Significant differences were found in this study in favor of the intervention group ($P<0.001$) in terms of improvement of cholesterol management. Patients in the intervention group also had better outcomes in subgroup analysis, which included women ($P<0.001$), men ($P<0.001$), age <70 ($P<0.001$), age ≥70 ($P<0.001$), urban pharmacy practice ($P<0.001$), rural pharmacy practice ($P=0.07$), diabetic patients ($P<0.001$) and nondiabetic patients ($P<0.001$).	3	Pharmacist services in the community care program achieved more improvement in cholesterol management

CVD = cardiovascular disease.

TABLE B11 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Hyperlipidemia*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Nola, 2000[57]	United States	Pharmacists provided a comprehensive program composed of diet, exercise evaluation, monitoring of cholesterol levels, monitoring of drug therapy, collaboration with physicians, and patient education. (25 patients)	Patients received usual care without involvement in the comprehensive program. (26 patients)	Both groups had an increase in patient HDL (8.3, 4.5, $P<0.01$) and patient knowledge (5.2, 1.8) with a decrease in serum triglycerides (4.4, 1.6).	3	The pharmacist can play an important role in managing patients with hyperlipidemia.
Paulos, 2005[58]	Chile	Pharmacists provided patients with a comprehensive pharmaceutical care service, which included obtaining total cholesterol and triglyceride levels, educating patients about the role of cholesterol in diseases and health, and providing education and counseling regarding each patient medication. (23 patients)	Patients received usual care with normal counseling from a pharmacist. (19 patients)	The pharmacist intervention group had a significant reduction in average blood cholesterol levels ($P=0.0266$) and triglyceride levels ($P=0.0169$); in the control group, patients had a nonsignificant reduction in cholesterol levels ($P=0.6624$) and slightly increased triglyceride levels ($P=0.1435$). The difference in patient quality of life was higher at the end of the study in favor of the pharmacist intervention group ($P=0.002$).	1	Pharmacists can improve patients' blood lipid values, CVD risk factors, and quality of life in the short term.
Peterson, 2004[53]	Australia	Pharmacists educated patients about their medication, goals, and benefits of cholesterol treatment. Patients also received advice about diet and lifestyle modification. (46 patients)	Patients in the control group did not have further contact until the 6-month follow-up appointment. (48 patients)	The pharmacist intervention group had a significant reduction in total cholesterol from baseline ($P<0.005$), while the control group had no significant changes (0.26). At the end of the study, the number of patients with a controlled cholesterol level (<4.0 mmol/L) was higher in the intervention group ($P=0.06$).	3	Pharmacists had a useful role in reducing morbidity and mortality associated with CHD in the community. This effect may double the benefits obtained from usual care.

CHD = coronary heart disease; CVD = cardiovascular disease; HDL = high-density lipoprotein; mmol/L = millimole per liter.

TABLE B12 *Randomized Controlled Trial Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Smokers*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Maguire, 2001[37]	United States	Smokers received a leaflet and a one-on-one interview. The follow-up advice was structured at weekly intervals for 4 weeks, then monthly for 3 months. (265 patients)	Smokers assigned to the control group were provided with normal pharmaceutical services with no structured pharmacist care. (219 patients)	Smokers in the intervention group had a significantly higher number of individuals who were abstinent for up to 12 months ($P<0.001$).	3	The structured pharmaceutical care for smoking cessation is an effective model, but questions remain about the proportion of pharmacists willing to be involved in this service.

TABLE B13 *Randomized Controlled Trial Conducted in an Outpatient Setting Using a Pharmacist-Led Intervention Model for Patients with Coronary Artery Disease*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Rothman, 2005[76]	United States	Pharmacists provided patients with intensive educational sessions, evidence-based algorithms, and proactive management of clinical parameters. (112 patients)	Patients received their usual care from their primary care physicians. (105 patients)	Patients in the intervention group had a significant reduction in their systolic blood pressure ($P=0.007$), diastolic blood pressure ($P=0.005$), HbA1c ($P=0.02$), and use of aspirin ($P<0.0001$). There were no significant changes found in total cholesterol measurements ($P=0.35$), use of clinical services, or potential adverse events.	3	Pharmacist-led disease management program targeting patients with diabetes mellitus was shown to be effective in improving patient outcomes.

HbA1c = hemoglobin A1c.

TABLE B14 *Randomized Controlled Trial Conducted in a Community Setting Using a Pharmacist Collaborative Model for Patients with Coronary Artery Disease*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Bond, 2007[62]	United Kingdom	Medical records of patients in the intervention group were reviewed by a pharmacist who recommended changes to the general practitioner by using a study referral form. (996 patients)	Patient medical records were not reviewed by a pharmacist. (1,018 patients)	The overall adherence to standard guidelines was good in both groups, with no significant differences except for antiplatelet prescribing ($P=0.076$). There were no differences between the 2 groups in terms of quality of life and costs, without including pharmacist time costs for all patients. When the pharmacist time costs were included, a significant difference was found in favor of the control group ($P<0.001$).	3	Benefits measured in the intervention group were small, and it was less than other studies measurement. This benefit was combined with minimal changes in prescribing, and the cost of the pharmacist group was higher without measuring pharmacist time cost.

TABLE B15 *Randomized Controlled Trial Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Coronary Artery Disease*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
The MEDMAN Study Group 2007[49]	United Kingdom	Pharmacists provided assessments of therapy, medication compliance, lifestyle (e.g., smoking cessation, exercise, and diet), and social support and recommendations to patient's general practitioner. (980 patients)	Patients received usual care from their general practitioners. (513 patients)	No significant differences were found between the 2 groups in terms of aspirin prescribed, lifestyle measures, lipid management, blood pressure, smoking, or alcohol use. The intervention group had a better result in terms of patient satisfaction ($P<0.01$) with a higher total National Health Service cost ($P<0.0001$).	3	The community pharmacist did not significantly improve the proportion of patients receiving appropriate medication, and it was more expensive.

TABLE B16 *Randomized Controlled Trial Conducted in an Inpatient Setting Using a Pharmacist Collaborative Model for Patients with Heart Failure*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Sadik, 2005[61]	United Arab Emirates	Pharmacists discussed drug therapy appropriateness and simplification of therapy regimens with physicians. Pharmacists also educated patients about their diseases, medications, symptom control, and provided lifestyle advice. (109 patients)	Patients received usual care without any advice from research pharmacists. (112 patients)	Patients in the intervention group had more improvement in many measures ($P<0.05$) than the control group, including exercise tolerance test, forced vital capacity, and patient quality of life. Intervention group patients also showed better adherence to their medications and lifestyle advice. Intervention groups also had lower total health care costs (Intervention £32,670 vs. Control £56,580).	3	Pharmaceutical care improved patients' quality of life, exercise capacity, pulmonary function, blood pressure, pulse, hospital admission rates, compliance with the prescribed heart failure medication and lifestyle advice.

TABLE B17 *Randomized Controlled Trials Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Heart Failure*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Bucci, 2003[60]	Canada	Pharmacists reviewed medication regimens and recommended changes. They also offered prevention and solution of drug-related problems, educated patients and health care providers about disease and medication use, and ensured continuity of care. (42 patiens)	Usual care was provided to patients without input from pharmacist. However, consultation with a specialized cardiology pharmacist was available for outstanding questions about appropriateness of drug use. (38 patients)	No significant differences were found between the 2 groups in terms of the medication appropriateness index. A directive guidance patients' survey showed that the intervention group had improved significantly in all survey components compared with the control group ($P<0.001$).	3	Pharmacist can be beneficial in the areas of education and goal setting, but it was difficult to affect the appropriateness of medication in short time due to highly appropriateness measured in the baseline.
Gattis, 1999[24]	United States	Pharmacists discussed patient cases and verbally provided therapeutic recommendations regarding optimization of therapy to the attending physician. (90 patients)	Patients received usual care, and a pharmacist did not provide any recommendations regarding drug therapy. (91 patients)	Patients in the intervention group had a lower rate of all the causes of mortality and heart failure events compared with the control group ($P=0.005$). Intervention group patients also had significantly higher angiotensin enzyme inhibitor (ACE I) doses than those in the control group ($P<0.001$), with a higher use of other vasodilators in patients with ACE I intolerance ($P=0.02$).	3	The study found that the clinical pharmacist is an important member of the multidisciplinary heart failure team and significantly improves patient care.
Varma, 1999[26]	United Kingdom	Pharmacists discussed with physicians the appropriateness of drug therapy and educated patients for better self-care. (42 patients)	Patients received usual standard care. (41 patients)	Patients in the intervention group showed more improvement in a 2-minute walking test ($P=0.03$) and blood pressure ($P=0.01$). The intervention group also had more improvement in some components of quality of life tests, including physical functioning ($P<0.05$), vitality ($P<0.05$), social functioning ($P<0.05$), and mental health ($P<0.05$). No significant differences between the 2 groups were found in term of forced vital capacity or pulse control.	3	Pharmacist improved patients` drug knowledge with fewer hospital admissions and improved outcomes. Further study in a large sample is required to provide additional evidence.

TABLE B18 *Randomized Controlled Trial Conducted in an Outpatient Setting Using a Pharmacist-Led Intervention Model for Patients with Heart Failure*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
López Cabezas, 2006[25]	Spain	A personal interview was performed that included information on the disease, diet education, and information on drug therapy. Pharmacists also performed follow-up phone calls on a regular basis and provided the patients with pharmacist contact details if any issues arose. (70 patients)	Patients in the control group received usual care without any intervention from a clinical pharmacist. (64 patients)	Patients in the intervention group had significant improvement in patient adherence and rate of hospital readmission and hospital stay at the 2- and 6-month follow-up visits compared with the control group. They also had a lower death rate at the 12-month follow-up and better patient satisfaction at the 2-month follow-up visit. No significant differences were found between the 2 groups in terms of quality of life.	3	Pharmacist providing postdischarge education for patients with heart failure reduced hospital re-admissions and the length of hospital stay and improved treatment compliance without increasing health care costs.

TABLE B19 *Randomized Controlled Trials Conducted in a Community Setting Using a Pharmacist-Led Intervention Model for Patients with Heart Failure*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Bouvy, 2003[22]	Netherlands	Patients were interviewed by a community pharmacist who discussed drug use, reasons for noncompliance, and encouraged compliance. Then the pharmacist sent a report to the general practitioner and contacted the patient on a monthly basis for 6 months. (74 patients)	Patients received usual care with no interview with the pharmacist. (78 patients)	Patients in the intervention group had greater compliance to prescribed diuretics, but no significant differences were found in terms of re-hospitalization, mortality, or disease specific quality of life.	3	Pharmacist-led intervention can have a positive effect on patient compliance for those with moderate to severe heart failure even if they are relatively high compliance.
Holland, 2007[23]	United Kingdom	Pharmacists arranged for home visits within 2 weeks of discharge; educated the patient/care giver about heart failure and drugs and gave basic exercise, dietary, and smoking cessation advice; encouraged completion of simple sign and symptom monitoring; distributed diary cards; removed discontinued drugs, fed back recommendations to the general practitioner and fed back to the local pharmacist for any need of drug adherence aids. (169 patients)	Usual care with no home visits from a pharmacist. (170 patients)	Patients in the intervention group did not have a significant decrease in the number of admissions ($P=0.28$) or death ($P=0.54$). In terms of quality of life, Eq-5D showed a better result for the intervention group while the Minnesota Living with Heart Failure Questionnaire showed a better improvement in the control group. None of these quality of life measure differences were significant.	3	Community pharmacist interventions did not improve heart failure outcome and reduce re-admission rates.

TABLE B20 *Randomized Controlled Trial Conducted in an Outpatient Setting Using a Pharmacist-Led Intervention Model to Identify Patients with Drug-Related Problems*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Jadad Score	Comments
Lee, 2006[42]	United States	Pharmacies provided medication education, dispensed medication by using adherence tools, and required follow-ups at 2-month intervals. The intervention was performed in phase 1 of the study and continued for patients in the randomized group. (83 patients)	Patients were randomized to the control group in phase 2, when they returned to receive the prestudy service (usual care). (76 patients)	At the end of phase 1, patients had significant improvements in medication adherence ($P<0.001$), systolic blood pressure ($P=0.02$), and LDL levels from baseline ($P=0.001$). After stopping the services for the control group, patients in the intervention group had a significant difference in medication adherence and systolic blood pressure.	3	Pharmaceutical care improved medication adherence, blood pressure, and lipid control, which continued after the services had ceased. The study results suggested that health care organisations should promote clinical pharmacy services.

LDL = low-density lipoprotein.

TABLE B21 *Nonrandomized Controlled Trials Conducted by Using a Pharmacist-Led Intervention Model for Patients with Diabetes Mellitus and Reporting Cost*

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Comments
Outpatient setting:					
Anaya, 2008[77]	United States	Pharmacists were responsible for diabetes education; initiating, changing, and monitoring medications; ordering all appropriate laboratory tests; scheduling and rescheduling patient visits with the pharmacist; and making referrals to other health care providers as needed.	Retrospective chart review was conducted that included patients with laboratory results of interest.	Patients receiving intervention from clinical pharmacists had significant improvements in HbA1c and blood glucose ($P\leq0.001$). They also had improvement in the number of emergency room visits, which resulted in decreased costs ($P=0.015$).	Pharmacist interventions under agreed protocol significantly improved diabetic patient control. This was combined with significant reduction in hospitalization and emergency room visits.
Community setting:					
Cranor, 2003[78]	United States	Patients met with a pharmacist who monitored treatment goals, provided diabetes education, home glucose meter training, information about adherence to their regimens and performed physical and laboratory assessments.	Baseline measurements for patients included in the study were used as a control.	Patients who received direct care from a clinical pharmacist had significant improvements in HbA1c concentration, especially in the first 2 follow-up visits ($P<0.0001$). A significant reduction was also found in LDL levels at the second follow-up visit and HDL at the third follow-up visit ($P=0.05$). Total mean drug costs were reduced per patient per year from baseline by $1,200 to $1,872.	Pharmacist interventions improved diabetic patient control with a decline in total medical cost during each year of follow-up. Patients with high levels of HbA1c were most likely to have benefits from these interventions.

HbA1c = hemoglobin A1c; HDL = high-density lipoprotein; LDL = low-density lipoprotein.

TABLE B22 Nonrandomized Controlled Trial Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Hypertension and Reporting Cost

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Comments
Erickson, 1997[79]	United States	Pharmacists reviewed patient medical records; obtained medical and drug histories; assessed patient specific drug issues; assessed compliance and patient knowledge about hypertension and lifestyle modification; monitored patient drug therapy; and discussed with physicians drug-related problems or any changes required.	Control group received usual care without any intervention from a pharmacist related to pharmaceutical care.	Patients in the intervention group had a significant decrease in their blood pressure compared with baseline in both systolic ($P=0.001$) and diastolic blood pressure ($P=0.01$). Patients in the control group did not have any significant differences in their blood pressure. When the changes in the 2 groups were compared, the only significant difference was found in systolic blood pressure ($P=0.05$). There were no significant differences found in quality of life (SF-36) except in physical activity ($P=0.03$).	Pharmacist care services targeting patients with hypertension can improve blood pressure control.

TABLE B23 Nonrandomized Controlled Trial Conducted in an Outpatient Setting Using a Pharmacist Collaborative Model for Patients with Hyperlipidemia and Reporting Cost

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Comments
Hilleman, 2004[80]	United States	Pharmacists sent letters to physicians regarding patient cholesterol, which included pharmacist recommendations. Pharmacists then made telephone follow-ups to confirm the application of these recommendations and achievement of target levels.	Patients in the control group did not receive any pharmacist recommendations.	Patients in the intervention group had a significantly higher level of statin use, clinic visits, and laboratory tests, which were reflected in a significantly higher number of patients achieving the target LDL level. The total cost for the intervention group was lower than for the control group ($1,576,898 vs. $1,968,674).	Concludes that pharmacist-made recommendation to physicians regarding statin therapy for patients with CHD was associated with an improvement in statin use, better LDL levels, and cost saving.

CHD = coronary heart disease; LDL = low-density lipoprotein.

TABLE B24 Nonrandomized Controlled Trial Conducted in an Inpatient Setting Using a Pharmacist Collaborative Model for Patients with Coronary Artery Disease and Reporting Cost

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Comments
Gandhi, 2001[81]	United States	Clinical pharmacists provided patient care in a coronary care unit from July 1998 to March 1999.	Patients admitted from October 1997 to June 1998 did not receive any pharmacist intervention.	Drug costs per admission were not reduced significantly in intervention period 1 from nonintervention period ($P > 0.1$). In intervention period 2, drug costs decreased significantly when compared with the nonintervention period ($P = 0.002$).	Clinical pharmacist can significantly decrease the estimated total drug cost in a coronary care unit.

TABLE B25 Nonrandomized Controlled Trial Conducted in a Community Setting Using Pharmacist-Led Intervention Model for Patients with Drug-Related Problems and Reporting Cost

Author, Year	Country	Description of Pharmacist Intervention (number of patients)	Description of Control (number of patients)	Result	Comments
Munroe, 1997[82]	United States	Pharmacists assessed patient adherence and educated patients regarding their condition, medication administration, role of medication, nondrug therapy, self-monitoring, and adverse effects. Pharmacists also assessed patient blood pressure, cholesterol determinations, blood glucose, and peak flow rate, weight, pulse, and respiratory rate. All information obtained by pharmacists was documented and regularly sent to patient's physician by letter or phone. Any recommendations or referrals required were included in the letters.	Patients did not receive any intervention from a pharmacist.	The study showed no significant differences between the 2 groups in terms of monthly prescription costs, except for patients with asthma ($P = 0.03$). For overall costs, pharmacist intervention resulted in significant differences from the control group ($P = 0.024$).	Pharmacist intervention can play an important role in decreasing health care cost, although this study showed a higher average of cost per prescription in the intervention group than the control group. This difference was not statistically significant except for patients with asthma. The average monthly medical costs were reduced in the intervention group, and pharmacist intervention was shown to reduce overall health care costs.

APPENDIX C Economic Studies Conducted to Measure the Pharmacist Impact in Treating Patients with CHD or CVD Risk Factors

Author	Scott, 2007[74]	Simpson, 2001[73]	Sinclair, 1999[68]	Taylor, 2005[71]
Type of economic evaluation	Cost minimization	Cost analysis	Cost-effectiveness analysis	Cost-effectiveness analysis
Perspective used	Health care system and patients perspective	Government and pharmacy manager perspective	Social perspective	Health care sector in general
Currency used	£ Sterling	$ Canadian	£ Sterling	$ Australian
Modeling	Regression modeling	No modeling	No modeling	No modeling
Description of pharmacist intervention	Pharmacist conducted interviews with patients and delivered medicine management service. This included medication review and lifestyle advice. Patient GPs were advised of any prescription changes and recommendations.	Pharmacists screened and identified CVD risk factors, provided verbal and written education on risk factors, with a referral to family physicians and monitoring of patients closely for 16 weeks.	Pharmacists gave detailed advice depending on the smoker cessation stage with appropriate follow-up.	Pharmacists provided medication review and documented any recommendations made for each patient.
Description of control	Patients in the control group did not have a structured interview with a pharmacist.	Patients received written material with general information about CVD risk factors with minimal follow-up.	Pharmacists gave standard advice and support for smoking cessation.	Patients received the standard of care as normal.
Source of effectiveness data	Single study	Single study	Single study	Single study
Source of resource use data	Single study	Single study	Single study	Single study
Source of unit cost data	Data from actual source	Combination of both	Data from actual source	Data from actual source
Link between cost and effectiveness data	Only cost data collected–very detailed.	Data relating to cost and effectiveness was collected prospectively and concurrently.	Prospective, concurrent collection of costs and effects data.	Data relating to cost and effectiveness was collected prospectively and concurrently.
Clinical outcomes measured and methods of valuation used	Outcomes measured in another study in term of medicine management and improving CHD patients' outcomes (nonsignificant).	Outcomes measured in terms of changes in cardiovascular risk by using the Framingham risk score.	Outcomes measured in term of quitters at 9 months.	Clinical outcomes measured in term of changes in HbA1c and glucose levels.
Comments	Suitability of CMA questionable.	Unconvincing study: authors have undertaken a "cost-identification" analysis assuming that improvement in risk factor management would translate into reduction in CV risk. Would need an improved study to make such a case.	A relatively old and limited study that highlighted contributions made by clinical pharmacists in achieving a cost-effective cessation in smoking.	Would have benefited from patient-level data and probabilistic sensitivity analysis and consideration of longer-term scenarios via modeling.
Authors' conclusions	The 1-year pharmacist-led medicine management was associated with a total cost increase with no changes in patient outcomes. The use of health care resources is unlikely to be efficient in this particular service.	Clinical pharmacy services in community were shown to be effective in terms of improving cholesterol management, systolic blood pressure, and reduction of the 10-year risk of CVD with a minimal increase in the incremental cost to the government health care system.	The study provided evidence of the community pharmacist cost-effectiveness in delivering smoking cessation advice to achieve national targets.	The study showed a significant reduction of HbA1c in favor of the intervention group at a cost of $A 383. It is likely to produce a cost saving to health care in the long term. The sustainability of the reduction in HbA1c if the service stopped after 9 months is unknown.
Author	Thavorn, 2008[69]	Boyd, 2009[70]	Cote, 2003[72]	Lowey, 2007[83]
Type of economic evaluation	Cost-effectiveness analysis	Cost-utility analysis	Cost-benefit analysis	Cost-effectiveness analysis
Perspective used	Health care system perspective	NHS perspective	Societal perspective	Hospital and patient perspectives
Currency used	Thai baht	£ Sterling	$ Canadian	£ Sterling
Modeling	Yes – Markov	Decision-analytic model	None	None

APPENDIX C Economic Studies Conducted to Measure the Pharmacist Impact in Treating Patients with CHD or CVD Risk Factors *(continued)*

Description of pharmacist intervention	Structured community pharmacist-based program for smoking cessation.	NHS support via the group-based service.	Modified factors that affect adherence to antihypertensive drug treatment, reinforced the use of nonpharmacological treatments, optimized pharmacological treatments.	Pharmacists met with patients and provided education and medicine management. Any changes made were recorded and issued to patient GPs after each visit.
Description of control	Usual care	Self quit	Participants not involved in pharmacist intervention program.	Patient data at baseline was used as control.
Source of effectiveness data	Review/synthesis	Review/synthesis	Single study	Single study
Source of resource use data	Review/synthesis	Single study	Single study	Single study
Source of unit cost data	Review/synthesis	Review/synthesis	Single study	Single study
Link between cost and effectiveness data	Costs derived prospectively; effectiveness data derived from systematic review.	Concurrent and prospective	Prospective, concurrent collection of costs and effects data.	Prospective and concurrent
Clinical outcomes measured and methods of valuation used	Probability of events was used to assess the efficacy of the smoking cessation program.	Outcomes measured in terms of changes in numbers of quitters.	Outcomes measured in terms of quitters at 9 months.	Outcomes measured in terms of blood pressure, cholesterol levels, CHD 10-year risk, and CVA 10-year risk.
Comments	Highlights other decision factors.	Good CUA – albeit without PSA.	CBA using WTP – useful as approach.	Very limited explanation and discussion of cost-effectiveness.
Authors' conclusions	Pharmacy program for smoking cessation was found to be cost saving and provided a gain in life years.	Both the pharmacy smoking cessation program and smoking cessation support group are considered to be very cost effective. A long-term study will be required to assess lifetime cost-effectiveness.	Pharmacist program seems promising in terms of improving patient blood pressure. This conclusion will require further research in order to be confirmed.	The study resulted in a significant reduction of CVA and CHD risk in diabetic patients in the intervention group.

CBA = cost benefits analysis; CHD = coronary heart disease; CMA = cost minimization analysis; CUA = cost utility analysis; CV = cardiovascular; CVA = stroke; CVD = cardiovascular disease; GP = general practitioner; HbA1c = hemoglobin A1c; NHS = National Health Service; PSA = probablistic sensitivity analysis; WTP = willingness to pay; $A = Australian dollar.