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COMMUNITY GUIDE REVIEW

Pharmacist Interventions for Medication Adherence: Community Guide Economic Reviews for Cardiovascular Disease

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Introduction: Adherence to medications for cardiovascular disease and its risk factors is less than optimal, although greater adherence to medication has been shown to reduce the risk factors for cardiovascular disease. This paper examines the economics of tailored pharmacy interventions to improve medication adherence for cardiovascular disease prevention and management.

Methods: Literature from inception of databases to May 2019 was searched, yielding 29 studies for cardiovascular disease prevention and 9 studies for cardiovascular disease management. Analyses were done from June 2019 through May 2020. All monetary values are in 2019 U.S. dollars.

Results: The median intervention cost per patient per year was $246 for cardiovascular disease prevention and $292 for cardiovascular disease management. The median change in healthcare cost per person per year due to the intervention was −$355 for cardiovascular disease prevention and −$2,430 for cardiovascular disease management. The median total cost per person per year was −$89 for cardiovascular disease prevention, with a median return on investment of 0.01. The median total cost per person per year for cardiovascular disease management was −$1,080, with a median return on investment of 7.52, and 6 of 7 estimates indicating reduced healthcare cost averted exceeded intervention cost. For cardiovascular disease prevention, the median cost per quality-adjusted life year gained was $11,298. There were no cost effectiveness studies for cardiovascular disease management.

Discussion: The evidence shows that tailored pharmacy-based interventions to improve medication adherence are cost effective for cardiovascular disease prevention. For cardiovascular disease management, healthcare cost averted exceeds the cost of implementation for a favorable return on investment from a healthcare systems perspective.

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INTRODUCTION

Greater adherence to medication is associated with a reduction in the risk factors for cardiovascular disease (CVD).[1–3] However, adherence to medications for CVD and CVD risk factors is less than optimal because the medications are not taken as prescribed.[4–6] Adherence is often indirectly measured using pharmacy dispensing data. A patient is commonly considered adherent to a medication if they have a supply of that medication ≥80% of the measured time period.[7] Among 1.8 million adults in 2001–2004 undergoing their first year of medication therapy, the percentage achieving adherence of ≥80% was 72.3% for hypertension, 65.4% for type 2 diabetes, and 54.6% for hypercholesterolemia.[8] A meta-analysis of >376,000 patients from 20 studies who were taking CVD-preventive medications over the long term reported adherence rates of 50% for those with no previous myocardial infarction and 66% for those who have had a myocardial infarction.[6]

Medication nonadherence is associated with higher healthcare costs. A recent review based on 12 studies (9 from the U.S.) of medication adherence for hypertension, dyslipidemia, and heart failure found that the mean annual incremental healthcare cost due to nonadherence ranged from $3,610 to just higher than $21,000.[9] A study by a large retail pharmacy chain found that higher medication costs incurred by adherent patients were recouped through lower overall healthcare costs for the group. The ratio of averted healthcare costs to medication costs for adherent patients was 10.1:1 for hypertension, 3.1:1 for dyslipidemia, 8.4:1 for congestive heart failure, and 6.7:1 for diabetes.[10]

Interventions that improve medication adherence can reduce CVD risk and reduce healthcare and other costs. Interventions delivered by pharmacists such as Medication Management Services,[11] including Medication Therapy Management services, have been proposed because Medication Therapy Management services can identify and address patient-level barriers to adherence.[12–14] These interventions are tailored when adherence barriers are identified for each patient, and they are provided guidance and services to reduce those barriers. In 2019, the Community Preventive Services Task Force (CPSTF), an independent, nonfederal panel of population health experts,[15] recommended tailored pharmacy-based adherence interventions on the basis of evidence from a systematic review of effectiveness in increasing patient adherence to medications for CVD prevention. CPSTF also found the intervention to be cost effective for CVD prevention on the basis of a systematic economic review.[16] There were no studies of cost–benefit or cost effectiveness analysis for CPSTF to consider an economic finding for CVD management. This study describes the process, results, and conclusions of the systematic economic review for CVD prevention and management.

The following research questions were addressed by the review:

1. What is the cost to implement the interventions?
2. What are the economic benefits of the interventions?
3. How do intervention costs compare to economic benefits?
4. Is the intervention cost effective?

METHODS

This study was conducted using established methods for systematic economic reviews developed by scientists at the Centers for Disease Control and Prevention and approved by CPSTF.[17] The study team included subject-matter experts on CVD from various agencies, organizations, and academic institutions; CPSTF members; and experts in systematic economic reviews from The Community Guide Office at the Centers for Disease Control and Prevention. Two reviewers independently screened the search yield, abstracted information from the included studies, computed economic estimates, and scored each estimate for quality. Disagreements were resolved through discussions with the larger team.

Tailored pharmacy-based interventions aim to help patients with CVD risk conditions take their medications as prescribed. In the interventions recommended by CPSTF, community or health system pharmacies use assessment tools or interviews to identify adherence barriers for each patient and provide tailored guidance and services to reduce those barriers. Tailored guidance includes either focused medication counseling or motivational interviews. Services include ≥1 of the following: patient tools such as pillboxes, medication cards, and calendars; medication refill synchronization; and enhanced follow-up. Interventions may include additional components that align with the Pharmacists' Patient Care Process such as patient education or communication and collaboration between the pharmacist and the patient's primary care provider. The interventions may be used alone, or they may be part of a broader intervention to reduce patients' CVD risk.[16]

Several outcomes reported in economic evaluations relate to present review's research questions. The definitions of these outcomes are provided next.

Intervention cost. Labor and materials are required to implement and deliver pharmacy-based adherence interventions. The intervention may be combined with additional interventions or may occur within interventions such as team-based care. The drivers of intervention cost are pharmacist and other staff salaries, the cost of patient education materials and adherence aids, and the cost of any added intervention.

Change in healthcare cost. Improved adherence to medications is associated with a reduction in risk factors such as high blood pressure (BP), blood glucose, and cholesterol and subsequent CVD and comorbidities such as diabetes, retinopathy,

neuropathy, and kidney failure and thereby associate with decreased utilization of healthcare resources related to these conditions. All components of healthcare utilization are expected to change because of the intervention and are therefore considered cost drivers. Although reductions in hospitalization and emergency department visits are expected in the longer term, the cost of medication, laboratory testing, and office visits may increase simply because of greater adherence and refills in the shorter term. The net effect on healthcare cost is thus an empirical question, at least in the short term.

Total cost and return on investment. Total cost is the sum of intervention cost and change in healthcare cost. Return on investment (ROI) is the ratio of the difference in intervention cost and change in healthcare cost to intervention cost. The ROI is from a healthcare systems perspective because the intervention cost is assumed to be borne by a healthcare payer, and the only benefit considered is averted healthcare cost. A favorable economic outcome is indicated by negative values of total cost or ROI >0.

Life years lived. Improved adherence to medications will prevent CVD and events and increase both quantity and quality of life years lived. Economic evaluations measure this outcome as quality-adjusted life years (QALY) gained or disability-adjusted life years (DALY) averted.

Productivity. Reduced morbidity and mortality also lead to greater productivity of patients at their work sites owing to both increased number of work hours and increased output per hour of work.

Cost effectiveness. Cost effectiveness is the total cost per QALY gained or the total cost per DALY averted. The CPSTF considers an intervention to be cost effective when the cost per QALY gained ≤$50,000[18] or the cost per DALY averted is less than or equal to per capita gross domestic product of the relevant country.[19]

Quality Assessment of Evidence

Quality assessment. Quality assessment was conducted for each estimate that contributed to the economic outcomes of interest: intervention cost and healthcare cost. Estimates that were modeled such as QALY were assessed for quality on the basis of a separate set of criteria. A quality assessment tool developed for the scope and objective of this review along with a full process description is in the Appendix (available online). Quality of capture was assessed as good, fair, or limited for each estimate for how well it captured the components that are deemed to be the drivers of magnitude. Quality of measurement was assessed as good, fair, or limited for each estimate for the appropriateness of design and statistical and analytic methods used to derive the estimates. The overall quality of an estimate was the lower of the quality assigned for capture and the quality assigned for measurement. Limited quality estimates were removed from the review. Finally, the quality assigned to estimates that were a combination of other estimates such as total cost per QALY gained was the lower of the quality assigned to total cost and QALY components. The key elements are briefly described in the following paragraph.

Quality based on the capture of drivers was assigned to each estimate as good, fair, or limited because it included most, some, or almost none of the components considered as drivers, respectively. The drivers of intervention cost were pharmacist and other staff wages and the cost of any additional intervention added to the pharmacy intervention. The drivers of healthcare cost were outpatient visits, inpatient stays, emergency department visits, medications, and laboratories. QALY estimates have no components, and hence they are not examined for drivers. Next, quality of measurement was assessed for each estimate of intervention cost and healthcare cost on the basis of limitation points for failing to follow appropriate measurement and statistical methods. Quality based on measurement was assigned to each estimate as good, fair, or limited because the number of limitations points were few, some, or many, respectively. The criteria for assessing limitation points were broadly classified into the domains of appropriate: population, analytic horizon, study or experiment design, data sources, and valuation. Briefly, limitation points for measurement were assigned for small sample size, populations that were predominantly young adults or seniors, time horizons that were too short to plausibly capture intervention effects, study designs that did not have an appropriate comparison group, economic outcomes that were not CVD related, and others. For the modeled estimates, additional criteria were considered for quality of measurement. Briefly, limitation points were assigned for model inputs not drawn from trials, short time horizons, model parameters without cited research, lack of sensitivity analysis, and others.

All monetary values are in 2019 U.S. dollars, adjusted for inflation using the Consumer Price Index from the Bureau of Labor Statistics,[20] and converted from foreign currency denominations using purchasing power parities from the World Bank.[21] Estimates are reported in per patient per year (PPPY) terms, wherever possible. Summaries of estimates are reported as medians along with interquartile intervals (IQIs) where there are ≥4 estimates. All analyses were conducted from June 2019 through May 2020.

Results are presented separately for studies of patients with existing CVD and studies with patients who are at risk for CVD. The rationale for the separation was the expectation that both the cost to implement the intervention and the effects on healthcare utilization, productivity, and life years lived would be different for CVD management and CVD prevention.

Search Strategy

A search of the peer-reviewed literature for economic evaluations was conducted with the following inclusion criteria: met the definition of the intervention, conducted in a high-income country,[22] written in English, and included ≥1 economic outcomes described in the research questions. Searches were conducted in PubMed, Embase, MEDLINE, Scopus, Cochrane, ERIC, CINAHL, Sociological Abstracts, and EconLit for papers published from the inception of databases to May 2019. Reference lists in included studies were screened, and subject-matter experts were consulted for additional studies. The detailed search strategy is available on The Community Guide website.[23]

RESULTS

Figure 1 shows the search yield for the economic review that resulted in the 38 included studies: 29 studies[24–52] for CVD prevention and 9 studies[50,53–60] for CVD management. Of the 15 studies of patients with diabetes, 6 studies[30,31,44,46,48,52] were for patients with a type 2

diabetes diagnosis, and 9[27,33,36,38,40,41,49–51] had patients with both type 1 and type 2 diabetes; the term diabetes will be used in this review to cover both types. Table 1 provides intervention and population characteristics. The median sample sizes were 169 patients for CVD prevention and 174 patients for CVD management. There were more female participants in the studies for CVD prevention than in those for CVD management (median=56% vs 45%), and the patients were younger (median age=57 vs 65 years). The CVD prevention studies included patients with high BP (10 studies),[25,26,28,29,35,37,39,42,44,47] dyslipidemia (4 studies),[28,33,44,48] diabetes (14 studies),[27,30,31,33,36,38,40,41,44,46,48,49,51,52] and a combination of CVD risk factors (9 studies).[24,32,34,43–45,49–51] The CVD management studies included patients with heart failure (3 studies),[56,57,60] CVD (5 studies),[53–55,58,59] and multiple cardiovascular conditions and diabetes (1 study).[50]

Studies were based in the U.S. (27 studies),[24,25,27–29,32,34,36–48,51–55,57,58] the Netherlands (2 studies),[26,50] the United Kingdom (2 studies),[49,59] Canada (2 studies),[35,60] China (Hong Kong; 2 studies),[30,33] Taiwan (1 study),[31] and Spain (1 study).[56] Studies were set in pharmacies (20 studies),[26,28,29,32,34–36,41,44,46–51,54,56,57,59,60] primary care clinics (13 studies),[24,25,30,31,33,37–40,42,52,53,55] a mixture of the 2 (1 study),[45] or the facilities of pharmaceuticals benefits managers (3 studies).[27,43,58] The majority were implemented in urban areas (19 studies),[24,25,28–31,33–38,40,41,45,51,53,54,57] and others were implemented in a mixture of urban and rural areas (9 studies).[27,32,39,43,44,47,48,50,58]

Pharmacist activities related to medication adherence occurred in every study because it was an inclusion criterion. Other pharmacist activities that were reported in each study are identified in the tables of results. The description of these activities are provided in greater detail in Appendix Table 1 (available online). The non-adherence-related actions taken by the pharmacist were patient education in 52% of CVD prevention studies[24,27–31,33,34,36,46–48,50–52] and 56% of CVD management studies,[50,56–58,60] lifestyle counseling in 34% of CVD prevention[24,25,28,30,33,37–39,42,46] and 56% of CVD management studies,[53,54,56,59,60] and the resolution of drug-related problems in 69% of CVD prevention[24,25,27–34,37–40,42,43,45,46,49,52] and 78% of CVD management studies.[53–55,57–60] Goal-setting activities were in 38% of CVD prevention studies[25,26,28,34,36,39,40,43,45,49,51] and in 22% of CVD management studies.[55,58]

Quality of estimates. Table 2 shows that most intervention cost estimates were of good quality (17 estimates), with the remainder being of fair quality (9 estimates). The most frequent limitations were failure to include the cost of patient education materials or adherence aids. Healthcare cost estimates were mixed in quality, with 15 being of good, 20 being of fair, and 5 being of limited quality (Table 2). The most frequently assessed limitations were failure to include inpatient or emergency department costs, the inclusion of

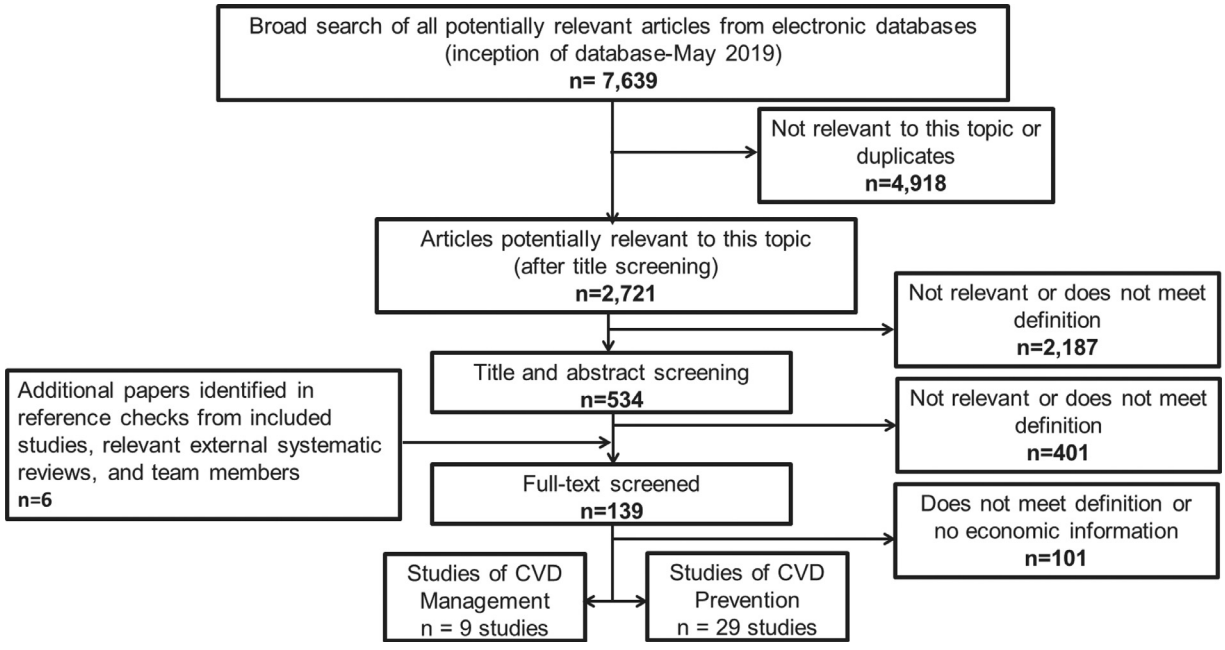

Figure 1. Search yield. CVD, cardiovascular disease.

Table 1. Patient and Intervention Characteristics

Study Country	Intervention sample size Settingurbanicity	Pharmacist activities other than adherence related	Mean age Percentage female	Non-White minority percent	Baseline mean clinical indicators	Baseline disease and risk factors
Altavela (2008)[24] U.S.	127 CL urban	PE, LC, DP	NR 65%	NR	NR	MCV
Borenstein (2003)[25] U.S.	98 CL urban	LC, DP, GS	61.5 y 61%	33.5%	SBP 159 DBP 91	BP
Bosmans (2019)[26] The Netherlands	85 RP NR	GS	60 y 52%	5%	SBP 145 DBP 88	BP
Brophy (2014)[27] U.S.	954 PBM mixed	PE, DP	NR 68.5%	56%	NR	DM
Bunting (2008)[28] U.S.	620 RP urban	PE, LC, PC, DP, GS	50 y 53%	18%	SBP 137.3 DBP 82.6	BP, LD
Carter (1997)[29] U.S.	25 RP urban	PE, PC, DP	67 y 76%	NR	SBP 146 DBP 83	BP
Chan (2012)[30] China (Hong Kong)	51 CL urban	PE, LC, DP	NR 41%	NR	SBP 141 DBP 75 A1c 9.7	DM
Chen (2016)[31] Taiwan	50 CL urban	PE, DP	72 y 50%	NR	SBP 135 DBP 75 A1c 9.22	DM
Christensen (2007)[32] U.S.	85 RP mixed	DP	68 y 63%	NR	NR	MCV
Chung (2011)[33] China (Hong Kong)	150 CL urban	PE, LC, DP	56 y 45%	NR	LDL 3.53	LD, DM
Connor (2009)[34] U.S.	100 RP urban	PE, PC, DP, GS	49 y 33%	61%	SBP 137 DBP 85 LDL 108 A1c 10.3	MCV
Côté (2003)[35] Canada	41 RP urban	PC	NR 65%	NR	NR	BP
Cranor (2003)[36] U.S.		PE, PC, GS	47.7 y 51%	17%	LDL 116 A1c 7.8	DM

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Table 1. Patient and Intervention Characteristics (*continued*)

Study Country	Intervention sample size Settingurbanicity	Pharmacist activities other than adherence related	Mean age Percentage female	Non-White minority percent	Baseline mean clinical indicators	Baseline disease and risk factors
	187 RP urban					
Dehmer (2018)[37] U.S.	148 CL urban	LC, DP	63 y 46%	13.4%	SBP 148 DBP 83	BP
Fabel (2019)[38] U.S.	602 CL urban	LC, PC, DP	NR NR	NR	SBP 150 DBP 94 A1c 12.1	DM
Fishman (2013)[39] U.S.	261 CL mixed	LC, DP, GS	NR 50%	17%	SBP 151.3 DBP 88.9	BP
Isetts (2012)[40] U.S.	823 CL urban	DP, GS	NR 60%	NR	NR	DM
Kraemer (2012)[41] U.S.	36 RP urban	None	56 y 39%	10%	SBP 136.3 DBP 80.6 LDL 99.5 A1c 7.28	DM
Kulchaitanaroaj (2017)[42] U.S.	399 CL NR	LC, DP	NR 57%	14%	SBP 151.4 DBP 86.9	BP
Moore (2013)[43] U.S.	2,250 PBM mixed	DP, GS	NR 60%	NR	NR	MCV
Oliveira (2010)[45] U.S.	9,068 CL and RP urban	DP, GS	NR 76%	NR	NR	MCV
Pringle (2014)a[44] U.S.	107 mixed	None	NR 57%	NR	NR	MCV, DM
Pringle (2014)b[44] U.S.	107 RP mixed	None	NR 57%	NR	NR	MCV, DM
Rashed (2010)[46] U.S.	22 RP NR	PE, LC, DP	57 y 59%	32%	LDL 140.4 A1c 8.99	DM
Shireman (2016)[47] U.S.	276 RP mixed	PE, PC	54 y 62%	100%	SBP 151 DBP 92	BP

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Table 1. Patient and Intervention Characteristics (*continued*)

Study Country	Intervention sample size Settingurbanicity	Pharmacist activities other than adherence related	Mean age Percentage female	Non-White minority percent	Baseline mean clinical indicators	Baseline disease and risk factors
Spence (2014)[48] U.S.	1,480 RP mixed	PE	56.5 y 51%	NR	LDL 134.5 A1c 9.28	LD, DM
Twigg (2019)[49] UK	378 RP NR	PC, DP, GS	NR 56%	NR	SBP 139.5 DBP 78.4	MCV, DM
Vegter (2014)[50] The Netherlands	Modeled RP mixed	PE	61 y 45%	NR	NR	MCV
Wertz (2012)a[51] U.S.	307 RP urban	PE, PC, GS	59 y 51%	50%	SBP 136.1 DBP 79.3 LDL 104.1	MCV, DM
Wertz (2012)b[51] U.S.	307 RP urban	PE, PC, GS	59 y 51%	50%	SBP 136.1 DBP 81 LDL 91.6 A1c 7.9	MCV, DM
Yu (2013)[52] U.S.	204 CL NR	PE, DP	55.5 y NR	NR	SBP 128.9: DBP 73.9 A1c 9.5	DM
Summary for CVD prevention studies Median (IQI)	Intervention sample size 169 (85–450)	Frequency: PE 16; LC 10; PC 10; DP 20; GS 12	Age 57 y (56–62 y) Percentage female 56% (50%–62%)	18% (14%–50%)	SBP 141 (136–150) DBP 83 (79–88) LDL 108 (102–125) A1c 9.3 (8.2–9.7)	Frequency: BP 9; LD 3; DM 16; MCV 11.
Delate (2010)[53] U.S.	628 CL urban	LC, PC, DP	61.7 y 33%	NR	NR	CVD
Ditusa (2001)[54] U.S.	300 RP urban	LC, DP	67 y 30%	NR	SBP 145 DBP 82 A1c 7.3	CVD
Ellis (2000)[55] U.S.	208 CL NR	PC, DP, GS	65 y 4%	NR	LDL 129.4	CVD
López Cabezas (2006)[56] Spain	70 HP NR	PE, LC	76 y 53%	NR	NR	HF
Murray (2007)[57] U.S.		PE, DP	61.4 y 68%	46	SBP 132.9 DBP 68.9	HF

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Table 1. Patient and Intervention Characteristics (*continued*)

Study Country	Intervention sample size Settingurbanicity	Pharmacist activities other than adherence related	Mean age Percentage female	Non-White minority percent	Baseline mean clinical indicators	Baseline disease and risk factors
	122 RP urban					
Polinski (2016)[58] U.S.	131 PBM mixed	PE, DP, GS	61.8 y 58%	30	NR	CVD
Scott (2007)[59] UK	980 RP NR	LC, DP	68.7 y 52.6%	NR	SBP 138.8 DBP 77.2	CVD
Tsuyuki (2004)[60] Canada	140 HP NR	PE, LC, DP	71 y 42%	NR	NR	HF
Vegter (2014)[50] The Netherlands	Modeled RP mixed	PE	61 y 45%	NR	NR	CVD, DM
Summary for CVD management studies Median (IQI)	Intervention sample size 174 (129–382)	Frequency: PE 5; LC 5; PC 2; DP 7; GS 2	Age 65 y (62–69 y) Percent female 45% (33%–53%)	38%[a]	SBP 139[a] DBP 76[a] LDL 129[a] A1c 7.3[a]	Frequency: HF 3; CVD 6; DM 1

[a]Mean.

A1c, glycated hemoglobin; BP, blood pressure; CL, clinic; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; DP, drug problem; GS, goal setting; HF, heart failure; HP, hospital pharmacy; IQI, interquartile interval; LC, lifestyle counseling; LD, dyslipidemia; LDL, low-density lipoprotein; MCV, multiple cardiovascular risk factors; NR, not reported; PBM, pharmacy benefits manager; PC, patient care; PE, patient education; RP, retail pharmacy; SBP, systolic blood pressure; UK, United Kingdom; y, year.

medication cost only, and estimates based on all causes rather than on only CVD and risk factors. Limited quality estimates were excluded from consideration.

Intervention cost. Table 2 shows that the median cost PPPY for interventions to prevent CVD was $246 (IQI= $95, $499) on the basis of 20 estimates from 19 studies.[26,30–33,35,37–39,41–43,45–51] The median cost PPPY for interventions to manage CVD was $292 (IQI=$96, $422) on the basis of 6 estimates from 6 studies.[50,53,56–59] Separating out the U.S. studies (not shown in the table), the median intervention cost PPPY was $467 (IQI=$254, $577)[32,37–39,41–43,45–48,51,52] and mean intervention cost PPPY was $514 (range=$372–$731)[53,57,58] for CVD prevention and CVD management, respectively. Intervention cost was substantially higher in the U.S. than in other high-income countries.

The dispersion of intervention cost was partly explained by the size of the intervention group, with smaller intervention cost associated with larger groups for both studies of CVD prevention and those of CVD management. For the CVD prevention studies, the median intervention cost for estimates of good quality was $256 (IQI=$146, $504),[31–33,35,37–39,41,42,46–51] not shown in the table. This median for higher-quality estimates was only marginally higher than the median of $246 reported for all estimates. There were too few estimates of intervention cost from the CVD management studies to compare between good- and fair-quality estimates.

The median intervention cost PPPY was higher for CVD management at $292 than for CVD prevention at $246 (Table 2). The difference was not due to sample size because the median sample size of 169 for CVD prevention is close to the 174 for CVD management. The table also shows that there was little difference between studies of CVD prevention and CVD management in terms of intervention setting or pharmacist activities to explain the difference in median cost.

Healthcare cost. Table 2 shows that the median change in healthcare cost PPPY for interventions to prevent CVD was −$355 (IQI= −$977, −$33) on the basis of the 21 estimates from 19 studies.[24,26,27,29–31,33,35,37,39,41,43–46,48–51] The median change in healthcare cost PPPY for interventions to manage CVD was −$2,430 (IQI= −$5,062, −$700) on the basis of the 7 estimates from 7 studies.[50,53,56–60] Separating out the U.S. studies (not shown in the table), the median healthcare cost averted PPPY was −$376 (IQI= −$898, −$112)[24,27,29,37,39,41,43–46,48,51] and mean healthcare cost averted PPPY was −$10,983 (range= −$26,216, −$2,430)[53,57,58] for CVD prevention and CVD management, respectively. Healthcare cost averted in CVD management was substantially larger in the U.S. than in other high-income countries.

The median of the good-quality estimates of change in healthcare cost for CVD prevention was −$376 (IQI= $741, −$249),[27,39,41,43,44,51] slightly higher than the median of −$355 reported for all estimates in absolute value. The median of the good-quality estimates in CVD management was −$2,283 (IQI= −$4,683, −$258),[50,57,59,60] lower than the median of −$2,430 reported for all estimates in absolute value. Somewhat counterintuitively, a better capture of drivers of healthcare cost such as emergency department visits and inpatient stays produced estimates of healthcare cost avoidance that were higher for prevention and lower for management.

By contrast, the averted healthcare cost for CVD management was higher, with a median of $2,430 than $355 for CVD prevention. The difference in effect on healthcare cost is not likely due to either setting or pharmacist activities because they did not differ between the 2 sets of studies (Table 2). Among the 9 studies[50,53–60] of CVD management, 1 study[53] reported that BP and low-density lipoprotein cholesterol control improved, 1 study[55] reported a reduction in low-density lipoprotein cholesterol, 1 study[59] found no change in guideline-concordant treatment, and 2 studies[50,57] did not report any clinical outcomes. A total of 2 studies were implemented among patients selected from hospital discharges. The study[56] for post–heart failure discharge found that the intervention group had 54% fewer all-cause readmissions at 2 months and 32% fewer at 6 months. The other study[58] for post–cardiovascular condition discharges found a risk ratio of 0.55 for 30-day readmission. The poor reporting of intermediate clinical outcomes related to the medications makes it difficult to draw a causal argument from the adherence improving intervention to healthcare cost averted.

Total cost and return on investment. Total cost was measured as the sum of the change in healthcare cost due to intervention and the cost of intervention; a negative value indicates that averted healthcare cost exceeds intervention cost. Estimates are shown in Table 3. The median total cost PPPY for interventions to prevent CVD was −$89 (IQI= −$656, $209) on the basis of 21 estimates from 20 studies.[25,26,28,30,31,33,35–37,39–41,43,45,46,48–52] The total cost estimates for CVD prevention were mixed, with 9 estimates[25,26,31,37,39,41,49–51] reporting positive total cost and 12 estimates[28,30,33,35,36,40,43,45,46,48,51,52] reporting negative total cost. The median total cost PPPY for interventions to manage CVD was −$1,080 (IQI= −$2,816, −$163) on the basis of the 7 estimates from 7 studies.[50,53,55–59] For all but 1[55] of the estimates, the

Table 2. Intervention Cost and Change in Healthcare Cost: Estimates, Components, and Quality of Estimates

Study	Intervention sample sizeIntervention duration in months	Pharmacist activities other than adherence related	Intervention cost per patient per year	Quality of intervention cost estimate	Drivers included in intervention cost	Change in healthcare cost per patient per year	Quality of healthcare cost estimate	Drivers included in healthcare cost
Altavela (2008)[24]	127 12	PE, LC, DP	NR	NA	NA	$2,846	Fair	OP, IP, ED, Med, lab
Borenstein (2003)[25]	98 12	LC, DP, GS	NR	NA	NA	$75[a]	Fair	OP, Med
Bosmans (2019)[26]	85 9	GS	$76	Fair	PL	$1,439	Fair	OP, IP, Med
Brophy (2014)[27]	954 12	PE, DP	NR	NA	NA	$662	Good	OP, IP, ED, Med
Bunting (2008)[28]	620 12	PE, LC, PC, DP, GS	NR	NA	NA	$89[a]	Fair	OP, IP, ED, Med, lab
Carter (1997)[29]	25 6	PE, PC, DP	NR	NA	NA	$224	Fair	OP, Med
Chan (2012)[30]	51 60	PE, LC, DP	$100	Fair	PL	$1,190	Fair	OP, IP, ED, Med, lab
Chen (2016)[31]	50 12	PE, DP	$81	Good	PL, PM	$13	Fair	OP, IP, Med
Christensen (2007)[32]	85 6	DP	$479	Good	PL	$105	Limited	Med
Chung (2011)[33]	150 12	PE, LC, DP	$144	Good	PL	$1,402	Fair	OP, IP, ED, Med, lab
Connor (2009)[34]	100 12	PE, PC, DP, GS	NR	NA	NA	$3,528	Limited	Med
Côté (2003)[35]	41 12	PC	$147	Good	PL, CDSS	$355	Fair	OP, IP, Med
Cranor (2003)[36]	187 60	PE, PC, GS	NR	NA	NA	$6,207[a]	Fair	OP, IP, ED, Med, lab
Dehmer (2018)[37]	148 12	LC, DP	$1,552	Good	PL	$413	Fair	IP, Med
Fabel (2019)[38]	602 12	PE, PC, DP	$238	Good	PL	$3,346	Limited	IP
Fishman (2013)[39]	261 12	LC, DP, GS	$467	Good	PL, TBC	$0	Good	OP, IP, ED, Med
Isetts (2012)[40]	823 12	DP, GS	NR	NA	NA	$576[a] median	Fair	OP, Med
Kraemer (2012)[41]	36 12	None	$259	Good	PL	$49	Good	OP, IP, ED, Med, lab
Kulchaitanaroaj (2017)[42]	399 Lifetime	LC, DP	$698	Good	PL, TBC	$4,047 lifetime	Good	OP, IP, ED, Med, lab

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Table 2. Intervention Cost and Change in Healthcare Cost: Estimates, Components, and Quality of Estimates (*continued*)

Study	Intervention sample sizeIntervention duration in months	Pharmacist activities other than adherence related	Intervention cost per patient per year	Quality of intervention cost estimate	Drivers included in intervention cost	Change in healthcare cost per patient per year	Quality of healthcare cost estimate	Drivers included in healthcare cost
Moore (2013)[43]	2,250 12	DP, GS	$559	Fair	NR	$1,216	Good	OP, IP, ED, Med
Oliveira (2010)[45]	9,068 120	DP, GS	$29	Fair	NR	$38	Fair	OP, IP, ED, Med
Pringle (2014)a[44]	107 12	None	NR	NA	NA	CVD related $370	Good	OP, IP, ED, Med
Pringle (2014)b[44]	107 12	None	NR	NA	NA	DM related $382	Good	OP, IP, ED, Med
Rashed (2010)[46]	22 36	PE, LC, DP	$435	Good	PL	$6,247	Fair	OP, IP, Med
Shireman (2016)[47]	276 6	PE, PC	$254	Good	PL	$208	Limited	Med
Spence (2014)[48]	1,480 12	PE	$17	Good	PL	$302	Fair	IP, ED, Med
Twigg (2019)[49]	378 12	PC, DP, GS	$214	Good	PL	$53	Fair	OP, IP, ED
Vegter (2014)[50]	Modeled	PE	$45	Good	PL	$33	Fair	OP, IP, Med
Wertz (2012)a[51]	307 12	PE, PC, GS	Heart health $577	Good	PL, TBC	HTN related −$315	Good	OP, IP, ED, Med
Wertz (2012)b[51]	307 12	PE, PC, GS	Diabetes care $655	Good	PL, TBC	DM and CVD related $977	Good	OP, IP, ED, Med
Yu (2013)[52]	204 12	PE, DP	NR	NA	NA	$984[a]	Good	OP, IP, ED, Med, lab
Summary for CVD prevention studies Median (IQI)	Intervention sample size 169 (85–450) Duration 12 (12 –12)	Frequency: PE 17; LC 9; PC 10; DP 20; GS 12	$246 ($95–$499)	Frequency: Good 16, fair 4, limited 0	Frequency: CDSS 1, PL 18, PM 1, TBC 4	$355 (−$977 –– $33)	Frequency: Good 10, fair 17, limited 4	Frequency: OP 25, IP 25, ED 30, Med 29, Lab 8
Delate (2010)[53]	628 12	LC, PC, DP	$439	Fair	PL	$26,216	Fair	OP, IP, ED, Med, lab
DiTusa (2010)[54]	300 6	LC, DP	NR	NA	NA	$175	Limited	Med
Ellis (2000)[55]	208 12	PC, DP, GS	NR	NA	PL	$570[a]	Good	OP, IP, Med, lab
López Cabezas (2006)[56]	70 12	PE, LC	$58	Fair	PL	$1,138	Fair	IP
Murray (2007)[57]		PE, DP	$372	Good	PL	$4,304	Good	

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Table 2. Intervention Cost and Change in Healthcare Cost: Estimates, Components, and Quality of Estimates (*continued*)

Study	Intervention sample sizeIntervention duration in months	Pharmacist activities other than adherence related	Intervention cost per patient per year	Quality of intervention cost estimate	Drivers included in intervention cost	Change in healthcare cost per patient per year	Quality of healthcare cost estimate	Drivers included in healthcare cost
	122 9							OP, IP, ED, Med, lab
Polinski (2016)[58]	131 1	PE, DP, GS	$731	Fair	PL	$2,430	Fair	IP
Scott (2007)[59]	980 12	LC, DP	$211	Fair	PL	$261	Good	OP, IP, Med
Tsuyuki (2004)[60]	140 6	PE, LC, DP	NR	NA	NA	$5,819	Good	OP, IP, ED, Med
Vegter (2014)[50]	Modeled	PE	$45	Fair	PL	$248	Good	OP, IP, Med, lab
Summary for CVD management studies Median (IQI)	Intervention sample size 174 (129−382) Duration 11 (6−12)	Frequency: PE 5; LC 5; PC 2; DP 7; GS 2	$292 ($96–$422)	Frequency: Good 1, fair 5, limited 0	Frequency: CDSS 0, PL 7, PM 0, TBC 0	$2,430 (−$5,062−–$700)	Frequency: Good 5, fair 3, limited 1	Frequency: OP 6, IP 8, ED 7, Med 7, Lab 4

[a]Healthcare cost includes intervention cost.

CDSS, clinical decision support system; CVD, cardiovascular disease; DM, diabetes mellitus; DP, drug problems; ED, emergency department; GS, goal setting; HTN, hypertension; IP, inpatient; IQI, interquartile interval; Lab, laboratory and imaging; LC, lifestyle counseling; Med, medication; NA, not applicable; NR, not reported; OP, outpatient; PC, patient care; PE, patient education; PL, pharmacist labor; PM, patient materials and adherence aid; TBC, team-based care.

reduced healthcare cost exceeded the cost of intervention. Separating out the U.S. studies (not shown in the table), the median total cost PPPY was −$187 (IQI= −$636, $176)[25,28,36,37,39−41,43,45,46,48,51,52] and −$2,816 (IQI= −$9,394, −$1,132)[53,55,57,58] for CVD prevention and CVD management, respectively. The total cost for CVD prevention was not much larger in the U'S than in other high-income countries, with the IQI crossing 0 in both cases. However, total cost took substantially larger negative values, indicating cost savings, for CVD management in U.S studies than for other high-income countries.

Of the 4 studies[53,55,57,59] of interventions to manage CVD that provided estimates for components of healthcare cost, 1 study[59] had inpatient cost accounting for >90% of the averted cost, 2 studies[53,57] had 70%, and 1 study[55] showed that 10% of healthcare cost savings was attributable to inpatient stays. The median ROI for CVD prevention was 0.01 (IQI= −0.83, 3.25) on the basis of 16 estimates from 15 studies.[26,30,31,33,35,37,39,41,43,45,46,48−51] The median ROI for CVD management was 7.52 (IQI=2.86, 16.62) on the basis of 6 estimates from 6 studies.[50,53,56−59] A value of ROI >0 indicates a favorable economic outcome from a healthcare systems perspective.

Cost effectiveness. The median cost per QALY gained for interventions to prevent CVD was $11,298 (IQI= $5,660, $28,416) on the basis of 5 estimates from 5 studies[26,39,42,49,50] (Table 3). The median and third quartile were below a conservative $50,000 benchmark.[18] Only 1 estimate[26] was above the threshold, and that study computed cost per QALY on the basis of health outcomes within a 9-month trial period. There were no studies that reported cost effectiveness outcomes for interventions to manage CVD; however, total cost estimates showed that 6 of 7 estimates for averted healthcare cost exceeded the intervention cost, substantially from averted inpatient stays as noted earlier.

DISCUSSION

This study reviewed the cost, benefit, cost−benefit, and cost effectiveness evidence for tailored pharmacy-based interventions to improve adherence to CVD medications. A separate assessment of the evidence was conducted for the interventions implemented to prevent CVD and the interventions to manage CVD. The evidence indicates that the interventions for the prevention of CVD were cost effective. There were no studies that reported cost effectiveness outcomes for CVD management; however, 6 of 7 studies found that the healthcare costs averted exceeded the intervention costs.

Tailored pharmacy-based medication adherence interventions are cost effective in improving medication adherence for CVD prevention, and it is inferred that improved health outcomes result from adherence.[61−68] From the perspective of a healthcare system, the healthcare cost averted exceeds the cost to implement the interventions for CVD management. These findings may be used to inform local consideration of tailored pharmacy-based interventions for patients at risk for CVD (i.e., hypertension, diabetes, dyslipidemia, and chronic kidney disease). For patients with new or existing CVD, pharmacy-based adherence support can complement other health system interventions, such as structured cardiac rehabilitation and mobile health programs[69,70] to reinforce provider messages and encourage patients in their treatment adherence efforts.

It was noted that the averted healthcare cost for CVD management was much larger than for prevention, with a median of $2,430 and $355, respectively. This is likely a consequence of the much higher probability of CVD events even in the near term among patients who were older (median age=65 vs 57 years) and with existing CVD conditions[71] such as heart failure in the studies for CVD management than among those for CVD prevention (Table 1). The interventions for CVD management where averted healthcare cost exceeds the intervention cost may also be cost effective from the societal perspective if the changes in QALY/DALY are in the favorable direction. This review therefore also examined the clinical indicators for BP, cholesterol, and blood glucose in the studies that reported the estimates of total cost, which is the sum of intervention cost and healthcare cost averted (Table 3). Although it could not be concluded from the relatively small number of studies that observed reductions in healthcare cost were directly a consequence of improved health, 2 studies did report favorable impacts on BP and cholesterol. Numerous other studies have shown the benefit of reducing BP, glucose, lipids, albuminuria, and serum creatinine on healthcare resource consumption, progression of disease, the incidence of comorbidities, and cardiovascular and renal events.[61−68] This suggests that adherence to medication therapy in accordance with evidence-based treatment guidelines is important to reducing cardiovascular and renal events.[72−78] However, additional research is needed to validate a causal relationship between tailored pharmacy-based interventions aimed at improving medication adherence and improved health and economic outcomes.

The availability of these interventions in the U.S. varies. Availability may be particularly limited for those without health insurance coverage. For individuals with health insurance coverage, there is significant variation in reimbursement and patient eligibility for pharmacist-provided services outside of dispensing.[79,80] Despite the

Table 3. Summary of Economic Outcomes: Total Cost, ROI, and Cost Effectiveness

Study	Intervention effects on clinical indicators and adherence	Pharmacist activities other than adherence related	Total cost per patient per year (quality of estimate)	ROI health systems perspective (quality of estimate)	Cost effectiveness Cost per QALY gained (time horizon) (quality of estimate)
Borenstein (2003)[25]	SBP/DBP reduced by 11.0/1.0 mmHg at 12 months Adherence not reported	LC, DP, GS	$75 (fair)	NR (NA)	NR
Bosmans (2019)[26]	SBP/DBP reduced by 0.3/2.2 mmHg at 9 months MARS-5 increased by 0.23	GS	$1,594 (fair)	−20.06 (fair)	$70,762 (9 months) (fair)
Bunting (2008)[28]	SBP/DBP reduced by 8.0/3.5 mmHg at 12 months Adherence not reported	PE, LC, PC, DP, GS	$89 (fair)	NR (NA)	NR
Chan (2012)[30]	SBP/DBP reduced by 3.2/2.1 mmHg and LDL reduced by 0.33 mmol/dL at 9 months Tablets taken/ Tablets needed increased by 20.5 PCT Pt	PE, LC, DP	$1,090 (fair)	10.92 (fair)	NR
Chen (2016)[31]	No clinical outcomes reported. Strict adherence claimed in a study with no details	PE, DP	$68 (fair)	−0.84 (fair)	NR
Chung (2011)[33]	LDL reduced by 0.49 mmol/dL at 24 months Percent adherent increased by 13.7 PCT Pt	PE, LC, DP	$1,258 (fair)	8.76 (fair)	NR
Côté (2003)[35]	No clinical outcomes were reported. Adherence not reported	PC	$208 (fair)	1.41 (fair)	NR
Cranor (2003)[36]	Percentage at optimal LDL increased by 15.8 PCT Pt at 60 months and optimal A1c increased by 18.2 PCT Pt at 36 months Adherence not reported	PE, PC, GS	$6,207 (fair)	NR (NA)	NR
Dehmer (2018)[37]	SBP/DBP reduced by 9.7/5.1 mmHg at 12 months	LC, DP	$1,140 (fair)	−0.73 (fair)	NR

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Table 3. Summary of Economic Outcomes: Total Cost, ROI, and Cost Effectiveness (*continued*)

Study	Intervention effects on clinical indicators and adherence	Pharmacist activities other than adherence related	Total cost per patient per year (quality of estimate)	ROI health systems perspective (quality of estimate)	Cost effectiveness Cost per QALY gained (time horizon) (quality of estimate)
	Adherence not reported				
Fishman (2013)[39]	SBP/DBP reduced by 8.9/3.6 mmHg at 12 months Adherence not reported	LC, DP, GS	$467 (good)	−1.00 (good)	$2,381[a] (patient lifetime) (good)
Isetts (2012)[40]	Percentage at DM care 5-point benchmark by 40% versus 17.5% statewide. 828 adherence-related problems resolved	DP, GS	$576 (fair)	NR (NA)	NR
Kraemer (2012)[41]	SBP/DBP reduced by 5.9/1.9 mmHg, LDL reduced 4.0 mmol/dL, A1c reduced by 0.34 PCT Pt at 12 months ASK-20 total barrier score reduced by 0.4	None	$209 (good)	−0.81 (good)	NR
Kulchaitanaroaj (2017)[42]	SBP reduced by 12 mmHg at 9 months Adherence not reported	LC, DP	NR (NA)	NR (NA)	$28,416 (patient lifetime) (good)
Moore (2013)[43]	No clinical outcomes were reported. Medication possession ratios at 12 months increased by 4.6 PCT Pt for HTN, 4.71 PCT Pt for dyslipidemia, and 2.37 PCT Pt for DM	DP, GS	$656 (fair)	1.17 (fair)	NR
Oliveira (2010)[45]	No clinical outcomes were reported. 33,706 encounters with 16.5% of drug-related problems identified as adherence	DP, GS	$8 (fair)	0.29 (fair)	NR
Rashed (2010)[46]	LDL reduced by 34.6 mmol/dL at 36 months. Study reports adherence improvement with no details	PE, LC, DP	$5,812 (fair)	13.36 (fair)	NR

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Table 3. Summary of Economic Outcomes: Total Cost, ROI, and Cost Effectiveness (*continued*)

Study	Intervention effects on clinical indicators and adherence	Pharmacist activities other than adherence related	Total cost per patient per year (quality of estimate)	ROI health systems perspective (quality of estimate)	Cost effectiveness Cost per QALY gained (time horizon) (quality of estimate)
Spence (2014)[48]	LDL reduced by 7.4 mmol/dL and A1c reduced by 0.34 PCT Pt at 12 months. Percentage of patients with DM adherent increased by 16.1 PCT Pt, and medication possession ratio of patients with dyslipidemia decreased by 1 PCT Pt	PE	$285 (fair)	17.14 (fair)	NR
Twigg (2019)[49]	SBP/DBP reduced by 2.9/1.8 mmHg at 12 months. MMAS-8 increased by 0.26	PC, DP, GS	$267 (fair)	−1.25 (fair)	$11,298 (12 months) (fair)
Vegter (2014)[50]	No clinical outcomes were reported. Nonadherence hazard by 0.47 for primary prevention of CVD	PE	$12 (fair)	−0.27 (fair)	$5,660 (patient lifetime) (fair)
Wertz (2012)a[51]	SBP/DBP reduced by 6.6/4.2 mmHg, LDL reduced by 6.9 mmol/dL at 12 months HTN Meds by 11 PCT Pt, Stations 11 by PCT Pt, Antidiabetic 8 PCT Pt	PE, PC, GS	$262 (good)	−0.45 (good)	NR
Wertz (2012)b[51]	SBP/DBP reduced by 5.7/4.7 mmHg, LDL reduced by 7.6 mmol/dL, A1c reduced by 0.8 PCT Pt at 12 months HTN Meds by 7.1 PCT Pt, Stations by 11 PCT Pt, and antidiabetic by 0 PCT Pt	PE, PC, GS	$322 (good)	0.49 (good)	NR
Yu (2013)[52]	OR of control for SBP/DBP and for LDL is 2.0; OR of control for A1c is 3.9 at 12 months. Percentage	PE, DP	$984 (good)	NR (NA)	Cost-saving (NR) (good)

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Table 3. Summary of Economic Outcomes: Total Cost, ROI, and Cost Effectiveness (*continued*)

Study	Intervention effects on clinical indicators and adherence	Pharmacist activities other than adherence related	Total cost per patient per year (quality of estimate)	ROI health systems perspective (quality of estimate)	Cost effectiveness Cost per QALY gained (time horizon) (quality of estimate)
	adherent increased by 15 PCT Pt				
Summary for CVD prevention studies Median (IQI)	—	Frequency: PE 11; LC 8; PC 6; DP 14; GS 11	$89 (−$656, $209) Quality: Good 5, fair 16, limited 0	0.01 (−0.83, 3.25) Quality: Good 4, fair 12, limited 0	$11,298 ($5,660, $28,416) Quality: Good 3, fair 3, limited 0
Delate (2010)[53]	Percentage with LDL<100 mg/dL is 70%, and percentage with SBP/DBP <140/90 is 70% Use of statins, beta-blockers, and antiplatelets after MI are 87%, 100%, and 97%, respectively	LC, PC, DP	$25,778 (fair)	58.77 (fair)	NR
Ellis (2000)[55]	LDL reduced by 10.6 mmol/dL compared with in the control. Resolved 55% of cases of drugs not taken as prescribed	PC, DP, GS	$570 (good)	NR (NA)	NR
López Cabezas (2006)[56]	12-month inpatient HF readmissions reduced by a mean of 3.7 days. Patients taking >85% of dose at 12 months increased by 11 PCT Pt versus in control	PE, LC	$1,080 (fair)	18.64 (fair)	NR
Murray (2007)[57]	Overall CVD MEMS increased by 10.9 PCT Pt	PE, DP	$3,933 (good)	10.58 (good)	NR
Polinski (2016)[58]	Risk ratio of 30-day readmission for CVD is 0.55 and respiratory is 0.61. Annual supply of Meds for intervention (control): 220.3 (207.4)	PE, DP, GS	$1,699 30 days (fair)	2.32 (fair)	NR
Scott (2007)[59]	No change in treatment meeting guidelines versus in control. No change in adherence versus in control	LC, DP	$50 (fair)	0.24 (fair)	NR

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Table 3. Summary of Economic Outcomes: Total Cost, ROI, and Cost Effectiveness (*continued*)

Study	Intervention effects on clinical indicators and adherence	Pharmacist activities other than adherence related	Total cost per patient per year (quality of estimate)	ROI health systems perspective (quality of estimate)	Cost effectiveness Cost per QALY gained (time horizon) (quality of estimate)
Vegter (2014)[50]	No clinical outcomes were reported. Nonadherence hazard ratio for secondary prevention of CVD is 0.54	PE	$275 (fair)	4.46 (fair)	NR
Summary for CVD management studies, median (IQI)	—	Frequency: PE 4; LC 3; PC 2; DP 5; GS 2	$1,080 (−$2,816, – $163) Quality: Good 2, fair 5, limited 0	7.52 (2.86, 16.62) Quality: Good 1, fair 5, limited 0	NA

[a]Versus SMBP, where SMBP dominated usual care.
A1c, glycosylated hemoglobin; ASK-20, Adherence Starts with Knowledge; CVD, cardiovascular disease; DBP, diastolic blood pressure; DM, diabetes mellitus; DP, drug problem; GS, goal setting; HF, heart failure; HTN, hypertension; IQI, interquartile interval; LC, lifestyle counseling; LDL, low-density lipoprotein; MARS, Medication Adherence Rating Scale; MEMS, Medication Event Monitoring System; MI, myocardial infarction; MMAS, Morisky Medication Adherence Scale; NA, not applicable; NR, not reported; PC, patient care; PCT pt, percentage point; PE, patient education; ROI, return on investment; QALY, quality-adjusted life year; SBP, systolic blood pressure; SMBP, self-measured blood pressure.

variations in reimbursement, some pharmacies may attempt to provide these services to enhance patient care. However, the lack of available reimbursement opportunities limits availability.[81]

Limitations

There were no cost effectiveness studies for CVD management. Most studies were implemented in urban areas, and it is unclear what the economic outcomes might be when implemented in rural settings. Most studies of the intervention for CVD management did not report clinical outcomes that may be associated with the observed reductions in healthcare cost. These economic evaluations would be more helpful to the field if they included patient health outcomes (e.g., BP, cholesterol) in their reports. The estimates for components of healthcare cost were often not reported in addition to the totals, thus precluding determination of which components of healthcare use led to the greatest changes in healthcare cost.

CONCLUSIONS

The systematic economic review finds that tailored pharmacy-based interventions to improve medication adherence to prevent CVD are cost effective on the basis of a median estimate of $11,298 per QALY gained, which is below a conservative $50,000 benchmark. For CVD management, economic evidence indicates that the healthcare cost averted exceeds the cost of implementation with a median ROI of 7.52 from a healthcare systems perspective.

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SUPPLEMENTAL MATERIAL

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