Pharmacist-led Chronic Disease Management: A Systematic Review of Effectiveness and Harms Compared to Usual Care

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PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at Nicole.Floyd@va.gov.


This report is based on research conducted by the Evidence-based Synthesis Program (ESP) Center located at the Minneapolis VA Medical Center, Minneapolis, MN, funded by the Department of Veterans Affairs, Veterans Health Administration, Office of Research and Development, Quality Enhancement Research Initiative. The findings and conclusions in this document are those of the author(s) who are responsible for its contents; the findings and conclusions do not necessarily represent the views of the Department of Veterans Affairs or the United States government. Therefore, no statement in this article should be construed as an official position of the Department of Veterans Affairs. No investigators have any affiliations or financial involvement (e.g., employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties) that conflict with material presented in the report.
EXECUTIVE SUMMARY

INTRODUCTION

Increased involvement of clinical pharmacists in patient care may offer increased access to health care and improved patient outcomes. Defined by Hepler and Strand in 1989, pharmaceutical care involves pharmacist collaboration with health team members to optimize therapeutic outcomes by identifying, solving, and preventing actual and potential drug therapy problems. Since 1995, the Department of Veterans Affairs has allowed Clinical Pharmacy Specialists (CPS) an expanded scope of practice with independent prescribing privileges. In this capacity, CPS have been detailed to perform “pharmaceutical care” or comprehensive medication management along with chronic disease state management services, in addition to more complex services such as patient medication counseling or responding to drug information questions. In the VA primary care setting, CPS are likely to be responsible for therapeutic outcomes for a multitude of conditions for any patient referred to CPS or proactively identified by CPS as a high-risk patient.

The purpose of this review is to determine the effectiveness and harms of pharmacist-led chronic disease management for community-dwelling adults. Chronic disease management aims to control symptoms and slow or stop disease progression. Chronic disease management is typically a multi-component intervention that includes medication therapy review, patient medication education, medication monitoring, immunizations, disease self-care and support, and/or prescribing authority.

This topic was nominated by Heather Ourth, PharmD, VACO Pharmacy Benefits Management Program Manager, on behalf of the National Clinical Pharmacy Research Group, chartered by the VACO Clinical Pharmacy Practice Office of VACO Pharmacy Benefits Management (PBM). We address the following key question developed with input from the topic nominator and a technical expert panel (TEP).

Key Question: What are the effectiveness and harms of pharmacist-led chronic disease management compared to usual care?

Population: Adults (age 18 or older)

Interventions: Chronic disease management; pharmacist takes responsibility for some component of the management or prevention of one or more chronic diseases (eg, chronic obstructive pulmonary disease [COPD], congestive heart failure [CHF], diabetes, hypertension, cancer, chronic kidney disease [CKD], pain, depression) (ie, pharmacist-led care)

Comparator: Usual care without the services provided by the pharmacists to the intervention group

Outcomes:
- Clinical Outcomes (including intermediate clinical measures): disease-specific clinical events (ie, severe hypoglycemia or hypotension requiring additional interventions), depression, mortality, health related quality of life, patient satisfaction, disease specific intermediate goal attainment such as glycated hemoglobin [HbA1c], blood pressure, and lipid levels
- Resource Use: office visits, urgent care or emergency room visits, hospitalizations, access to care, and costs
Pharmacist-led Chronic Disease Management Evidence-based Synthesis Program

- Medications: appropriate medications and dosages, drug interactions, (non)adherence, other
- Timing: No minimum follow-up required
- Setting: Interventions that take place within the United States and are provided to outpatients by pharmacists based in healthcare facilities

METHODS

Data Sources and Searches

We searched MEDLINE (Ovid), CINAHL, the Cochrane Library, and the International Pharmaceutical Abstracts (IPA) database for articles published from 1995 through June 2015. We obtained additional articles by hand-searching the reference lists of systematic reviews and included studies and we also received reference suggestions from peer reviewers.

Study Selection

Abstracts from MEDLINE were independently reviewed in duplicate by investigators and research associates. All other abstracts were reviewed by a single co-investigator or research associate. We included studies of any design that reported on the effectiveness or harms of pharmacist-led chronic disease management in adult outpatients with, or at risk for, a chronic disease. We excluded studies that did not test an intervention that was pharmacist-led (ie, where the pharmacist was responsible for a component of patient care), studies without a comparator, studies that did not take place in a healthcare facility in the US (eg, studies set in retail pharmacies), and studies of anticoagulation clinics because pharmacist management is considered standard care.

Full-text reports of studies identified as potentially eligible based on abstract review were obtained for further review. Each article was independently reviewed by 2 investigators or research associates.

Data Abstraction and Risk of Bias Assessment

Study characteristics (target population, inclusion/exclusion criteria, intervention goal, follow-up duration, primary outcomes, pharmacist type, setting, and intervention and comparator descriptions) and outcomes (primary and secondary outcomes reported in the studies and broadly categorized as clinical, resource use, and medications) were extracted into evidence tables by one investigator or research associate and verified by another. We assessed the risk of bias based on the following criteria: allocation of subjects to comparison groups, allocation concealment, risk of bias from confounding (for non-randomized studies), blinding, completeness of outcome reports including losses to follow-up, and selective outcome reporting – a modification of the Cochrane approach to determining risk of bias.

Data Synthesis and Analysis

We organized evidence tables by disease state of the study population. We described and qualitatively summarized the characteristics and findings of included studies. Outcomes data were pooled where possible. However, pooled analyses were not appropriate for many outcomes due to heterogeneity of interventions and outcome reporting.
We rated the overall strength of the body of evidence across chronic disease conditions for disease-specific clinical events, patient satisfaction, target goal attainment, urgent care/emergency department visits and hospitalizations, and medication adherence using the method reported by Owens et al.

**RESULTS**

**Results of Literature Search**

We reviewed 1,342 abstracts, 504 from MEDLINE and the remaining from additional databases. We excluded 1,151 abstracts and reviewed the full text of 191 articles. During full-text review we excluded 134 articles leaving 57 eligible for inclusion. Hand-searching reference lists of pertinent trials and systematic reviews and peer reviewer suggestions identified an additional 13 references.

We included 70 papers representing 62 studies with 64 unique study populations (k) in cardiovascular diseases (k=6), chronic kidney disease (k=4), chronic obstructive pulmonary disease (k=1), depression (k=4), diabetes mellitus (k=24), dyslipidemia (k=7), hypertension (k=15), and polypharmacy/high risk (k=3). An overview of study characteristics is presented in Executive Summary Table 1.

**Summary of Results**

**Overall findings: (Executive Summary Tables 1-3)**

- Most studied interventions included pharmacist-led medication monitoring, medication therapy review, prescribing authority, and/or disease self-care and support.

- Interventions were typically delivered by pharmacists in-person and over multiple times. However, interventions varied in composition, delivery mode, and intensity, making it difficult to draw conclusions about important intervention characteristics.

- Studies were generally short-term and designed to assess intermediate outcomes such as blood pressure, cholesterol, and/or glucose goal attainment in patients with diabetes, hypertension, or cardiovascular disease rather than other clinical or resource use outcomes.

- Many of the outcomes reported in this review were not primary study endpoints supported by rigorous research methods or statistical inferences. Findings based on analyses of outcomes other than the study-defined primary outcomes should be interpreted with caution.

- Most trials reporting disease-specific clinical events found pharmacist-led care and usual care to be similar. However, only 3 of the included studies were designed to assess clinical events, outcomes were sporadically and inconsistently reported, and there were few events (low strength of evidence). Eight studies reported mortality with all finding similar mortality in the pharmacist-led care and control groups.

- Compared to usual care, pharmacist-led care was associated with similar incidences or rates of office, urgent care or emergency department visits, and hospitalizations (moderate strength of evidence) and medication adherence (low strength of evidence).
• There was insufficient evidence to evaluate the effect of pharmacist-led care on patient satisfaction. There was limited reporting of quality of life outcomes.

• No studies reported typical measures of access to care (e.g., wait time for appointment or percentage of appointments within a specified window of a desired appointment time). Four studies reported either patient satisfaction with reaching someone in an emergency or availability of advice about health condition (both significantly higher in the intervention group) or patient perceptions of communication with the care team and problems getting care (intervention and control groups similar).

• There was limited reporting of harms or other drug-related problems (defined for this review as inappropriate medication or dosage and drug interactions). Studies that reported harms often did not provide data for the control group participants.

• Reported cost outcomes included total costs, medication costs, cost savings per patient, and program costs, but few studies found significant differences between intervention and control groups.

• Patients in the pharmacist-led care groups generally received a greater number or dose of medications although it was difficult to evaluate whether increased number or dose of medications was an indicator of better care quality.

• Compared to usual care, pharmacist-led care improved study-selected glycemic, blood pressure, and lipid goal attainment (moderate strength of evidence).
## Executive Summary

### Table 1. Summary of Included Studies

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>(Risk of) Cardiovascular Disease</th>
<th>Chronic Kidney Disease</th>
<th>Chronic Obstructive Pulmonary Disease</th>
<th>Depression</th>
<th>Diabetes Mellitus</th>
<th>Dyslipidemia</th>
<th>Hypertension</th>
<th>Polypharmacy/High Risk</th>
<th>Total</th>
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<td></td>
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<td>24</td>
<td>7</td>
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<td>2,920</td>
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<td>926</td>
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<td>3</td>
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<td>2</td>
<td>13</td>
<td>3</td>
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<td>Non-VA</td>
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<td>Patient Medication Education</td>
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<td>0</td>
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<td>9</td>
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<td>4</td>
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<td>3</td>
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<td>2</td>
<td>2</td>
<td>1</td>
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<td>In-Person</td>
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<td>0</td>
<td>14</td>
<td>4</td>
<td>8</td>
<td>2</td>
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<td>Mixed</td>
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<td>1</td>
<td>3</td>
<td>8</td>
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<td><strong>Intervention Frequency</strong></td>
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<td>One-time</td>
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<td>0</td>
<td>0</td>
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<td>0</td>
<td>0</td>
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<td>Multiple</td>
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<td>4</td>
<td>20</td>
<td>6</td>
<td>15</td>
<td>3</td>
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<td><strong>Risk of Bias</strong></td>
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<td></td>
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<td></td>
<td></td>
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<tr>
<td>Low</td>
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<td>1</td>
<td>0</td>
<td>1</td>
<td>5</td>
<td>0</td>
<td>2</td>
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<tr>
<td>Medium</td>
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<td>2</td>
<td>15</td>
<td>3</td>
<td>12</td>
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<td>High</td>
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<td>0</td>
<td>1</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>0</td>
<td>12</td>
</tr>
</tbody>
</table>

RCT = randomized controlled trial; VA = Veterans Affairs

*2 studies reported separate results for 2 different disease conditions
### Executive Summary Table 2. Number of Studies Reporting Each Outcome (and Study-Defined Primary Outcome)\(^a\)

<table>
<thead>
<tr>
<th>Condition (number of included studies)</th>
<th>Clinical Events</th>
<th>Resource Use</th>
<th>Medication</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Clinical Issues</td>
<td>Resource Use</td>
<td>Medication</td>
</tr>
<tr>
<td></td>
<td>Depression</td>
<td>All-Cause Mortality</td>
<td>Health-Related Quality of Life</td>
</tr>
<tr>
<td>Cardiovascular Diseases (k=6)</td>
<td>2</td>
<td>2 (1)</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Kidney Disease (k=4)</td>
<td>2</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Chronic Obstructive Pulmonary Disease (k=1)</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Depression (k=4)</td>
<td>2 (2)</td>
<td>3</td>
<td>4 (1)</td>
</tr>
<tr>
<td>Diabetes (k=24)</td>
<td>4</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Dyslipidemia (k=7)</td>
<td></td>
<td>7 (3)</td>
<td>4</td>
</tr>
<tr>
<td>Hypertension (k=15)</td>
<td>6</td>
<td>1</td>
<td>7 (2)</td>
</tr>
<tr>
<td>Polypharmacy/High-risk (k=3)</td>
<td>1</td>
<td>2 (2)</td>
<td>2 (1)</td>
</tr>
<tr>
<td>TOTAL (64 unique study populations)(^c)</td>
<td>15</td>
<td>2 (2)</td>
<td>8 (1)</td>
</tr>
</tbody>
</table>

\(^a\) Some studies didn’t have one of our outcomes as their primary outcome and some had more than one primary outcome; table entries are number of studies reporting that outcome as their primary outcome.

\(^b\) Access to care assessed as patient satisfaction (reaching someone in an emergency, availability of advice) or patient perceptions (communication with the care team and problems getting care).

\(^c\) 2 studies reported separate results for 2 different disease conditions.
**Executive Summary Table 3. Strength of Evidence**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Strength of Evidence</th>
<th>Direction</th>
<th>Number of RCTs (N)</th>
<th>Summary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease-specific clinical events&lt;sup&gt;b&lt;/sup&gt;</td>
<td>Low</td>
<td>Similar</td>
<td>12 (3,355)</td>
<td>Most trials found similar outcomes between pharmacist-led care and usual care. Outcomes were sporadically and inconsistently reported and there were few events. Overall risk of bias was moderate.</td>
</tr>
<tr>
<td>Patient satisfaction</td>
<td>Insufficient</td>
<td>Mixed</td>
<td>16 (12,793)</td>
<td>Results were inconsistent for measures of patient satisfaction between pharmacist-led care and usual care. There was variation in how patient satisfaction was reported (scale score or proportions), some measures may not be validated, and some trials used a single item from a multi-item scale. Overall risk of bias was moderate. Given these limitations, conclusions regarding the strength of evidence for patient satisfaction cannot be determined.</td>
</tr>
<tr>
<td>Urgent care/ER and hospitalizations</td>
<td>Moderate</td>
<td>Similar</td>
<td>Urgent care/ER 16 (7,166) Hospitalizations 12 (7,455)</td>
<td>Incidence or rates of urgent care/ER visits or hospitalizations were similar between pharmacist-led care and usual care. Overall risk of bias was moderate.</td>
</tr>
<tr>
<td>Non-adherence to medications</td>
<td>Low</td>
<td>Similar</td>
<td>17 (5,933)</td>
<td>In most trials medication non-adherence was similar between pharmacist-led care and usual care. Overall risk of bias was moderate. Pooled results from 7 (n=1479) demonstrated a substantial relative reduction but findings were imprecise, not significant, and had substantial heterogeneity (RR 0.58 [95% CI 0.33, 1.01]; I² = 82%).</td>
</tr>
<tr>
<td>Goal attainment</td>
<td>Moderate</td>
<td>Improved in pharmacist-led care groups</td>
<td>19 (5,816)</td>
<td>Pharmacist-led care improved the proportion of patients achieving guideline-recommended laboratory or physiologic treatment goals versus usual care, 51% vs 34% (RR 1.56 [95% CI 1.37, 1.78]; I² = 48%). Results were precise and fairly consistent. Cluster RCTs, CCTs, and cohort studies not included in the pooled analysis generally reported improved goal attainment in the pharmacist-led care group. Overall risk of bias was moderate.</td>
</tr>
</tbody>
</table>

<sup>a</sup> Strength of evidence determined for specific outcomes across all chronic disease conditions  
<sup>b</sup> *ie*, severe hypoglycemia or hypotension requiring additional interventions
**Condition-specific Findings**

**Cardiovascular Disease or Risk Factors (4 RCTs, 2 Cohort Studies)**

- Pharmacist-led care
  - resulted in mortality and rates of disease-specific clinical events that were similar to usual care; only one study reported a clinical event as a primary outcome,
  - was associated with mixed results for maintenance or attainment of HbA1c and blood pressure goals compared to usual care,
  - resulted in hospitalization rates that were similar to usual care; there were mixed results for office visits, urgent care visits, and costs; only one study reported resource use as a primary outcome, and
  - was associated with mixed results for medication use and adherence as compared to usual care.
- No studies reported on access to care, or drug interactions or other drug-related problems.

**Chronic Kidney Disease (2 RCTs, 2 Cohort Studies)**

- Pharmacist-led care
  - improved kidney disease-related quality of life at one year but not 2 years among patients at a university-affiliated dialysis center but resulted in similar quality of life for Veterans with CKD in primary care.
  - lowered medication use in the intervention group in the dialysis study,
  - increased use of anti-hypertensive medications in the VA study with intervention and control groups similar on blood pressure goal attainment,
  - resulted in similar all-cause mortality between groups in both studies, and
  - to manage anemia due to CKD was associated with a lower weekly dose of EPO (k=1), more medication adjustments if hemoglobin levels were low (but not high) (k=1), cost savings (k=2), and better attainment of target hemoglobin (k=2) and iron saturation values (k=1) versus usual care; intervention and control sites reported similar rates of adverse events (k=1).
- No studies reported on office or emergency department visits, access to care, or drug interactions or other drug-related problems.

**Chronic Obstructive Pulmonary Disease (1 RCT)**

- Multifaceted pharmacist-led care from 8 VA Medical centers
  - resulted in health-related quality of life, number of new medications, number of emergency department visits, and a rate of hospitalization that were similar to usual care,
  - decreased office visits, and
  - resulted in mixed findings for patient satisfaction (ie, significant differences on some subscales).
- Effects on drug-related problems were reported only for the intervention group.
- All-cause mortality, disease-specific clinical events, access to care, and costs were not reported.
Depression (3 RCTs, 1 non-RCT)

- Pharmacist-led care
  - was similar to usual care for depressive symptoms and health-related quality of life,
  - was similar to usual care for medication adherence (2 RCTs reporting); self-reported use of antidepressant medications and changes in antidepressant medications were more frequent in the pharmacist-led care groups,
  - resulted in numbers/rates of primary care or urgent care visits that were similar to usual care, and
  - increased patient satisfaction with availability of advice.
- All-cause mortality, hospitalizations, costs, inappropriate prescriptions, drug interactions and other drug-related problems and harms were not compared.

Diabetes (12 RCTs, 2 CCTs, 10 Cohort Studies)

- Pharmacist-led care
  - resulted in all-cause mortality, disease-specific clinical events, and health-related quality of life that was similar to usual care, although few studies reported these outcomes,
  - improved rates of goal attainment for HbA1c, blood pressure, and lipids; the 3 studies in VA settings reported increased attainment of HbA1c and blood pressure goals in patients receiving pharmacist-led care,
  - resulted in significantly higher numbers and/or doses of medications, and
  - resulted in resource use (office visits, urgent care or emergency department visits, and hospitalizations) that was similar to usual care.
- One study reported access to care favoring the intervention group; no studies reported drug interactions or other drug-related problems.

Dyslipidemia (2 RCTs, 2 CCTs, 3 Cohort Studies)

- Pharmacist-led care
  - improved goal attainment (typically LDL < 100 mg/dL) compared to usual care although pooled results from 2 RCTs showed groups were similar,
  - was associated with increased medication use; one study reported adherence in the intervention group but not the usual care group, and
  - led to mixed results for office visits and similar results for urgent care or emergency department visits and costs as usual care.
- No studies reported other clinical outcomes (ie, mortality, disease-specific clinical events, health-related quality of life, and patient satisfaction), hospitalizations, access to care, inappropriate prescriptions, or drug interactions or other drug-related problems.

Hypertension (13 RCTs, 1 CCT, 1 Case-Control Study)

- Pharmacist-led care
  - resulted in similar health-related quality of life as usual care; patient satisfaction results were mixed and few studies reported other clinical outcomes,
  - increased medication use but adherence was similar to usual care,
Pharmacist-led Chronic Disease Management Evidence-based Synthesis Program

- led to mixed results for resource use outcomes including office visits and costs; few studies reported urgent care or emergency room visits, and
- resulted in patient perceptions similar to usual care for “had problems getting needed care.”
- No studies reported drug interactions or other drug-related problems; one study reported inappropriate medications for the intervention group but not the control group.

**Polypharmacy/High Risk for Drug-related Problems (3 RCTs)**

- Pharmacist-led care
  - resulted in health-related quality of life; patient satisfaction, and rates/numbers of disease-specific clinical events that were similar to usual care; goal attainment was improved,
  - resulted in similar medication use as usual care; results were mixed for medication adherence; significance of other medication findings could not be determined, and
  - increased the number of office visits compared to usual care but decreased use of urgent care facilities; results were mixed for hospitalizations and costs.
- No studies reported all-cause mortality or access to care.

**DISCUSSION**

**Summary of Findings and Strength of Evidence**

We rated strength of evidence for disease-specific clinical events (low strength of evidence that pharmacist-led care and usual care were similar), patient satisfaction (insufficient evidence), urgent care/emergency department visits and hospitalizations (moderate strength of evidence that pharmacist-led care and usual care were similar), non-adherence to medications (low strength of evidence that pharmacist-led care and usual care were similar), and goal attainment (moderate strength of evidence that pharmacist-led care increased the proportion of patients achieving glycemic, blood pressure, and cholesterol goals compared to usual care). While we did not formally assess strength of evidence on other outcomes we did find that pharmacist-led care was also similar to usual care for depression, health-related quality of life, all-cause mortality, and cost outcomes. However, due to differences in costs reported across studies (program costs, medication costs, visit costs), it is difficult to reach a conclusion about costs. Very few studies reported drug-related problems (inappropriate medication or dosage, drug interactions). Patients in the pharmacist-led care groups generally received a greater number or dose of medications although it was difficult to evaluate whether increased number or dose of medications was an indicator of better care quality.

**Applicability**

The chronic disease conditions addressed in the included studies (cardiovascular disease, chronic kidney disease, COPD, depression, diabetes mellitus, and hypertension) are common among Veterans. Seventeen studies were conducted in VA facilities. The model of pharmacist-led care reported in these studies varied but likely is similar to ongoing programs in VA.
Limitations/Research Gaps/Future Research

Many of the outcomes reported in this review were not the study-defined primary endpoints and therefore were not supported by rigorous research methods or statistical inferences. Among studies included in our review, sample sizes were too small and follow-up periods too short to detect differences in mortality. There was limited reporting of other clinical events, health-related quality of life, and patient satisfaction. When assessed, authors used varied methods for determining health-related quality of life and patient satisfaction. Scale scores were often not validated, of unknown clinical importance, or included selected findings from subscales. Interventions varied in composition, delivery mode, and intensity as did the usual care comparator, making it difficult to draw conclusions about important intervention characteristics.

One hypothetical benefit of pharmacist-led care for chronic diseases is increased access to care for patients. None of the included studies reported typical measures of access and only 4 studies (2 in patients with depression and one each in patients with hypertension or diabetes) reported patient satisfaction or patient perception measures related to access (eg, satisfaction with ability to reach someone in an emergency or satisfaction with availability of advice). Intervention-based increases in the number of scheduled visits or telephone calls may not represent improved access. Further research is needed with conventional measures of access.

A consistent definition of an office visits outcome is needed to distinguish regularly scheduled office visits, study-related office visits, and unplanned office visits. In many cases it was unclear whether the visit was with a pharmacist or primary care provider. Also, a consistently reported cost outcome that includes all of the important economic factors involved in pharmacist-led care would facilitate comparisons across studies and provide more accurate cost-effectiveness estimates.

There was limited reporting of important drug-related problems, in particular drug interactions and inappropriate medications and/or dosages. Some studies did report on adherence with mixed, inconclusive results. Despite existing definitions of polypharmacy, an isolated measure of the number of medications is not an indicator of quality of care as there are situations where adding medications and/or increasing dosages may be helpful. Similarly, de-prescribing medications that emerging evidence suggests are not beneficial and may provide harm may also be helpful. Further research is needed to define and describe these interventions and their association with patient outcomes and value.

Finally, the demonstrated improvement in laboratory and physiologic goal attainment due to pharmacist-led care is potentially encouraging. Intervention group pharmacists successfully achieved the intended study objectives. The target goals were based, in part, on recommendations from selected existing clinical practice guidelines and performance measures. The results indicate that future pharmacist-led programs are likely to achieve intended goals. However, there is conflicting evidence that target goals for glycemic, blood pressure, or cholesterol control have long-term beneficial effects on patient outcomes including clinical events, satisfaction, access, hospitalizations, and costs. Therefore, future research needs to carefully assess whether the magnitude of effect on selected intermediate laboratory and physiologic goals translates to improved patient outcomes including clinical events, satisfaction, access, hospitalizations, and costs. Few studies reported differences in potential harms. Thus the available evidence does not answer the question about whether the benefits of pharmacy-led
interventions justify potential harms and costs. Ideally, future studies will be designed to fully and accurately address final patient outcomes and cost effectiveness.

**Conclusions**

Evidence is limited on the effectiveness and harms of pharmacist-led chronic disease management compared to usual care for clinical outcomes (*i.e.*, clinical events, all-cause mortality, patient satisfaction, quality of life, and resource utilization). Moderate-strength evidence indicates that pharmacist-led chronic disease management increases goal attainment for HbA1c, blood pressure, and cholesterol levels. Moderate- or low-strength evidence also indicates that pharmacist-led chronic disease management and usual care were similar for urgent care visits or hospitalizations, clinical events, and adherence to medications. Evidence was insufficient for patient satisfaction. There was little reporting of access to care and drug-related problems. These results suggest that future programs are likely to achieve intended laboratory and physiologic goals. However, to accurately assess health care value, future research studies and implementation projects that utilize intermediate laboratory and physiologic goals as measures of effectiveness need to be certain that these goals are clearly linked to improved patient outcomes including clinical events, satisfaction, access, hospitalizations, costs, medication adherence, and drug-related problems without undue harms and costs.

**ABBREVIATIONS TABLE**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>BP</td>
<td>Blood pressure</td>
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<tr>
<td>CCT</td>
<td>Controlled clinical trial (non-randomized)</td>
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<tr>
<td>CPS</td>
<td>Clinical Pharmacy Specialist</td>
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<td>HbA1c</td>
<td>Hemoglobin A1c</td>
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<tr>
<td>HTN</td>
<td>Hypertension</td>
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<tr>
<td>HDL, HDL-C</td>
<td>High density lipoprotein cholesterol</td>
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<tr>
<td>LDL, LDL-C</td>
<td>Low density lipoprotein cholesterol</td>
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<tr>
<td>MTM</td>
<td>Medication Therapy Management</td>
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<tr>
<td>PharmD</td>
<td>Doctor of Pharmacy</td>
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<tr>
<td>RCT</td>
<td>Randomized controlled clinical trial</td>
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<td>RR</td>
<td>Risk ratio</td>
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<td>VA</td>
<td>Veterans Affairs</td>
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