Cardiovascular Disease: Tailored Pharmacy-based Interventions to Improve Medication Adherence

Community Preventive Services Task Force
Finding and Rationale Statement
Ratified April 2019

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CPSTF Finding and Rationale Statement

**Intervention Definition**
Tailored pharmacy-based interventions aim to help patients with cardiovascular disease risk conditions take their medications as prescribed. Community or health system pharmacies use assessment tools or interviews to identify adherence barriers for each patient. Pharmacists then provide tailored guidance and services to reduce those barriers.

Tailored guidance includes either focused medication counseling or motivational interview sessions. Services include one or more of the following: patient tools such as pillboxes, medication cards and calendars, medication refill synchronization, and enhanced follow-up.

Interventions may include additional components such as communication between the pharmacist and the patient’s primary care provider, or patient education materials. Interventions may be used alone, or they may be part of a broader intervention to reduce patients’ cardiovascular disease risk.

**CPSTF Finding (April 2019)**
The Community Preventive Services Task Force (CPSTF) recommends tailored pharmacy-based adherence interventions based on strong evidence of effectiveness in increasing patient adherence to medications for cardiovascular disease prevention. Studies of interventions delivered by pharmacists in community and health system pharmacies found meaningful increases in the proportion of patients who reported taking medications as prescribed.

**Rationale**

**Basis of Finding**
The CPSTF finding is based on evidence from a systematic review of 48 studies (search period through August 2018). The Community Guide review focused on four primary outcomes: (1) medication adherence, (2) cardiovascular disease risk conditions including blood pressure and cholesterol, (3) health care utilization, and (4) cardiovascular disease morbidity and mortality.

Studies had to measure intervention effects on medication adherence to be included in the review. Included studies used a variety of measurements to evaluate adherence precluding an overall summary effect estimate.

In 27 studies, adherence measures were converted into dichotomous patient outcomes (i.e., adherent or non-adherent) based on whether patients possessed, took, or refilled their prescribed cardiovascular prevention medications at least 80% of the time. The proportion of patients considered adherent increased by a median of 6.9 percentage points [Interquartile interval (IQI): 3.4 to 14.0 percentage points]. Subsets of these 27 studies reported different adherence measures and used uncontrolled before-after designs. Results are presented in Table 1.
Table 1: Medication Adherence Outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Proportion of patients achieving high medication adherence (&gt;80%)</td>
<td>Overall (27 studies)</td>
</tr>
<tr>
<td>Subset: Proportion of days covered &gt;80% (9 studies)*</td>
<td>Median increase of 4.9 percentage points (IQI: 3.4 to 14.9 percentage points)</td>
</tr>
<tr>
<td>Subset: Medication possession ratio &gt;80% (8 studies)*</td>
<td>Median increase of 3.7 percentage points (IQI: -0.4 to 7.1 percentage points)</td>
</tr>
<tr>
<td>Subset: Other Measures &gt;80% count or score (7 studies)*</td>
<td>Median increase of 11.6 percentage points (IQI: 7.1 to 15.1 percentage points)</td>
</tr>
<tr>
<td>Subset: Uncontrolled Before-After studies (3 studies)</td>
<td>Median increase of 23.2 percentage points (Range: 3.4 to 69 percentage points)</td>
</tr>
</tbody>
</table>

Count or score: Includes pill count thresholds or maximum adherence scores using validated MMAS-8 and MMAS-4 self-report tools

IQI = interquartile interval

*Greatest or moderate quality of design

The remaining 21 studies examined intervention effectiveness for medication adherence based on mean patient differences or changes in various adherence measurements or tools. In ten studies, patient adherence measures were determined through objective provider counts or records. In seven studies, adherence measures were determined from patient self-reported tools or counts. The final four studies used unique measures and were evaluated separately; two studies reported favorable improvements and two studies found no significant effect on medication adherence. Results are presented in Table 2.

Table 2: Additional Medication Adherence Outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Provider or pharmacy determined proportion of doses taken as prescribed* (11 studies)</td>
<td>Median increase of 5.4 percentage points (IQI: 4.0 to 11.4 percentage points)</td>
</tr>
<tr>
<td>Patient self-reported proportion of doses taken as prescribed** (6 studies)</td>
<td>Median increase of 17.1 percentage points (IQI: -2.8 to 19.7 percentage points)</td>
</tr>
</tbody>
</table>
| Other measures on medication adherence (4 studies) | Two studies reported statistically significant increases in adherence
Two studies reported no significant effect on adherence |
Four studies used mean proportion of days covered, four studies recorded each dose taken, one study used medication possession ratio, one study recorded pill counts, and one study recorded refill rates.

Three studies used the patient-reported MMAS-4 adherence tool, two studies used MMAS-8 reports, and one study used patient self-reported pill counts.

IQI = interquartile interval

Subsets of the included studies evaluated intervention effects on blood pressure control (13 studies) and lipid control (4 studies). Most of these studies included a tailored adherence intervention as part of a broader cardiovascular disease prevention intervention. The proportion of patients who achieved blood pressure control increased by a median of 13.9 percentage points (IQI: 5.8 to 28.2 percentage points). Effects on LDL (3 studies) or total cholesterol (1 study) were mixed. Results are presented in Table 3.

Table 3: Cardiovascular Risk Outcomes

<table>
<thead>
<tr>
<th>Outcome Measure</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood pressure at goal</td>
<td>Median increase of 13.9 percentage points (IQI: 5.8 to 28.2 percentage points)</td>
</tr>
<tr>
<td>(13 studies)</td>
<td></td>
</tr>
<tr>
<td>Lipids at goal</td>
<td>Studies examined different lipid outcomes with mixed findings</td>
</tr>
<tr>
<td>(4 studies)</td>
<td></td>
</tr>
</tbody>
</table>

IQI = interquartile interval

The review team assessed additional evidence for healthcare, morbidity, and mortality from studies that used different outcomes or inconsistent units of measure, or didn’t report baseline information. Six studies (7 estimates) measured emergency room visits and showed mixed results (5 favorable, 1 no change, 1 unfavorable). Nine studies reported on hospitalizations (e.g., number of admissions, days in hospital) and showed mixed results (5 favorable, 3 no change, 1 unfavorable). Four studies (5 estimates) measured death and incidence of disease and were mostly favorable but not significant (4 favorable, 1 no change).

Most of the studies used a team-based care approach that provided patients with contact, communication, or feedback from a primary care provider (29 studies). The remaining studies either did not use team-based care or did not indicate if they used team-based care (19 studies).

Interventions delivered counseling face-to-face (18 studies), by telephone (8 studies), or both in person and by phone (17 studies). Patients participated in three to five sessions (19 studies), fewer than two sessions (13 studies), or six or more sessions (8 studies). Interventions were delivered by pharmacists (41 studies) or a combination of pharmacy residents and pharmacy technicians (7 studies). Study duration ranged from 6 months (18 studies), to 7-11 months (8 studies), to 12 months (22 studies).

Applicability and Generalizability Issues

The 48 included studies were conducted in the United States (23 studies), Europe (12 studies), Canada (5 studies), Hong Kong (4 studies), and Australia (4 studies).

Studies were implemented in community pharmacies (27 studies), health system pharmacies (14 studies), or a combination of both (5 studies). In two studies, health systems implemented an adherence telephone support service.
for patients. While some studies specifically included rural (5 studies), or urban (12 studies) pharmacies, most of the studies did not report this information (28 studies). Included studies evaluated outcomes in fewer than 100 patients (10 studies), 100-500 patients (21 studies), or more than 500 patients (16 studies); one study did not report sample size.

Across all studies, the median age for patients was 61.6 years (IQR: 59.0 to 66.8; 43 studies); 52.1% were female (IQR: 39.3 to 61.3; 46 studies). The cardiovascular disease risks or conditions most commonly reported were hypertension (high blood pressure; 27 studies), hyperlipidemia or dyslipidemia (abnormal amounts of lipids in blood; 18 studies), diabetes combined with hyperlipidemia or dyslipidemia (10 studies), and cardiovascular disease (8 studies).

Ten studies from the United States also provided information about patients’ demographic characteristics. Of the seven studies that provided information about race and ethnicity, six reported a median of 43% African-American patients (IQR: 34.6% to 60.3%) and one study reported a majority of patients were African-American. Five studies that provided information about patients’ educational achievement reported a median of 38.7% of patients had less than a high school degree (IQR: 26% to 44.5%). Of the four studies that provided information about household income, three reported a median of 34.6% of patients (range: 19.0% to 51.0%) had household incomes less than $25,000, and one study reported patients’ average household income was $30,000.

Data Quality Issues
Of the 48 included studies, 26 were randomized controlled trials, seven were other design with concurrent comparison, one was before and after with comparison, six used a retrospective cohort, and eight were before and after without a comparison. Trials randomized recruited pharmacies (17 studies) or patients within pharmacies (9 studies). Most studies assigned patient recruitment to study pharmacists, introducing potential for selection and recruitment biases. In general, studies provided little information about the demographic characteristics of recruited patients except for age, gender, and cardiovascular disease risks and conditions. Baseline information was not consistently reported in some studies.

Potential Benefits
None of the included studies reported or examined additional benefits of tailored interventions. The CPSTF postulates potential benefits could include improved pharmacist-patient communication, which could increase patient reporting of all medication issues, including side effects. Similarly, interventions involving communication between pharmacists and primary care providers could create opportunities for team-based patient care.

Potential Harms
None of the included studies reported or examined potential harms of tailored interventions. The CPSTF did not postulate any harms of these interventions.

Related Reviews and Recommendations
The CPSTF did not identify any systematic reviews of pharmacy-based adherence interventions based on individualized patient assessment and tailored counseling and support. Several published systematic reviews examined the effectiveness of related approaches such as pharmacist interventions for chronic disease management (Milosavljevic et al., 2018) and adherence interventions implemented in ambulatory settings, regardless of the implementer (Van Driel et al., 2018).
Considerations for Implementation

The Joint Commission of Pharmacy Practitioners developed the Pharmacists’ Patient Care Process [https://www.pharmacist.com/sites/default/files/files/PatientCareProcess.pdf] in 2014 that outlines steps to optimize patient health and medication outcomes. The steps in this process (i.e., collect, assess, plan, implement, follow-up, and monitor) closely align with the process for selecting tailored actions to remove or reduce patient adherence barriers to medication adherence.

Pharmacies may want to implement tailored pharmacy-based interventions to increase medication adherence as part of a broader pharmacist-patient care process. CDC has a resource guide to help pharmacies implement this process:


The Million Hearts Initiative® provides action guides [https://millionhearts.hhs.gov/tools-protocols/medication-adherence.html] that detail organizational considerations and ways to increase medication adherence for cardiovascular disease prevention.

Several previous CPSTF recommendations relate to the current finding by identifying additional, effective approaches or complementary interventions to address gaps. For example, pharmacist-provider communications were a frequent component of the studies identified in this review. The CPSTF also recommends complementary intervention approaches. A review of team-based care to improve blood pressure control [https://www.thecommunityguide.org/findings/cardiovascular-disease-team-based-care-improve-blood-pressure-control] reported greater effects when pharmacists were included on teams. And the review of text messaging interventions to increase medication adherence among patients with chronic diseases [https://www.thecommunityguide.org/findings/health-information-technology-text-messaging-medication-adherence-chronic-disease] included cardiovascular risk conditions.

Medication costs are a common and substantial barrier to adherence for patients. Pharmacists may have limited options to address this barrier, and when identified in patient assessments, additional support may be necessary. The CPSTF recommends interventions that combine reduced out-of-pocket costs for blood pressure and cholesterol medications with additional components aimed at improving patient–provider interaction and patient knowledge (e.g., team-based care with medication counseling, patient education).

The studies identified in this review did not evaluate adherence to medications for smoking cessation. Counseling and assisting tobacco-using patients to quit are important contributors to cardiovascular disease risk reduction (USPSTF [https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions1] 2015). While this review did not evaluated adherence to medications for smoke cessation, pharmacists can play an important role in supporting patient efforts to obtain, initiate, and complete cessation treatments (Saba et al., 2014).

Pharmacists delivered and guided the tailored interventions in the studies identified in this review. While pharmacists or pharmacy residents may need to be involved in decisions about counseling content and additional adherence services for patients, implementers might consider how other staff, such as pharmacy technicians, can support the interventions. Pharmacy technicians might be able to conduct tool-based assessments of patient barriers, provide instruction on the use of patient adherence tools, and deliver adherence reminders.

Pharmacies may have limited space to provide tailored interventions to patients, particularly in community settings. Several studies in this review provided space in the patient’s primary care setting to enable confidential assessments and tailored counseling, and a few studies delivered tailored interventions over the phone.

Evidence Gaps
Additional research and evaluation are needed to answer the following questions and fill existing gaps in the evidence base.

- How does intervention effectiveness vary with different intervention components? Are interventions more effective when tailored options include system-level approaches, such as refill synchronization or blister packaging?
- Within a tailored approach, are some adherence barriers commonly addressed by specific intervention options? Does evidence indicate that some adherence barriers can be removed with a specific component, allowing for some standardization in tailored interventions?
- How effective are tailored interventions when targeted to specific patients at risk for adherence barriers, such as patients with low income or low health-literacy?
- How effective are tailored interventions when implemented in pharmacies that serve minority and low-income communities?
- How effective are tailored interventions that engage community health workers and pharmacy technicians in appropriate assessment, coaching, or follow-up roles?

References


Disclaimer

The findings and conclusions on this page are those of the Community Preventive Services Task Force and do not necessarily represent those of CDC. Task Force evidence-based recommendations are not mandates for compliance or spending. Instead, they provide information and options for decision makers and stakeholders to consider when determining which programs, services, and policies best meet the needs, preferences, available resources, and constraints of their constituents.

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