

# Heart Disease and Stroke Prevention: Tailored Pharmacy-based Interventions to Improve Medication Adherence

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## 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.

The CPSTF finds the intervention is cost-effective for cardiovascular disease prevention based on a median estimate of \$11,298 per quality adjusted life year (QALY) saved, which is below a conservative threshold of \$50,000.

## 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**

Outcome Measure		Results
Proportion of patients achieving high medication adherence (>80%)	Overall (27 studies)	Median increase of 6.9 percentage points (IQI: 3.4 to 14.0 percentage points)
	Subset: Proportion of days covered >80% (9 studies)*	Median increase of 4.9 percentage points (IQI: 3.4 to 14.9 percentage points)
	Subset: Medication possession ratio >80% (8 studies)*	Median increase of 3.7 percentage points (IQI: -0.4 to 7.1 percentage points)
	Subset: Other Measures >80% count or score (7 studies)*	Median increase of 11.6 percentage points (IQI: 7.1 to 15.1 percentage points)
	Subset: Uncontrolled Before-After studies (3 studies)	Median increase of 23.2 percentage points (Range: 3.4 to 69 percentage points)

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**

Outcome Measure	Results
Provider or pharmacy determined proportion of doses taken as prescribed* (11 studies)	Median increase of 5.4 percentage points (IQI: 4.0 to 11.4 percentage points)
Patient self-reported proportion of doses taken as prescribed** (6 studies)	Median increase of 17.1 percentage points (IQI: -2.8 to 19.7 percentage points)
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**

Outcome Measure	Results
Blood pressure at goal (13 studies)	Median increase of 13.9 percentage points (IQI: 5.8 to 28.2 percentage points)
Lipids at goal (4 studies)	Studies examined different lipid outcomes with mixed findings

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).

### Economic Evidence

Economic evidence shows tailored pharmacy-based adherence interventions to prevent cardiovascular disease are cost-effective. For patients with existing cardiovascular disease, the evidence shows averted healthcare cost exceeds the cost of intervention for a favorable return on investment (ROI) from a healthcare system perspective.

The economic review included 38 studies (search period through May 2019). Twenty-nine studies evaluated interventions to prevent cardiovascular disease. Nine studies focused on patients with existing cardiovascular disease or cardiovascular disease management. All monetary values are reported in 2018 U.S. dollars.

Studies were based in the United States (27 studies), the Netherlands (3 studies), the United Kingdom (2 studies), Canada (2 studies), Hong Kong (2 studies), Taiwan (1 study), and Spain (1 study). Studies were set in pharmacies (21 studies), primary care clinics (13 studies), a mix of the two (1 study), or the facilities of pharmaceuticals benefits managers (3 studies). The majority of studies (21 studies) were implemented in urban areas.

The median sample sizes were 232 for cardiovascular disease prevention and 174 for cardiovascular disease management. There were more females in the studies for cardiovascular disease prevention compared to those for cardiovascular disease management (56% versus 42%) and the patients were younger (58 years versus 65 years). The cardiovascular disease prevention studies included patients with high blood pressure (10 studies), dyslipidemia (4 studies), type 2 diabetes (14 studies), and a combination of cardiovascular risk factors (8 studies). The cardiovascular disease management studies included patients with heart failure (3 studies), coronary heart disease (2 studies), and multiple cardiovascular conditions or type 2 diabetes (4 studies).

The economic review team assessed the quality of evidence by considering how well each estimate captured the components considered to be drivers of magnitude and the appropriateness of measurement and valuation; the lower of the two assessments was used to determine overall quality. The majority of intervention cost estimates were of good quality (17 estimates); the remaining were of fair quality (9 estimates). The most frequent limitation was failure to include cost of patient education materials or adherence aids.

The healthcare cost estimates were mixed in quality, with 14 good, 19 fair, and 5 of limited quality. The most frequently assessed limitations were failure to include inpatient or emergency department costs, inclusion of medication cost only, and cost assessments based on all causes of healthcare use rather than use related to cardiovascular disease and risk factors.

### Intervention Cost

- The median cost per patient per year for interventions to prevent cardiovascular disease was \$246 (IQI: \$95 to \$499), based on 20 estimates from 19 studies.
- The median cost per patient per year for interventions to manage cardiovascular disease was \$292 (IQI: \$96 to \$422), based on 6 estimates from 6 studies.

### Healthcare Cost

- The median change in healthcare cost per patient per year for interventions to prevent cardiovascular disease was -\$355 (IQI: -\$981 to -\$23), based on 25 estimates from 25 studies.
- The median change in healthcare cost per patient per year for interventions to manage cardiovascular disease was -\$1784 (IQI: -\$4683 to -\$258), based on 8 estimates from 8 studies.

### *Total Cost*

Total cost is measured as the sum of the change in healthcare cost due to intervention and the cost of intervention. A negative value indicates averted healthcare cost exceeds intervention cost.

- The median total cost per patient per year for interventions to prevent cardiovascular disease was -\$49 (IQI: -\$636 to \$249), based on 22 estimates from 21 studies. The total cost estimates for cardiovascular disease prevention were inconsistent, with ten estimates reporting positive total cost and twelve estimates reporting negative total cost.
- The median total cost per patient per year for interventions to manage cardiovascular disease was -\$1080 (IQI: -\$2816 to -\$163), based on 7 estimates from 7 studies. For all but one of the estimates, the reduced healthcare cost exceeded the cost of intervention indicating net cost savings when implemented for patients with existing cardiovascular disease.

### *Cost-effectiveness*

- The median cost per QALY saved for interventions to prevent cardiovascular disease was \$11,298 (IQI: \$5660 to \$28,416), based on 5 estimates from 5 studies. The median and third quartile were below a conservative \$50,000 threshold. Only one estimate was above the threshold and the study that reported this result computed cost per QALY based on health outcomes within a 9-month trial period.
- There were no studies that reported cost-effectiveness outcomes for interventions to manage cardiovascular disease.

The systematic economic review finds pharmacy-based adherence interventions to prevent cardiovascular disease are cost-effective based on a median estimate of \$11,298 per QALY saved, which is below a conservative \$50,000 threshold. For patients with existing cardiovascular disease, economic evidence indicates that the healthcare cost averted exceeds the cost of implementation for a favorable return on investment (ROI) from a healthcare systems perspective.

### **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) [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:

- [Using the Pharmacists' Patient Care Process to Manage High Blood Pressure: A Resource Guide for Pharmacists](https://www.cdc.gov/dhds/pubs/docs/pharmacist-resource-guide.pdf) [https://www.cdc.gov/dhds/pubs/docs/pharmacist-resource-guide.pdf]

The Million Hearts Initiative® provides [action guides](https://millionhearts.hhs.gov/tools-protocols/medication-adherence.html) [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) [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) [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) [https://www.uspreventiveservicestaskforce.org/Page/Document/UpdateSummaryFinal/tobacco-use-in-adults-and-pregnant-women-counseling-and-interventions1] 2015). While this review did not evaluate 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.

Community health workers might also be able to play a role. The CPSTF recommends [engaging community health workers for cardiovascular disease prevention](https://www.thecommunityguide.org/findings/cardiovascular-disease-prevention-and-control-interventions-engaging-community-health) [https://www.thecommunityguide.org/findings/cardiovascular-disease-prevention-and-control-interventions-engaging-community-health]. Implementation research could evaluate coordinated work between community health workers and community-based pharmacies in underserved communities.

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?
- Are these interventions cost-effective for patients with existing cardiovascular disease?
- What are the economic outcomes when interventions are implemented in rural areas?
- What are the clinical outcomes associated with reductions in healthcare costs and increases in quality adjusted life years? Economic evaluations will be more helpful if they include patient health outcomes (e.g., blood pressure, cholesterol) in their reports.
- Which components of healthcare use lead to the greatest changes in healthcare cost following implementation?

## References

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## Disclaimer

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