Medication Adherence Interventions: Comparative Effectiveness

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RTI International – University of North Carolina Evidence-based Practice Center
AHRQ Comparative Effectiveness Review Process

Topic Nomination

Systematic Review

- Public Comment
- Expert Input
- Peer Review
4. Medication Adherence Interventions: Comparative Effectiveness

Closing the Quality Gap: Revisiting the State of the Science

Background
Achieving the goal of quantitatively improving the quality and effectiveness of health care for all Americans requires both knowledge and tools. Although medical researchers have demonstrated many efficacious medical treatments to improve health outcomes, a recent Institute of Medicine report identified a disquieting discrepancy between present treatment success rates and those thought to be achievable. This gap has been attributed partly to barriers that providers face in implementing best practice guidelines. Patients’ adherence to treatment, however, provides an additional explanation for the mismatch between recommended treatment and actual treatment outcomes.

Poor medication adherence is relatively common. Studies have shown consistently that 20 to 30 percent of medication prescriptions are never filled and that, on average, 50 percent of medications for chronic disease are not taken as prescribed. This lack of adherence to medications is not only prevalent, but also has dramatic effects on individual and population-level health. Nonadherence has been estimated to cost the U.S. health care system between $300 billion and $529 billion annually in direct costs. Strong evidence suggests that benefits attributable to improved self-management of chronic diseases could result in a cost-savings ratio of approximately 1:10.3,23

Evidence-based Practice Program
The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States. The reports and assessments provide organizations with comprehensive, science-based information on common, costly medical conditions and new health care technologies. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

AHRQ expects that the EPC evidence reports and technology assessments will inform individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

The full report and this summary are available at www.effectivehealthcare.ahrq.gov/reports/final.pdf.
Learning Objectives

• Identify factors that influence medication adherence.

• Describe the adverse consequences of medication nonadherence.

• Summarize the effectiveness of interventions on medication adherence and health outcomes.

• Apply this information to interventions on medication adherence with your patients.
What to Expect

Background
- Definition, prevalence, causes, and outcomes of medication nonadherence

Methods
- Grading the strength of a body of evidence

Key Questions
- Clinical questions addressed

Results
- What was found

Conclusions
- What was learned about medication-adherence interventions

Clinical Practice
- How to use these findings
What is medication adherence?

What is the prevalence of nonadherence?

What are the causes of nonadherence?

What are the outcomes of nonadherence?
The extent to which patients take medication as prescribed by their health care providers
Prevalence of Medication Nonadherence

Prescriptions
20%-30% Never Filled

Prescriptions for Chronic Conditions
50% Not Taken as Prescribed
Outcomes of Medication Nonadherence

- Complications
- Quality of Life
- Mortality
Effect on Health Care Costs

Nonadherence costs between $100 and $289 billion annually in direct costs.
Factors that Influence Medication Adherence

- Patient
- Health Care Provider
- Medication Nonadherence
- Health Policy
- Health System
Health Policies

- Health policies support health care systems and influence broader societal factors that affect the patient’s ability to adhere to medication recommendations.
Causes of Medication Nonadherence

Health System

- The health system influences clinicians’ behaviors and broader infrastructural features, such as communication systems for interdisciplinary teams.
• The health care provider may provide insufficient instructions about the proper use and purpose of medications.
Causes of Medication Nonadherence

Patient

- Many patient factors underlie nonadherence, including inability to understand why or how to take the medication, lack of motivation, lack of resources that support adherence, substance abuse, depression, lack of medical insurance, competing demands on time, or erratic daily schedules.
Medication Nonadherence

Health and Health Care Disparities
# Components of Medication Adherence Interventions

<table>
<thead>
<tr>
<th>Component</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Knowledge-based</td>
<td>General Information about behavior-related health consequences, use of individualized information, increase in understanding/memory enhancement</td>
</tr>
<tr>
<td>Awareness-based</td>
<td>Risk communication, self-monitoring, reflective listening, behavioral feedback</td>
</tr>
<tr>
<td>Social influence</td>
<td>Information about peers or social influence of peers</td>
</tr>
<tr>
<td>Attitudes</td>
<td>Targets attitudes toward behavior</td>
</tr>
<tr>
<td>Self-efficacy</td>
<td>Modeling, practice, verbal persuasion, coping responses, graded tasks, reattribution of success/failure</td>
</tr>
<tr>
<td>Self-monitoring skills</td>
<td>Teaching skills in self-monitoring and self-management</td>
</tr>
<tr>
<td>Intention formation</td>
<td>General intention, medication schedule, goals, behavioral contract</td>
</tr>
<tr>
<td>Action control</td>
<td>Cues/reminders, self-persuasion, social support</td>
</tr>
</tbody>
</table>
## Components of Medication Adherence Interventions

<table>
<thead>
<tr>
<th>Component</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maintenance</td>
<td>Maintenance goals, relapse prevention</td>
</tr>
<tr>
<td>Facilitation</td>
<td>Ongoing professional support, dealing with adverse effects, individualizing/simplifying regimen (fewer pills, fewer medications, less frequent dosing, timing of dosing to fit individual schedule), reducing environmental barriers</td>
</tr>
<tr>
<td>Contingent reward</td>
<td>Payment or other reward for conducting behavior</td>
</tr>
<tr>
<td>Motivational interviewing</td>
<td>Client-centered yet directive counseling style that facilitates behavior change through helping clients resolve ambivalence</td>
</tr>
<tr>
<td>Stress management</td>
<td>Methods to reduce or manage stress, such as biofeedback</td>
</tr>
<tr>
<td>Organizational learning strategies</td>
<td>Use of implementation toolkits or learning collaboratives</td>
</tr>
<tr>
<td>Systems change – clinical champion</td>
<td>Use of clinician patient advocate</td>
</tr>
<tr>
<td>Systems change – quality</td>
<td>Continuous quality improvement system</td>
</tr>
</tbody>
</table>
Scope of the Review

Population

• Adults prescribed self-administered medication for secondary or tertiary prevention of chronic diseases.

Interventions

• Any intervention intended to improve adherence with prescribed self-administered medications.
• Any intervention intended to address policy barriers.

Comparators

• Usual care.
• Medication-adherence intervention.

Outcomes

• Medication adherence, adverse events, mortality, morbidity, QOL, patient satisfaction, health care utilization (and associated costs), biomarkers.
Strength of the Evidence

**High**
- High confidence that the evidence reflects the true effect. Further research is very unlikely to change the confidence in the estimate of effect.

**Moderate**
- Moderate confidence that the evidence reflects the true effect. Further research may change the confidence in the estimate of effect and may change the estimate.

**Low**
- Low confidence that the evidence reflects the true effect. Further research is likely to change the confidence in the estimate of effect and is likely to change the estimate.

**Insufficient**
- Evidence either is unavailable or does not permit estimation of an effect.
### Key Questions

<table>
<thead>
<tr>
<th>KQ 1</th>
<th>A: Among patients with chronic diseases with self-administered medication prescribed by a provider, what is the comparative effectiveness of interventions aimed at patients, providers, systems, and combinations of audiences in improving medication adherence?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B: Is improved medication adherence associated with improvement in patient outcomes?</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>KQ 2</th>
<th>A: Among patients with chronic diseases with self-administered medication prescribed by a provider, what is the comparative effectiveness of policy interventions in improving medication adherence?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>B: Is improved medication adherence associated with improvement in patient outcomes?</td>
</tr>
</tbody>
</table>
### Key Questions

| KQ 3 | A: How do medication-adherence intervention characteristics (e.g., mode of delivery, intervention target, intensity) vary? | B: To what extent do the effects of adherence interventions vary based upon their characteristics? |
| KQ 4 | To what extent do the effects of adherence interventions vary based on differences in vulnerable populations? |
| KQ 5 | What unintended consequences are associated with interventions to improve medication adherence? |
Key Questions in Relation to Each Other

**Intervention Characteristics**

- KQ 3a
  - KQ 1a, KQ 3b interventions: directed at patients, providers, and systems
  - KQ 2a, KQ 3b interventions: directed at policy

**Outcomes**

- Biomarkers of clinical outcomes
- Clinical outcomes: Mortality, Morbidity
- Quality of life
- Patient satisfaction
- Healthcare utilization
- Quality of care

**Vulnerable Populations**

**Adverse Events**
What are Medication Adherence Interventions?

- Education
- Counseling
- Behavioral
- Case management

- Simplified dosing
- Reminders
- Formulation change
- Medication charts

- Dose-dispensing units
- Shared decision making
- Augmented pharmacy services
- System changes

- Rewards
- Changes in copay
- Changes in refill practices
- Changes in formularies
Studies Addressing the Key Questions

- **Patient, provider, and systems interventions**
  - 57 studies

- **Policy interventions**
  - 5 studies

- **Features of interventions**
  - 4 studies

- **Specific populations**
  - 15 studies

- **Adverse effects**
  - 3 studies
1A: What is the comparative effectiveness of interventions aimed at patients, providers, and systems in improving medication adherence?

1B: Is improved medication adherence associated with improvement in patient outcomes?
Findings Related to Clinical Conditions

- Hypertension: 17 studies
- Diabetes: 5 studies
- Hyperlipidemia: 9 studies
- Heart failure: 4 studies
- Reactive airway: 8 studies
- Depression: 11 studies
- Glaucoma: 1 study
- Musculoskeletal: 3 studies
- Myocardial infarction: 1 study
- Multiple sclerosis: 1 study
- Unspecified or multiple conditions: 4 studies
### Effective Interventions for Improving Medication Adherence (low strength of evidence)

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blister packaging</td>
<td>1 study</td>
</tr>
<tr>
<td>Case management</td>
<td>3 studies</td>
</tr>
<tr>
<td>Education</td>
<td>8 studies</td>
</tr>
</tbody>
</table>

### Effects on Health Outcomes (low to moderate strength of evidence)

- Improved systolic and diastolic blood pressure
Patient, Provider, and Systems Interventions: Heart Failure

### Effective Interventions for Medication Adherence

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case management</td>
<td>(1 study)</td>
</tr>
<tr>
<td>Multicomponent pharmacist-led</td>
<td>(1 study)</td>
</tr>
<tr>
<td>Reminders</td>
<td>(1 study)</td>
</tr>
</tbody>
</table>

### Effects on Health Outcomes

<table>
<thead>
<tr>
<th>Effect</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Improved patient satisfaction</td>
<td></td>
</tr>
<tr>
<td>Reduced emergency department or hospital admissions</td>
<td></td>
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</tbody>
</table>
### Effective Interventions for Medication Adherence (low to moderate strength of evidence)

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<tr>
<th>Intervention</th>
<th>Number of Studies</th>
</tr>
</thead>
<tbody>
<tr>
<td>Case management</td>
<td>3 studies</td>
</tr>
<tr>
<td>Collaborative care</td>
<td>3 studies</td>
</tr>
<tr>
<td>Reminders</td>
<td>1 study</td>
</tr>
</tbody>
</table>

### Effects on Health Outcomes (low to moderate strength of evidence)

<table>
<thead>
<tr>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Symptom improvement</td>
</tr>
<tr>
<td>Increased patient satisfaction</td>
</tr>
</tbody>
</table>
**Effective Interventions for Medication Adherence**  
*(low to moderate strength of evidence)*

<table>
<thead>
<tr>
<th>Intervention</th>
<th>Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-management</td>
<td>(5 studies)</td>
</tr>
<tr>
<td>Shared or clinical decision making</td>
<td>(1 study)</td>
</tr>
</tbody>
</table>

**Ineffective Interventions for Medication Adherence**  
*(low strength of evidence)*

<table>
<thead>
<tr>
<th>Intervention</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pharmacist or physician access to adherence records</td>
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</table>

**Effects on Health Outcomes**  
*(low strength of evidence)*

<table>
<thead>
<tr>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Variable depending upon intervention</td>
</tr>
</tbody>
</table>
### Patient, Provider, and Systems Interventions: Other Conditions

<table>
<thead>
<tr>
<th>Condition</th>
<th>Interventions</th>
</tr>
</thead>
</table>
| Diabetes                   | • Improved adherence  
                              | • Improved Hb1Ac                                     |
| Hyperlipidemia             | • Improved adherence  
                              | • Improved patient satisfaction                       |
| Myocardial infarction      | • Improved adherence                                 |
| Glaucoma                   | • Improved adherence                                 |
| Multiple sclerosis         | • Improved adherence                                 |
| Musculoskeletal diseases   | • Improved adherence                                 |

All results shown had low strength of evidence.
Findings Related to Interventions

- Blister packaging
- Case management
- Collaborative care by telephone
- Collaborative care in person
- Counseling
- Decision aids
- Education by pharmacist
- Education with behavioral support
- Education with social support
- Health coaching
- Multicomponent interventions
- Outreach
- Patient access to records
- Pharmacist or physician access to adherence records
- Reminders
- Risk communication
- Self-management
- Shared or clinical decision making
- Telemonitoring
- Virtual clinic
Interventions that had a Positive Effect on Medication Adherence

- **Educational** (low to moderate strength of evidence)
  - Asthma
  - Hypertension
  - Hyperlipidemia
  - Myocardial infarction

- **Case Management** (low to moderate strength of evidence)
  - Diabetes
  - Heart failure
  - Hypertension
  - Depression

- **Reminders** (low strength of evidence)
  - Heart failure
  - Depression

- **Multicomponent** (low strength of evidence)
  - Heart failure
  - Glaucoma
Key Question 2

A: Among patients with chronic diseases with self-administered medication prescribed by a provider, what is the comparative effectiveness of policy interventions in improving medication adherence?

B: Is improved medication adherence associated with improvement in patient outcomes?
Policy Interventions

Medication costs

Adherence

Cardiovascular Conditions (5 studies) or Diabetes (3 studies)
(moderate strength of evidence)
Key Question 3

A: How do medication-adherence intervention characteristics (e.g., mode of delivery, intervention target, intensity) vary?

B: To what extent do the effects of adherence interventions vary based upon their characteristics?
Key Intervention Characteristics

- Mode
- Target
- Agent
- Intensity
- Duration
- Components
Characteristics of Medication-Adherence Interventions
Only four studies compared individual features of an intervention.

► Based on one of these studies done among patients with asthma, we concluded with low strength of evidence that:
  o Shared decision making had a greater effect on medication adherence than did a clinician decision making approach.
  o Both approaches were more efficacious than usual care.
  o Shared decision making improved pulmonary function tests when compared with clinical decision making.

► The remaining three studies had insufficient evidence.
Vulnerable Populations

Key Question 4: To what extent do the effects of adherence interventions vary based on differences in vulnerable populations?
Vulnerable Populations

15 studies of vulnerable populations

- 12 studies included vulnerable populations only
- 3 studies performed subgroup analyses from a larger study sample

6 studies looked at severe disease, persistent disease, or coexisting conditions

- 1 looked at severe or persistent depression
- 1 looked at patients with diabetes plus hypertension
- 4 looked at depression with a co-existing condition, 1 of which was conducted among African Americans

9 studies in other groups

- 5 studies were conducted among the elderly
- 2 studies in rural communities
- 2 studies among patients with major depression
Outcomes for Vulnerable Populations

Interventions improved medication adherence for:

- Major or Severe Depression
- Multiple Chronic Conditions
- Depression + Hypertension
- African Americans with Diabetes + Depression
- Elderly Populations with Diabetes, Hyperlipidemia, Heart Failure, or Hypertension

All results shown had low strength of evidence.
Adverse Effects

Key Question 5

What unintended consequences are associated with interventions to improve medication adherence?
Adverse Events

3 studies evaluated adverse effects of interventions

Studies involved varied conditions and interventions

No evidence of greater adverse events from intervention

Evidence is insufficient to draw conclusions
Conclusions

What did we learn?
Conclusions: Adherence

Hypertension
- Blister packaging
- Case management
- Education

Heart Failure
- Case management
- Reminders
- Multicomponent pharmacist-led program

Depression
- Case management*
- Reminders
- Collaborative care*

Asthma
- Self-management*
- Shared or clinician decision making
- Reduced medication copayments
- Improved prescription drug coverage

Cardiovascular Conditions
- Reduced medication copayments*
- Improved prescription drug coverage*

*Denotes moderate strength of evidence.
Conclusions: Health Outcomes

<table>
<thead>
<tr>
<th>Condition</th>
<th>Interventions</th>
<th>Improved Outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>• Case management</td>
<td>• Adherence</td>
</tr>
<tr>
<td></td>
<td>• Face-to-face education by pharmacists</td>
<td>• Systolic and diastolic blood pressure</td>
</tr>
<tr>
<td>Heart Failure</td>
<td>• Pharmacist-led multicomponent intervention</td>
<td>• Adherence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Emergency department visits</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient satisfaction</td>
</tr>
<tr>
<td>Depression</td>
<td>• Case management</td>
<td>• Adherence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Symptoms of depression</td>
</tr>
<tr>
<td>Depression</td>
<td>• Collaborative care</td>
<td>• Adherence</td>
</tr>
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<td>• Symptoms of depression</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Patient satisfaction</td>
</tr>
<tr>
<td>Asthma</td>
<td>• Shared decisionmaking</td>
<td>• Adherence</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Symptoms</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Pulmonary function</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Health care use</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Quality of care</td>
</tr>
</tbody>
</table>
Findings in Relation to What is Already Known
Limits and Applicability

Relatively applicable because of the wide variety of included populations, clinical conditions, and interventions.

Not applicable to children and adolescents, or to populations with HIV infection, AIDS, schizophrenia, bipolar disorder, substance abuse, or acute conditions.

Study designs and populations included in available studies as well as the complexity of the interventions and uncertainty about reproducibility may also limit applicability.
Research Gaps

Paucity of evidence for some clinical conditions

Lack of evidence on conditions with episodic symptomatology (symptom-free periods that alternate with the presence of symptoms)

Limited evidence on harms, health outcomes, QOL, costs, and health care utilization

Limited evidence on long-term outcomes
How can I apply this information to my patients?
Clinical Application of Review Results

- Educate the patient about the benefits of taking medications as directed.
- Ensure that patients have access to their medications.
- Provide clear instructions on the correct use of each medication.
- Continue to educate and monitor medication usage at all office visits.
Continuing Education and Wrap Up
Continuing Education Credit

• To obtain credit:
  ► Complete the online evaluation.
  ► Pass the posttest with a grade of 75% or higher.

If you have any problems receiving certification, please contact:

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Fax: (303) 858-8848
Email: information@pimed.com