

# Modes of Delivery for Interventions to Improve Cardiovascular Medication Adherence

Sarah L. Cutrona, MD, MPH; Nitesh K. Choudhry, MD, PhD; Michael A. Fischer, MD, MPH; Amber Servi, BA; Joshua N. Liberman, PhD; Troyen A. Brennan, MD, JD; and William H. Shrank, MD, MSHS

**N**onadherence to essential chronic medication therapy for cardiovascular disease and diabetes is common, leading to substantial morbidity, mortality, and healthcare costs.<sup>1-3</sup> Evidence-based efforts to improve adherence are needed. Previous studies have demonstrated the effectiveness of reduced dosing demands and complex, multifactorial interventions,<sup>4,5</sup> but there is little evidence available comparing modes of delivery for adherence interventions.

Evidence-based information on modes of delivery would enhance the construction of adherence interventions in several domains: the communication channel (eg, written, electronic, phone, in person), the purveyor of information (eg, lay person, pharmacist, physician), and the optimal setting (hospital, home, pharmacy, clinic). The mode of delivery is closely linked to an intervention's cost and therefore to its long-term viability. Careful consideration of the comparative efficacy and intensity of different approaches is needed to develop evidence-based strategies.

We conducted a systematic review of interventions that sought to improve adherence to medications for cardiovascular disease and diabetes, a cardiovascular disease equivalent. We focused on the mechanism of information transfer to patients. By evaluating the effects of (1) the purveyor of information, (2) the channel of information, and (3) the setting of transfer, we offer to payers, providers, and policy makers additional guidance on the development of adherence interventions.

## METHODS

We performed a systematic search of articles published in peer-reviewed, healthcare-related journals between 1966 and December 31, 2008. The search was performed using MEDLINE and EMBASE, with the help of a professional librarian. We limited our search to randomized controlled trials.

We used search terms related to the type of study (randomized controlled trial), adherence (ie, "adherence" OR "compliance" OR "medication adherence" or "treatment adherence"), prescription drugs (ie, "drug" OR "medication" OR "antihypertensive" OR "antihyperlipidemic" OR "hypoglycemic agents"), and cardiovascular disease and diabetes (myocardial infarction, coronary heart disease, heart failure; hypertension; hyperlipidemia; and diabetes). Articles with

**Objective:** To determine the optimal modes of delivery for interventions to improve adherence to cardiovascular medications.

**Study Design:** Systematic review.

**Methods:** We conducted systematic searches of English-language, peer-reviewed publications in MEDLINE and EMBASE, 1966 through December 31, 2008. We selected randomized controlled trials of interventions to improve adherence to medications for preventing or treating cardiovascular disease or diabetes. Articles were classified based on mode of delivery of the main intervention as (1) person-independent interventions (mailed, faxed, or hand distributed; or delivered via electronic interface) or (2) person-dependent interventions (nonautomated phone calls, in-person interventions).

**Results:** We identified 6550 articles. Of these, 168 were reviewed in full and 51 met inclusion criteria. Among person-independent interventions (56% successful), electronic interventions were most successful (67%). Among person-dependent interventions (52% successful), phone calls showed low success rates (38%). In-person interventions at hospital discharge were more effective (67%) than clinic interventions (47%). In-person pharmacist interventions were effective when held in a pharmacy (83% successful), but were less effective in clinics (38%).

**Conclusions:** Future medication adherence studies should explore new electronic approaches and in-person interventions at the site of medication distribution. Identifying times of increased patient receptivity to the adherence message such as hospital discharge also will be important.

(*Am J Manag Care.* 2010;16(12):929-942)

### In this issue

Take-Away Points / p930

[www.ajmc.com](http://www.ajmc.com)

Full text and PDF

Web exclusive

eAppendix

For author information and disclosures, see end of text.

### Take-Away Points

Interventions designed to improve adherence to cardiovascular medications may require a person to deliver them (in-person counseling, phone calls), or the delivery may be person independent (mailed information, electronic interface). The mode of delivery directly affects cost and long-term viability.

- Among person-independent interventions, we found electronic approaches to be most effective at improving adherence.
- For interventions delivered by a person, we found high success rates for in-person interventions delivered at a pharmacy or at the time of hospital discharge.

at least 1 search term in 3 of the main categories (study type AND adherence AND either drug OR disease) met criteria for the title/abstract review (see the [eAppendix](#) at [www.ajmc.com](#)).

Search terms and parameters were adjusted for both databases while maintaining a common overall architecture. Search results from MEDLINE and EMBASE were combined and screened for duplicate entries.

### Study Selection

Studies were included if they reported the results of randomized controlled trials that examined interventions to improve adherence to medications used for the prevention or treatment of cardiovascular disease or diabetes. Studies were limited to adult subjects (aged  $\geq 18$  years) in either the outpatient setting or at the inpatient/outpatient transition. Data were gathered on outpatient adherence for all patients. Studies were excluded if they described an intervention characterized by regimen simplification (either unit-of-use packaging or changes in dose frequency or formulation), as they could not be placed into the study categorization, and previous studies have demonstrated their effectiveness.<sup>4</sup> Studies were excluded if they were written in a language other than English. Those with a duration of less than 24 weeks were excluded because cardiovascular medications typically require long-term adherence.

After exclusions, 51 articles ([Figure](#)) were classified by the mode of delivery of the intervention. Person-independent interventions included (1) mailed, faxed, or hand-distributed interventions and (2) interventions delivered via electronic system. Person-dependent interventions included (1) interventions delivered via nonautomated phone calls and (2) in-person interventions (classified based on site of delivery, ie, home, work site, pharmacy, clinic, or hospital). Person-dependent interventions were further classified based on the level of training required of the person administering the intervention: (1) trained lay person, (2) nurse, (3) pharmacist, (4) physician, or (5) not specified.

For those studies that incorporated 2 or more modes of intervention, we assigned categories based on what appeared

to be the main mode of intervention. Where categories appeared to be equivalent, we assigned priority in the following order: person dependent (in person, followed by phone) and person independent (electronic system, followed by mailed, faxed, or hand distributed).

### Data Extraction

Data were extracted by 2 investigators (SLC, WHS) with disagreements resolved by consensus. We assessed a number of variables related to the organization and outcome of studies, including the study design, setting, characteristics of population studied, the number of participants, characteristics of intervention, methods used to measure medication adherence, clinical outcomes, and medication adherence outcomes. We report confidence intervals (CIs) when available and *P* values when no CIs were available.

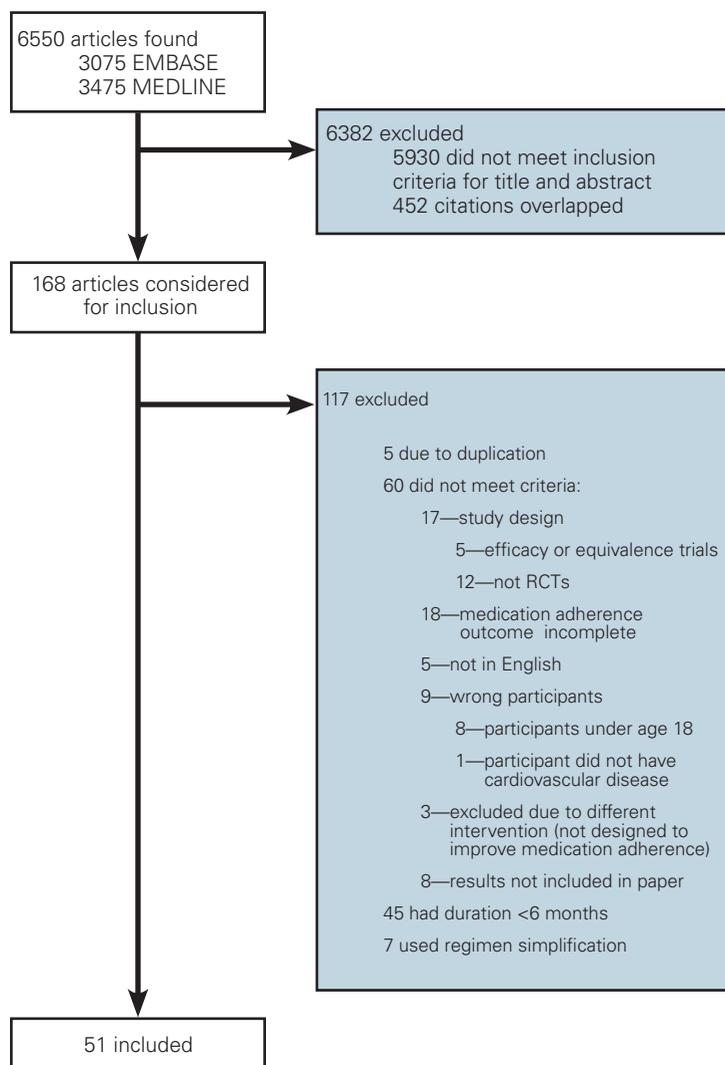
## RESULTS

Our search retrieved a total of 6550 articles. Of these articles, 168 were reviewed in full and 51 met inclusion criteria<sup>6-56</sup> ([Figure](#), [Table 1](#), [Table 2](#)). The majority (55%) of interventions were aimed at subjects with hypertension. Other patient populations studied included those with diabetes (8%), coronary artery disease (8%), congestive heart failure (14%), and dyslipidemia (10%); 6% of the studies evaluated patients with a mix of cardiovascular and noncardiovascular diseases.

### Person-Independent Interventions: Mailed, Faxed, or Hand-Distributed Material

There were 3 studies<sup>6-8</sup> in which the main intervention was delivered via mail, fax, or hand distribution of paper or video information; 1 was successful.<sup>6</sup> Smith et al followed 907 patients after discharge from a hospital stay for myocardial infarction; 2 letters sent to patients and to primary care providers describing the importance of beta-blocker use yielded improved adherence as measured by pharmacy claims data. Patients receiving mailings were 17% more likely to have 80% of days covered (relative risk = 1.17; 95% CI = 1.02, 1.29). The 2 unsuccessful studies described direct patient mailings of written information on hypertension<sup>7</sup> or video information on 1 of 4 medications (2 blood pressure agents, an antihyperlipidemic, and transdermal estrogen).<sup>8</sup> Takala defined adherent patients as those still under treatment after 2 years,<sup>7</sup> and Powell and Edgren studied mean medication possession ratios.<sup>8</sup>

■ **Figure. Study Selection Criteria**



RCT indicates randomized controlled trial.

**Person-Independent Interventions:  
Electronic Systems**

There were 6 studies<sup>9-14</sup> that examined a range of electronic interventions, including use of electronic pillboxes with programmable reminders, automated phone calls with interactive components, computer-generated individualized interventions, and home automatic blood pressure monitoring. Overall, this group included more positive studies than the mailed/faxed/hand-delivered group (4 out of 6 showed improved adherence).

Rosen et al<sup>14</sup> studied 33 people with diabetes whose baseline adherence was less than 80%. This study tested use of electronic pill caps with a time display and programmable

beeper compared with electronic pill caps alone. Participants with programmable beeper pill caps showed improved adherence (80% intervention vs 60% control;  $P = .017$ ).

Friedman et al<sup>10</sup> and Piette et al<sup>13</sup> studied the effect of automated phone calls. Friedman and colleagues followed 299 hypertensive patients, randomizing patients to an interactive computer-based home telemonitoring system versus usual care. Patients called in weekly, shared information by phone regarding automated blood pressure readings and adherence, and received targeted education and motivational counseling (all automated), with responses forwarded to doctors. Adherence, measured by pill count, was not significantly different between groups in unadjusted analysis; adjustment for age, sex, and baseline adherence yielded significant differences (17.7% adherence in intervention group vs 11.7% in control group;  $P = .03$ ). Piette et al randomized 280 patients to biweekly automated interactive phone calls with structured messages that were adjusted based on patient responses, followed by targeted nurse calls versus usual care. Differences from Friedman et al’s intervention include outgoing calls to patients (Friedman et al required patients to call in) and limited nonautomated phone follow-up. Piette and colleagues found that intervention patients were “substantially less likely to report adherence problems” (based on self-report using modified Morisky scale) ( $P = .003$ , no adherence percentages given) but did not provide baseline adherence (56% reported “any medication problem” at baseline).

Johnson et al<sup>11</sup> followed 404 adults, describing the impact of a computer program designed to mimic the reasoning and problem-solving of humans based on an integrative model of behavioral change (the transtheoretical model) and incorporating an individualized computer-generated report mailed to patients. They found an improvement in adherence at 18 months (odds ratio = 2.86,  $P < .05$ ). Emmett et al<sup>9</sup> studied 217 patients newly diagnosed with hypertension who were randomized in a factorial manner to a computerized decision analysis intervention, mailed video and leaflet, both, or neither. Neither the decision analysis nor the mailed video and leaflet resulted in significant improvement. Marquez-Contreras et al<sup>12</sup> examined use of home automatic blood pressure monitoring (along with a phone call with instructions on use) in 250 patients with uncontrolled or newly diagnosed hypertension. At the end of 6 months,

**Table 1. Person-Independent Interventions<sup>a</sup>**

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
<b>Paper Information: Mailed, Faxed, or Handed Out</b>				
Smith et al, <sup>6</sup> 2008 (US urban centers)	907 patients at hospital discharge post-MI, with $\beta$ -blocker prescriptions  9 months	2 mailings to patients, PCPs addressed importance of $\beta$ -blockers, guidelines	Percentage of patients with $\geq 80\%$ of days covered in the 9 months after 1st mailing; pharmacy claims and other electronic data	Treatment patients were 17% more likely to have 80% of days covered (RR 1.17; CI 1.02, 1.29)
Takala, <sup>7</sup> 1983 (Southwest Finland)	147 untreated HTN patients  2 years	Mailed information on HTN	2 years after intervention, asked if "still under treatment after 2 years"	Adherent: I: 90% C: 79% <i>P</i> = NS
<b>Video Information: Mailed or Handed Out</b>				
Powell et al, <sup>8</sup> 1995 (Midwestern, US)	4246 patients on benazepril, metoprolol, simvastatin, or estrogen  9 months	Mailed 1 of 4 educational videotapes	MPR; pharmacy claims	No significant between-group differences in mean MPRs
<b>Electronic System</b>				
Emmett et al, <sup>9</sup> 2005 (Bristol, England)	217 newly diagnosed HTN patients, primary care practices  3 years	1. Decision analysis (DA) 2. Video and leaflet 3. DA and video/leaflet vs usual care	Proportion of patients who report taking all their medications	DA: 90% Adjusted OR 1.56 CI 0.49, 4.96 <i>P</i> = .45 Video plus leaflet: 94% Adjusted OR 0.53 CI 0.15, 1.84 <i>P</i> = .32
Friedman et al, <sup>10</sup> 1996 (Boston, MA)	299 HTN patients  6 months	Interactive computer-based home monitoring; patient self-BP checks, weekly calls to counsel on adherence	MPR (expressed as percentage); home pill count	Mean $\Delta$ adherence, unadjusted: C: -0.4% I: 2.4%, <i>P</i> = .29 Adjusted for baseline adherence: I: 17.7% C: 11.7%, <i>P</i> = .03
Johnson et al, <sup>11</sup> 2006 (Massachusetts and Rhode Island)	404 adults with hyperlipidemia  18 months	Population-based, computer-generated individualized intervention; report mailed to patient	Responses to 5 questions (on Likert scale) summed to create a continuous measure; calculated odds of appropriate adherence; self-report	Adherence as continuous measure: 6-month OR 2.03 <i>P</i> > .05 18-month OR 2.86 <i>P</i> < .05
Marquez-Contreras et al, <sup>12</sup> 2006 (Spain)	250 HTN patients from primary care centers  6 months	Home automatic BP monitoring	MPR (expressed as percentage); Adherence was >80%; MEMS	Percent adherent patients: I: 92 (SD 14.2) C: 74 (SD 18.1) <i>P</i> = .0007
Piette et al, <sup>13</sup> 2000	280 DM patients on hypoglycemic medications; included Spanish-speaking patients  12 months	Biweekly automated assessment/education calls: hierarchically structured messages (positive feedback for adherence, questions on adherence barriers, advice); targeted nurse follow-up calls	Abbreviated Morisky Index <sup>b</sup> patients considered nonadherent if they sometimes forgot or stopped taking medication; phone interviews, self-report	I: "substantially less likely" to report adherence problems ( <i>P</i> = .003)
Rosen et al, <sup>14</sup> 2004 (Connecticut)	33 DM patients on metformin with <80% adherence  28 weeks	Cue-dose training: given electronic pill caps programmed to beep, instruction on other cues	Mean MPR (doses needed to be taken on time); electronic pill bottles	16 weeks of intervention: I: 80% C: 60% <i>P</i> = .017 No numbers given for 28 weeks (graph provided)

BP indicates blood pressure; C, control group; CI, confidence interval; DM, diabetes mellitus; HTN, hypertension; I, intervention group; MEMS, medication electronic monitoring system; MI, myocardial infarction; MPR, medication possession ratio (medication doses taken divided by doses prescribed); NS, not significant; OR, odds ratio; PCP, primary care practitioner; RR, relative risk.

<sup>a</sup>Controls received usual care unless otherwise specified. Duration indicates time until last follow-up in which adherence was measured. The CI was 95% unless otherwise specified. Studies took place in United States unless otherwise indicated.

<sup>b</sup>The Morisky scale has 4 questions, with 1 point for every "yes" response. 1. Do you ever forget to take your medication? 2. Are you careless at times about taking your medication? 3. When you feel better, do you sometimes stop taking your medication? 4. Sometimes if you feel worse when you take your medication, do you stop taking it?

## Cardiovascular Medication Adherence

**Table 2. Person-Dependent Interventions**

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
<b>Phone Call (Nonautomated)</b>				
<b>Call by Lay Person</b>				
Stewart et al, <sup>15</sup> 2005 (Johannesburg, South Africa)	83 HTN patients, majority indigent  36 weeks	Support of physiotherapist and family member by phone	Self-described as adherent to medications	I: 82.4% C: 86.7% P = .56
Schechtman et al, <sup>16</sup> 1994 (Milwaukee, WI)	162 patients with hyperlipidemia  6 months	Weekly phone counsel in 1st month of therapy by medical assistant; each group also randomized to niacin vs bile acid sequestrants	MPR; pharmacy claims	Adherence, bile acid sequestrants: I: 88% (SD 4) C: 82% (SD 4) P = .32 Adherence, niacin: I: 90% (SD 2) C: 84% (SD 3) P = .07
<b>Call by Nurse</b>				
Hamet et al, <sup>17</sup> 2002 (Canada)	4864 patients with essential HTN on irbesartan  12 months	Behavioral modification program: phone nurse counsel, reminder letters, BP diaries, mailed education brochures	"Are you taking your Avapro every day?" (no = nonadherent); self-report	Nonadherent patients: I: 25.4% (CI 23.7, 27.2) C: 25.5% (CI 23.8, 27.3) Between-group difference: -0.1% (-2.6 to 2.3) P = .94
<b>Call by Pharmacist</b>				
Faulkner et al, <sup>18</sup> 2000 (Omaha, NE)	30 patients post CABG, PTCA, or both (7-30 days)  2 years	Weekly phone contact for 12 weeks; all received lovastatin daily and colestipol twice daily	Patients returning more than 20% of prescribed pills, and those failing to fill 80% or more of scripts at 1 and 2 years, were considered nonadherent; pharmacy records	Adherent patients Lovastatin: I: 1 year: 67% 2 years: 60% C: 1 year: 33% 2 years: 27% P < .05 for all values (colestipol findings similar, not shown here)
Mehos et al, <sup>19</sup> 2000 (Colorado)	36 HTN patients from clinic in which pharmacist provides direct clinical services  6 months	Home BP monitors, diary for BP and missed doses; pharmacist evaluated BP by phone monthly	MPR (mean), expressed as percentages; pharmacy refill data	I: 82% C: 89% P = .29
<b>Caller Not Specified</b>				
Antonicelli et al, <sup>20</sup> 2008 (Italy)	57 hospitalized CHF patients, aged >70 y  12 months	Home telemonitoring managed by specialized CHF team	Percentage of adherent patients (no further definition)	I: 91% C: 46% P < .03
Sclar et al, <sup>21</sup> 1991 (Delaware, Texas, and Wisconsin)	453 HTN patients on atenolol  180 days	On refill, educational material given; phone contact, refill reminder, mailings; 4 arms, each group divided (previously treated/newly diagnosed)	MPR: multiplied the number of requested atenolol refills by 30 and divided by 180	MPR (SD): Previously treated: C: 0.48 (0.06) I: 0.82 (0.04) Newly diagnosed: C: 0.52 (0.06) I: 0.93 (0.05) P < .05
Guthrie, <sup>22</sup> 2001 (Ohio)	13,100 patients with elevated total cholesterol  6 months	Postal, phone reminders about coronary risk reduction and medication adherence	Taking pravastatin as prescribed per self-report: yes/no	Taking as prescribed: I: 79.7% C: 77.4% Authors conclude: "no meaningful difference"

(Continued)

■ **Table 2.** Person-Dependent Interventions (*Continued*)

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
<b>In person</b>				
<b>Home</b>				
<b>Lay Person</b>				
Saunders et al, <sup>23</sup> 1991 (Soweto, South Africa)	115 HTN patients  6 months	Appointment reminders sent; patient-retained BP and medication records; targeted field worker home visit follow-up	MPR based on clinic instructions Adherent: ≥80% consumed	I: 31% C: 15% P = .19
Johnson et al, <sup>24</sup> 1978 (Hamilton, Ontario, Canada)	140 people with persistently elevated DBP  6 months	2x2 factorial: 1. self-recorded BP 2. monthly home visits 3. self-recorded BP and monthly home visits Control (neither)	Percent adherence estimated by comparing pills on hand with prescription records; self-report, pill count	Mean Δ adherence (SD): 1. self-recorded BP: 11.8% (4.5%) 2. monthly home visits: 2.2% (5.6%) 3. self-recorded BP and home visits: 10.1% (4.9%) Control: 1.0% (7.0%). P = NS
Morisky et al, <sup>25</sup> 1985 (Baltimore, MD)	290 HTN patients  18 months	Family support: home interview, training with family member	Scale <sup>b</sup> : 0-4 (1 point per yes answer) (4 = lower compliance); self-report	Intervention group had improved scores (0.876 vs 1.932, P < .01)
<b>Nurse</b>				
Kirscht et al, <sup>26</sup> 1981 (Tecumseh, MI)	417 patients with HTN  3 years	Assigned to 4 interventions in a factorial design: 3 × 2 × 3 × 2 1. Printed messages 2. Nurse phone reminder and reinforcement 3. Self-monitoring with charts 4. Nurse worked with support person	MPR; pharmacy records; averaged over the set of HTN medications	<i>Printed information:</i> I: 0.689 C: 0.684 Between group: NS <i>Nurse phone contact:</i> I: 0.749 C: 0.690 Between group P < .05 <i>Self-monitoring:</i> Charts: 0.683 BP: 0.665 C: 0.665 Between group: NS <i>Nurse support:</i> I: 0.654 C: 0.545 Between group P < .05
<b>Work Site</b>				
<b>Nurse</b>				
Logan et al, <sup>27</sup> 1979 (Toronto, Canada)	457 HTN patients selected from various work sites  6 months	I: work-site care: nurse working under physician supervision managed all aspects of HTN	Adherence: ≥80% of prescribed medications were consumed (pill count) and patient claimed to be taking the medication as instructed (self-report)	Adherent patients: I: 67.6% C: 49.1% P < .005
Logan et al, <sup>28</sup> 1983 (Toronto, Canada)	194 HTN patients  1 year	I: work-site care by physician plus nurse; nonadherents were counseled on medication diary, tailored regimen, home BPs; increased visit frequency	Percentage of adherent patients (≥80% of prescribed medication taken); home pill count	I: 55.4% C: 55.7% P = NS

(Continued)

■ **Table 2.** Person-Dependent Interventions (Continued)

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
<b>Doctor</b>				
Sackett et al, <sup>29</sup> 1975 (Hamilton, Ontario)	230 Canadian steel workers with HTN detected on screening  6 months	Augmented convenience (AC) HTN treated by work-site doctor Additional education (AE) program on HTN, pill-taking reminders C: no AC, no AE I-1: AC, no AE I-2: no AC, AE I-3: AC, AE	Adherence: MPR in 6th month; pill count; adherent was MPR ≥0.8	Compliant at 6 months C: no AC, no AE: 48% I-1: AC, no AE 62% I-2: no AC, AE 53% I-3: AC, AE 48% P = NS
<b>Pharmacy</b>				
<b>Pharmacist</b>				
Lee et al, <sup>30</sup> 2006 (Walter Reed Army Medical Center)	159 patients with HTN, hyperlipidemia, other diseases  6 months	Pharmacy care (education, blister packs, meeting with clinical pharmacist)	Mean MPR for all chronic diseases; pill count	Mean (SD): I: 95.5% (SD 7.7%) C: 69.1% (SD 16.4%) P <.001
Murray et al, <sup>31</sup> 2007 (Indianapolis, IN)	314 HTN patients from inner-city practice  12 months	Pharmacist medication history, knowledge assessment, verbal, written education	Percentage of prescribed medication taken; MEMS	During intervention: I: 78.8% C: 67.9% Difference: 10.9% CI 5.0%, 16.7% Postintervention difference: 3.9% CI -2.8%, 10.7%
Blenkinsopp et al, <sup>32</sup> 2000 (England)	282 HTN patients from community pharmacies  6 months	Pharmacist counsel: structured, questions, medication advice, HTN teaching	Percentage of adherent patients; modified version of Horne's Medication Adherence Report Scale used	I: 62.9% C: 50.0% P <.05
Vrijens et al, <sup>33</sup> 2006 (Belgium)	392 patients with hyperlipidemia on atorvastatin  12 months	I: pharmacy program: medication history educational reminders, written information C: written information	Percentage of days that medication container opening was recorded; MEMS	I: 95.89% CI 90.28%, 98.66% C: 89.37% CI 69.70%, 96.33% P <.001
Community Pharmacy Medicines Management Project Evaluation Team, <sup>34</sup> 2007 (England)	1493 CAD patients from primary care organizations  12 months	Community pharmacist assessed therapy, adherence, lifestyle, social support	Adherence score (12-60) based on 12 questions; self-report	I: 59 (57-60 IQR) C: 59 (57-60 IQR) OR = 1.0, 95% CI 0.61, 1.65 P = .99
Bouvy et al, <sup>35</sup> 2003 (The Netherlands)	152 CHF patients, inpatient and outpatient  6 months	Community pharmacist: structured interview using computerized record, discussed medications, nonadherence	Adherence based on percentage of days without opening pill bottle; nonadherence defined as <80% of days; MEMS	Nonadherent patients: I: 0% C: 14% RR 0.5 CI 0.4, 0.6
<i>(Continued)</i>				

92% of the intervention group had adherence greater than 80% (assessed using electronic pillboxes) compared with 74% of the control group ( $P <.05$ ).

**Person-Dependent Interventions: Nonautomated Phone Calls**

Eight studies described the use of nonautomated phone calls to improve adherence. Calls were made by trained lay people,<sup>15,16</sup> nurses,<sup>17</sup> pharmacists,<sup>18,19</sup> or a nonspecified caller.<sup>20-22</sup> Overall, 5 of these studies showed a nonsignificant improvement in adherence, a single study<sup>20</sup> showed significant

improvement but did not clearly define its adherence outcome measure, and 2 showed significant improvement with clearly defined outcomes.

Neither phone calls by trained lay people nor calls by a nurse yielded significant improvements in adherence. Pharmacist calls showed mixed results. Faulkner et al<sup>18</sup> described 12 weeks of weekly phone calls from a pharmacist for patients after cardiac surgery or angioplasty and found a significant improvement in adherence as measured by pharmacy refills (60% adherence for the phone call group vs 27% adherence for the control group at 2 years for lovastatin). Mehos et al<sup>19</sup> evaluated the effect of

■ **Table 2.** Person-Dependent Interventions (*Continued*)

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
<b>Clinic</b>				
<b>Lay Person</b>				
Ogedegbe et al, <sup>36</sup> 2008 (New York, NY)	190 HTN patients, African Americans, most women  12 months	Motivational interviewing with patient-centered counseling by research assistants	MPR, expressed as percentage; MEMS	I: 60% C: 47% P = .054 Intent-to-treat analysis showed model-predicted rates: I: 57% C: 43% P = .027
Haynes et al, <sup>37</sup> 1976 (Canada)	39 noncompliant HTN patients (pill count <80% at baseline)  12 months	Visits every 2 weeks with research assistant; home BP self-checks, medication and BP charting; tailoring regimen	Proportion of prescribed pills removed from their containers	Mean (SD): I: 65.8% (8.2%) Within group P = 0.001 C: 43.2% (10.1%) Within group P = NS Between group P = .025
<b>Nurse</b>				
Schroeder et al, <sup>38</sup> 2005 (Avon, UK)	245 HTN patients  6 months	Nurse-led adherence support sessions	MPR (expressed as percentage); MEMS, used for 1 medication only	I: 95.6 (SD 16.4) C: 95.6 (SD 15.7) P = .76
Rudd et al, <sup>39</sup> 2004 (California)	150 patients on medication for HTN  6 months	I: physician-directed, nurse-managed, algorithm-based home HTN management, based on self-BP checks	Adherence: average percentage of days on which the correct number of doses were taken; electronic pill monitors	Mean (SD): I: 80.5% (23.0%) C: 69.2% (31.1%) P = .03
<b>Pharmacist</b>				
Vivian, <sup>40</sup> 2002 (Philadelphia, PA)	56 male HTN patients, majority African American  6 months	Monthly pharmacist counseling: changed drugs, adjusted doses	Nonadherence was failure to refill within 2 weeks of scheduled refill date or missing >3 doses in 1 week; pharmacy records	Adherent patients: I: 85% C: 93% P >.42
Phumipamorn et al, <sup>41</sup> 2008 (Krabi Province, Thailand)	135 Muslim DM patients  8 months	Pharmacist meeting day of doctor visit; visit reminder 3 days prior; given refills, lifestyle and medication education	MPR (expressed as percentage); pill count	Mean difference (CI): I: 6.8% (2.1%, 11.4%) P = .005 C: -2.8% (-7.31%, 1.7%) P = 0.29 Between group mean difference P = .004
Hunt et al, <sup>42</sup> 2008 (Oregon)	463 patients with uncontrolled HTN  12 months	Pharmacists managed HTN in PCP office with physician input	Percentage with high adherence, categorized by Morisky scale <sup>b</sup> ; self-report	I: 67% C: 69% P = .77 Change in I: P = .08 Change in C: P = .52
Taylor et al, <sup>43</sup> 2003 (Alabama)	81 patients with ≥3 diseases (HTN, dyslipidemia, DM were most common)  1 year	Pharmacy care medical history, medication review, and education; monitoring; simplified regimens, devised reminders	Estimated MPR; self-report; mean compliance score calculated from scores for each medication	I: 100% C: 88.9% (6.3%) P = .115
Hawkins et al, <sup>44</sup> 1979 (San Antonio, TX)	200 HTN patients on a diuretic with or without methyldopa  29 months	I: Clinical pharmacist managed HTN in place of physician	Percentage of adherent patients (MPR >0.80 considered adherent); pharmacy records	Diuretic only: I: 60.5% C: 52.9% P ≤.7 Diuretic plus methyldopa: I: 84.6% C: 65.4 P ≤.2

(Continued)

## Cardiovascular Medication Adherence

■ **Table 2.** Person-Dependent Interventions (*Continued*)

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
Odegard et al, <sup>45</sup> 2005 (Seattle, WA)	77 subjects with A1C $\geq$ 9 taking DM medication.  12 months	Pharmacist developed care plan, regular pharmacist-patient communication on DM care, medication problems	Adherence based on 2 questions: "Do you ever find it difficult to remember to take (medication name)?" If yes, "How many times over the last 2 weeks have you missed a dose?"	Control showed better adherence than intervention group throughout study ( $P = .003$ )
Sookaneknun et al, <sup>46</sup> 2004 (Urban and rural Thailand)	235 HTN patients from pharmacy and primary care  6 months	Research pharmacist consult: assessed medication understanding, adherence, counseled on use, lifestyle; educational leaflets, diary	Calculated MPR, expressed as percentage; $\geq$ 80% necessary to be considered adherent	Adherent patients: I: 63.64% C: 55.56% $P = .014$
Solomon et al, <sup>47</sup> 1998 (multiple sites)	133 HTN patients  6 months	Standardized pharmacy care: patient assessment, regular interventions for disease management and education	Adherence score based on 4-point Morisky scale <sup>b</sup> ; self-report	Mean (SD): I: 0.23 (0.054) C: 0.61 (0.094) $P < .05$ compared within and between groups
<b>Doctor</b>				
Birtwhistle et al, <sup>48</sup> 2004 (Urban, rural Canada)	614 HTN patients  36 months	3-month vs 6-month physician follow-up	Morisky scale <sup>b</sup> questions including "Ever forget blood pressure pills?"; self-report	I-3 months: 30% I-6 months: 27% Difference: 2.96% (SE 3.92%) 90% CI -3.48%, -9.41%
Yilmaz et al, <sup>49</sup> 2005 (Ankara, Turkey)	202 patients on statin for secondary prevention  15 months	Education that included physician conversation on statins	Odds of being on continuous statin (after median of 15 months); self-report	I: more likely to be on continuous statin OR 1.977 CI 1.127, 3.468
Avanzini et al, <sup>50</sup> 2002 (Italy)	1771 treated HTN patients  1 Year	Physicians treating intervention group wrote guidelines on HTN management Control: patients of physicians who did not write guidelines	Percentage of patients with poor adherence; self-report (not defined further)	I: 3.8% C: 9.5% $P = .004$
<b>Hospital (or Combination of Hospital and Clinic)</b>				
<b>Lay Person</b>				
Tsuyuki et al, <sup>51</sup> 2004 (Canada)	276 patients with CHF discharged from hospital  6 months	Education; adherence aids (organizer, schedule), phone, mail follow-up C: pamphlet	MPR for ACE inhibitor, expressed as percentage; pharmacy records	I: 83.5% (SD 31.2%) C: 86.2% (SD 29.0%) $P = .691$
<b>Nurse</b>				
Krantz et al, <sup>52</sup> 2008 (Denver, CO)	64 CHF patients with ejection fraction $<$ 40%  6 months	Pre-hospital discharge carvedilol initiation and nurse counseling with outpatient nurse management	Beta-blocker "utilization"; on medication (yes/no); pill count	<i>Beta-blocker utilization:</i> C: Hospital discharge: 9.4% 6 months: 47.8% I: Hospital discharge: 96.9% 6 months: 96.2% Utilization significantly higher in intervention group at all time periods, $P < .001$
<b>Pharmacist</b>				
Lopez Cabezas et al, <sup>53</sup> 2006 (Barcelona, Spain)	134 hospitalized patients with CHF  1 year	Pharmacist program: educational interview with patient and caregiver at discharge, follow-up phone calls	Adherent: 95%-100% of prescribed doses taken	Adherent patients at 1 year: I: 85.0% C: 73.9% $P = NS$

(Continued)

■ **Table 2.** Person-Dependent Interventions (*Continued*)

Source (Site)	Participants, Duration	Intervention	Adherence Measures	Outcome(s)
Sadik et al, <sup>54</sup> 2005 (Al-Ain, United Arab Emirates)	221 CHF patients  12 months	Structured pharmacist counsel (in clinic or hospital); CHF and medication education, booklet; self-monitoring: 1-month card (told to bring to PCP)	"Patient self-report on missing dose or taking extra doses without medical advice"; no further definition	Number of compliant patients I: 85 C: 35 <i>P</i> <.05
Varma et al, <sup>55</sup> 1999 (Northern Ireland)	83 elderly CHF patients followed after hospital discharge  12 months	Pharmacist counseling on CHF medications, adherence, lifestyle; dose simplification; symptom monitoring	Adherence defined as 80%-120% of medications taken for all CHF drugs assessed; pharmacy records	Adherent patients: I: 76.9% C: 30% <i>P</i> = .039
<b>Nurse-Pharmacist Team</b>				
Edworthy et al, <sup>56</sup> 2007 (Calgary, Alberta, Canada)	2643 cardiac patients after hospitalization  19 months	In-hospital individual and group counseling on medications and medical conditions; videos, printed materials; developed long-term medication plans	Percentage of adherent patients (not further defined); self-report Data on medication use collected by: I: Nurses C: Nonmedical staff	Beta-blockers I: 89% C: 80% <i>P</i> <.01 Lipid-lowering agents I: 83% C: 78% <i>P</i> <.05
<p>A1C indicates glycosylated hemoglobin; ACE, angiotensin-converting enzyme; BP, blood pressure; C, control group; CABG, coronary artery bypass graft; CAD, coronary artery disease; CHF, congestive heart failure; CI, confidence interval; DM, diabetes mellitus; HTN, hypertension; I, intervention group; IQR, interquartile range; MEMS, medication electronic monitoring system; MPR, medication possession ratio (medication doses taken divided by doses prescribed); NS, not significant; OR, odds ratio; PCP, primary care practitioner; PTCA, percutaneous transluminal coronary angioplasty; RR, relative risk.</p> <p><sup>a</sup>Controls received usual care unless otherwise specified. Duration indicates time until last follow-up in which adherence was measured. The CI was 95% unless otherwise specified. Studies took place in United States unless otherwise indicated.</p> <p><sup>b</sup>The Morisky scale has 4 questions, with 1 point for every "yes" response. 1. Do you ever forget to take your medication? 2. Are you careless at times about taking your medication? 3. When you feel better, do you sometimes stop taking your medication? 4. Sometimes if you feel worse when you take your medication, do you stop taking it?</p>				

monthly pharmacist phone calls in conjunction with home blood pressure monitoring in a group of hypertensive patients who all received direct clinical services from a pharmacist, and found no significant improvement.

Three studies did not specify the identity of the caller. Antonicelli et al<sup>20</sup> described a home telemonitoring intervention managed by a specialized congestive heart failure team that included doctors and nurses, without specifying the actual caller. The study reported significant improvement in adherence (91% in the intervention group vs 46% in the control group, *P* <.03), but did not adequately define how adherence was measured. Sclar et al<sup>21</sup> used phone calls in which adherence was reinforced and monthly mailings delivered to patients with previously treated and newly diagnosed hypertension, and found statistically significant improvements in both intervention groups (previously treated, 82% adherence intervention vs 48% control; newly treated, 93% vs 52%; *P* <.05 for both). Guthrie<sup>22</sup> used phone reminders along with mailings to patients with elevated cholesterol and found no significant difference in self-reported pravastatin use.

**Person-Dependent Interventions:  
In-Person Meetings**

We identified 34 in-person interventions<sup>23-56</sup> (Table 2). These interventions included those conducted in the home,<sup>23-26</sup>

at work sites,<sup>27-29</sup> at pharmacies,<sup>30-35</sup> and at medical facilities.<sup>36-56</sup> Overall, in-person interventions were more likely (56%) than phone calls (38%) to result in significant improvement.

Morisky et al<sup>25</sup> examined the effect of a trained lay person (a health educator) visiting the home of a patient to provide education to both family members and the patient, and found a significant improvement in self-reported adherence scores. Saunders et al<sup>23</sup> also incorporated visits by trained lay persons. They sent reminder letters to patients with hypertension and used patient-recorded blood pressure and medication records, adding field worker home visits after 2 reminder letters went unanswered, but did not find significant improvement. Kirscht et al<sup>26</sup> applied a factorial design to multiple educational and behavioral strategies (Table 2) and found a significant improvement in adherence among patients who received nurse-administered home visits aimed at a support person as well as the patient (adherence 65% vs control 55%, *P* <.05). Johnson et al<sup>24</sup> examined monthly home visits with or without home blood pressure monitoring (the training of the home visitor was not identified) and found no significant improvement. Both effective in-home interventions incorporated family member involvement, in contrast to the 2 unsuccessful interventions.

The 3 work site interventions provided hypertension care by a nurse<sup>27,28</sup> or a physician<sup>29</sup>; improvement was shown only

**Table 3.** Modes of Delivery for Adherence Interventions and Associated Success Rates

Study Type	No. of Studies	No. (%) Showing Improved Adherence
<b>Person Independent: Mailed, Faxed, or Hand-Distributed Information</b>		
Paper	2	1 (50)
Video	1	0
Electronic system	6	4 (67) <sup>a</sup>
<b>All person-independent interventions</b>	<b>9</b>	<b>5 (56)</b>
<b>Person Dependent</b>		
Phone call by:		
Lay person	2	0
Nurse	1	0
Pharmacist	2	1 (50)
Caller not specified	3	2 (67)
All phone calls	8	3 (38)
In-person visit (by site)		
Home		
Lay person	3	1 (33)
Nurse	1	1 (100)
Work site		
Nurse	2	1 (50)
Doctor	1	0
Pharmacy		
Pharmacist	6	5 (83)
Clinic		
Lay person	2	1 (50) <sup>b</sup>
Nurse	2	1 (50)
Pharmacist	8	3 (38)
Doctor	3	2 (67)
Hospital		
Lay person	1	0
Nurse	1	1
Pharmacist	3	2 (67)
Nurse-pharmacist team	1	1 (100)
All in-person visits	34	19 (56)
<b>All person-dependent interventions</b>	<b>42</b>	<b>22 (52)</b>

<sup>a</sup>Friedman et al<sup>10</sup> showed nonsignificant improvement in unadjusted analyses and we classified this study as unsuccessful; however, after adjustment for age, sex, and baseline adherence, significant improvement was realized.  
<sup>b</sup>Ogedegbe et al<sup>96</sup> showed nonsignificant improvement in analysis of study completers, and we classified this study as unsuccessful; however, intent-to-treat analysis did predict significant improvement in intervention group adherence.

in the study in which a nurse acted with relative autonomy.<sup>27</sup> Logan et al<sup>27</sup> examined the effect of hypertension care administered to 457 patients by a specially trained nurse at the work site. All aspects of blood pressure management were handled directly by the nurse, and the intervention demonstrated improved adherence (68% vs 49% had at least 80% of medications consumed based on pill count).

We identified 6 interventions<sup>30-35</sup> that were conducted in pharmacies, all administered by pharmacists. All but 1 study in this group showed success at improving adherence. Although methods of measuring adherence differed between studies, the successful interventions improved adherence by 7% to 27% (Table 2). Interventions in this group were similar, involving an in-person meeting with a pharmacist in which patient-centered medication histories were obtained, medication knowledge was elicited and expanded upon, and disease and lifestyle teaching was conducted, sometimes with accompanying written information. All 6 studies lasted between 6 and 12 months.

Lee et al<sup>30</sup> made use of blister packaging in addition to clinical pharmacist meetings and medication education for 159 patients with hypertension, hyperlipidemia, and other diseases, and found 96% adherence at 6 months in intervention patients compared with 69% in controls ( $P < .001$ ). Murray et al<sup>31</sup> found an adherence improvement of 11% (95% CI = 5%, 17%) among 314 patients with hypertension over 12 months, but noted that the difference declined to a nonsignificant level after the intervention was discontinued. Blenkinsopp et al<sup>32</sup> followed 282 patients with hypertension recruited by community pharmacists over 6 months (63% adherence in intervention group vs 50% in control group,  $P < .05$ ). Bouvy et al<sup>35</sup> followed 152 patients with congestive heart failure, defining nonadherence as fewer than 80% of days without opening the electronic pill bottle, and found all patients in the intervention group took pills more than 80% of days, whereas 86% in the control group reached that threshold (relative risk = 0.5, 95% CI = 0.4, 0.6). Vrijens et al<sup>33</sup> followed 392 patients with hyperlipidemia and found that intervention patients had higher adherence at follow-up (96% vs 89%,  $P < .001$ ). The study of patients with coronary artery disease<sup>34</sup> used a self-reported score to measure adherence (making comparison with other studies difficult) and reported very high baseline and follow-up adherence scores. For this reason, the nonsignificant findings in this study may not be representative of the group of pharmacist interventions.

We identified 15 in-person studies<sup>36-50</sup> that were conducted in a clinic setting. Among in-person clinic interventions conducted by a lay person or nurse,<sup>36-39</sup> 50% of studies showed significant improvement over the control group (Table 2). Whereas in-person pharmacist interventions showed high success rates when

conducted in a pharmacy, in-person pharmacist interventions in clinics<sup>40-47</sup> showed the lowest rate of success among clinic interventions (38% compared with 50% to 67% for other in-clinic interventions). All 3 successful clinic interventions<sup>41,46,47</sup> were carried out at clinics that also had medication-dispensing capabilities. The 5 unsuccessful clinic interventions<sup>40,42-45</sup> were carried out at primary care offices and neighborhood clinics that did not dispense medications.

Three in-person clinic interventions were carried out by physicians.<sup>48-50</sup> Although 2 of these studies were successful,<sup>49,50</sup> neither used a rigorous method of assessing adherence. Yilmaz et al<sup>49</sup> studied the impact of verbal advice on statin benefits from an “expert physician.” At the end of the study there was an increased likelihood of being on continuous statin therapy (63% intervention vs 46% control), but the authors did not define the outcome or the data source. Avanzini et al<sup>50</sup> studied 1771 patients with hypertension, randomized to care by (1) doctors who had the opportunity to educate themselves extensively on hypertension and then designed and implemented hypertension management guidelines or (2) doctors without this experience. At follow-up, 4% of intervention vs 10% of control patients “admitted poor compliance,” but the authors give no further information on how this outcome was calculated. Birtwhistle et al<sup>48</sup> randomized patients with hypertension to every-3-month versus every-6-month physician follow-up and found no significant difference in adherence. In-person interventions for patients at the point of hospital discharge<sup>51-56</sup> (67% successful) showed lower success rates than interventions carried out in a pharmacy (83%) but higher success rates than those carried out in a clinic setting (47%). However, although 4 out of 6 studies showed significant improvement in adherence,<sup>52,54-56</sup> 2 of the successful studies had unclear definitions of adherence.

Of the 6 studies, 4 recruited in-hospital patients exclusively and followed them after discharge. Two studies recruited patients from both in-hospital sites and outpatient clinics.

Tsuyuki et al<sup>51</sup> found a nonsignificant effect of educational meetings with a research assistant prior to hospital discharge, accompanied by adherence aids, and phone and mail follow-up. Krantz et al<sup>52</sup> found a significantly higher rate of beta-blocker utilization (96% intervention vs 48% control) after predischarge nurse counseling and outpatient nurse follow-up, but the term “utilization” was not clearly defined. Significant improvement was shown by 2 of the 3 pharmacist interventions,<sup>54,55</sup> although Sadik et al,<sup>54</sup> who evaluated pharmacist education for congestive heart failure, did not clearly define the way self-reported adherence was calculated. The study by Varma et al,<sup>55</sup> a successful pharmacist intervention that defined adherence as 80% to 120% of all congestive heart failure drugs taken at 12 months, found a significant effect (77% intervention vs 30% control). Edworthy et al<sup>56</sup> followed 2643 cardiac patients after hospitalization, giv-

ing in-hospital counsel on medications and medical conditions by nurses and pharmacists along with video, printed material, and phone follow-up by both a nurse and a pharmacist. Significant improvement in adherence was seen for both beta-blockers (intervention 89% vs control 80%,  $P < .01$ ) and lipid-lowering agents (intervention 83% vs control 78%,  $P < .05$ ).

## DISCUSSION

Our review of interventions to improve adherence to cardiovascular and diabetes medications yielded a highly diverse group of interventions. Several themes arose regarding the effectiveness of different approaches that may inform future intervention development.

Among person-independent interventions, those that used electronic interventions showed promise. Effective electronic interventions included those that were designed to be individualized using either computer-generated algorithms or hierarchically structured messages, and 1 study effectively combined hierarchical phone messages and targeted phone follow-up by a nurse. Home automatic blood pressure monitoring and programmable pill caps with reminder cues also demonstrated promising results. Adherence interventions delivered via paper or video showed minimal effectiveness unless targeted at a group (in this case, hospitalized patients after myocardial infarction) that was especially likely to be sensitive to the message.

Among person-dependent interventions, the results of phone call interventions were not encouraging. Only a minority were effective. These interventions targeted groups at a time in their lives when they should have been particularly sensitive to the message (eg, immediately after bypass surgery, percutaneous intervention, or hospitalization for congestive heart failure, or after a new diagnosis of hypertension).

In-person interventions yielded some interesting patterns. Home visits, an expensive intervention, were only effective in half the studies identified; both of the effective studies sought to target a family member as a support person, whereas neither of the ineffective studies did so. The data on worksite interventions were limited, and no recent studies were identified. Interventions carried out in the pharmacy (all by pharmacists) were almost uniformly effective and were a fairly homogenous group in both the nature of the services rendered and in duration of follow-up. Interestingly, when we looked at the group of interventions carried out in the clinic by pharmacists, only 3 out of 8 were effective. All 3 of these were carried out in clinics that also had dispensing abilities and therefore may have been more similar to the group of in-person pharmacy interventions. Interventions that targeted patients at the point of hospital discharge were more effective than those that focused on clinic patients, although the lower number of in-person hospital studies should be noted (6 com-

pared with 15 clinic studies).

Person-dependent administration of an adherence intervention can be costly, whether carried out by a lay person, nurse, pharmacist, or physician. We found the success rate of person-dependent interventions comparable to or lower than that of person-independent interventions. We interpret this result cautiously, given the presence of fewer person-independent interventions overall.

The wide heterogeneity of the adherence intervention studies that we identified should prompt us to interpret all comparisons with caution. We included studies with differing populations (patients from different countries and with different cardiovascular diseases; nonadherent vs all patients; hospitalized vs outpatient patients), and we encountered a wide variety of study designs, including some with idiosyncracies that limited their generalizability. In addition, although a detailed discussion of comparative adherence measurement methods is outside the scope of this study, we found inconsistencies in methods of adherence measurement across the studies reviewed, demonstrated most clearly in our tables. Direct comparison of the magnitude of the intervention effects is complicated by this heterogeneity. Although we were able to consider some aspects of healthcare setting in our analysis, stratification by healthcare facility size was not possible because of inconsistencies in reporting. Finally, although more than 40% of the identified studies reported no significant improvement, publication bias also may be playing a role in our findings.

We suggest that future research focus on (1) the life events causing increased patient receptiveness to the adherence message (ie, hospital stays, particularly after a serious cardiac event); (2) the psychological factors present during an acute illness and hospital stay as they relate to a patient's willingness to modify adherence behavior; (3) in-person pharmacist counsel delivered at the site of medication dispensing (so that arriving for an appointment to discuss adherence can be combined with retrieving the medication); and (4) new and innovative ways to take advantage of electronic technologies.

We saw few interventions that capitalized on lay-person social networks, either electronic or in person. Research on adherence to other medically recommended behaviors including cancer screening has indicated that this may be a promising direction,<sup>57</sup> and the same may be true for medication adherence interventions.

In conclusion, among interventions to improve adherence to cardiovascular medications, electronic interventions, in-person pharmacist interventions held at a site of medication dispensing, and in-person interventions targeted to patients at the point of hospital discharge showed the highest rates of success. Future studies should explore new electronic approaches and in-person interventions at the site of medication distribution. A focus on

identifying times of increased patient receptivity to the adherence message also will be important.

**Author Affiliations:** From the Division of Pharmacoepidemiology and Pharmacoeconomics (SLC, NKC, MAF, AS, WHS), Brigham and Women's Hospital, Boston, MA; Tri County Medical Associates Hospitalist Group (SLC) Milford Regional Medical Center, Milford, MA; Division of Strategic Research (JNL, TAB), CVS Caremark, Hunt Valley, MD; and Center for American Political Studies (WHS), Harvard University, Boston, MA.

**Funding Source:** This work was supported by a research grant from CVS Caremark. Dr Shrank is supported by a career development award from the National Heart, Lung and Blood Institute (HL-090505).

**Author Disclosures:** Drs Liberman and Brennan are employees of CVS Caremark, the funder of the study. Dr Brennan also reports holding options and stock in the company. Dr Choudhry reports receiving multiple grants to conduct studies on patterns and predictors of medication adherence. Dr Fischer reports a potential study of adherence with Surescripts. Dr Shrank reports receiving grants from CVS Caremark. The other authors (SLC, AS) report no relationship or financial interest with any entity that would pose a conflict of interest with the subject matter of this article.

**Authorship Information:** Concept and design (SLC, NKC, MAF, AS, TAB, WHS); acquisition of data (SLC, AS, TAB, WHS); analysis and interpretation of data (SLC, NKC, MAF, AS, JNL, WHS); drafting of the manuscript (SLC, TAB, WHS); critical revision of the manuscript for important intellectual content (SLC, NKC, MAF, AS, JNL, WHS); statistical analysis (WHS); obtaining funding (JNL, WHS); and administrative, technical, or logistic support (AS, WHS).

**Address correspondence to:** Sarah L. Cutrona, MD, Milford Regional Medical Center, TCMA Hospitalists, 14 Prospect St, Milford, MA 01757. E-mail: slcutrona@gmail.com.

## REFERENCES

1. Ho PM, Spertus JA, Masoudi FA, et al. Impact of medication therapy discontinuation on mortality after myocardial infarction. *Arch Intern Med.* 2006;166(17):1842-1847.
2. Ho PM, Rumsfeld JS, Masoudi FA, et al. Effect of medication nonadherence on hospitalization and mortality among patients with diabetes mellitus. *Arch Intern Med.* 2006;166(17):1836-1841.
3. Rasmussen JN, Chong A, Alter DA. Relationship between adherence to evidence-based pharmacotherapy and long-term mortality after acute myocardial infarction. *JAMA.* 2007;297(2):177-186.
4. Kripalani S, Yao X, Haynes RB. Interventions to enhance medication adherence in chronic medical conditions: a systematic review. *Arch Intern Med.* 2007;167(6):540-550.
5. Haynes RB, Ackloo E, Sahota N, McDonald HP, Yao X. Interventions for enhancing medication adherence. *Cochrane Database Syst Rev.* 2008;(2):CD000011.
6. Smith DH, Kramer JM, Perrin N, et al. A randomized trial of direct-to-patient communication to enhance adherence to beta-blocker therapy following myocardial infarction. *Arch Intern Med.* 2008;168(5):477-483.
7. Takala J. Screening, treatment and adherence to treatment for hypertension. *Scand J Prim Health Care.* 1983;1(3-4):114-119.
8. Powell KM, Edgren B. Failure of educational videotapes to improve medication compliance in a health maintenance organization. *Am J Health Syst Pharm.* 1995;52(20):2196-2199.
9. Emmett CL, Montgomery AA, Peters TJ, Fahey T. Three-year follow-up of a factorial randomised controlled trial of two decision aids for newly diagnosed hypertensive patients. *Br J Gen Pract.* 2005;55(516):551-553.
10. Friedman RH, Kazis LE, Jette A, et al. A telecommunications system for monitoring and counseling patients with hypertension—impact on medication adherence and blood pressure control. *Am J Hypertens.* 1996;9(4 pt 1):285-292.
11. Johnson SS, Driskell MM, Johnson JL, et al. Transtheoretical model intervention for adherence to lipid-lowering drugs. *Dis Manag.* 2006;9(2):102-114.
12. Marquez-Contreras E, Martell-Claros N, Gil-Guillen V, et al; Compliance Group of the Spanish Society of Hypertension (SEE). Efficacy of a home blood pressure monitoring programme on therapeutic compliance in hypertension: the EAPACUM-HTA study. *J Hypertens.* 2006;24(1):169-175.

13. **Piette JD, Weinberger M, McPhee SJ, Mah CA, Kraemer FB, Crapo LM.** Do automated calls with nurse follow-up improve self-care and glycemic control among vulnerable patients with diabetes? *Am J Med.* 2000;108(1):20-27.
14. **Rosen MI, Rigsby MO, Salah JT, Ryan CE, Cramer JA.** Electronic monitoring and counseling to improve medication adherence. *Behav Res Ther.* 2004;42(4):409-422.
15. **Stewart A, Noakes T, Eales C, Shepard K, Becker P, Veriawa Y.** Adherence to cardiovascular risk factor modification in patients with hypertension. *Cardiovasc J S Afr.* 2005;16(2):102-107.
16. **Schectman G, Hiatt J, Hartz A.** Telephone contacts do not improve adherence to niacin or bile-acid sequestrant therapy. *Ann Pharmacother.* 1994;28(1):29-35.
17. **Hamet P, Campbell N, Curnew G, Eastwood C, Pradhan A.** AVAPROMISE: a randomized clinical trial for increasing adherence through behavioural modification in essential hypertension. *Exp Clin Cardiol.* 2002;7(4):165-72.
18. **Faulkner MA, Wadibia EC, Lucas BD, Hilleman DE.** Impact of pharmacy counseling on compliance and effectiveness of combination lipid-lowering therapy in patients undergoing coronary artery revascularization: a randomized, controlled trial. *Pharmacotherapy.* 2000;20(4):410-416.
19. **Mehos BM, Saseen JJ, MacLaughlin EJ.** Effect of pharmacist intervention and initiation of home blood pressure monitoring in patients with uncontrolled hypertension. *Pharmacotherapy.* 2000;20(11):1384-1389.
20. **Antonicelli R, Testamata P, Spazzafumo L, et al.** Impact of telemonitoring at home on the management of elderly patients with congestive heart failure. *J Telemed Telecare.* 2008;14(6):300-305.
21. **Sciar DA, Chin A, Skaer TL, Okamoto MP, Nakahiro RK, Gill MA.** Effect of health-education in promoting prescription refill compliance among patients with hypertension. *Clin Ther.* 1991;13(4):489-495.
22. **Guthrie RM.** The effects of postal and telephone reminders on compliance with pravastatin therapy in a national registry: results of the first myocardial infarction risk reduction program. *Clin Ther.* 2001;23(6):970-980.
23. **Saunders LD, Irwig LM, Gear JS, Ramushu DL.** A randomized controlled trial of compliance improving strategies in Soweto hypertensives. *Med Care.* 1991;29(7):669-678.
24. **Johnson AL, Taylor DW, Sackett DL, Dunnett CW, Shimizu AG.** Self-recording of blood pressure in the management of hypertension. *Can Med Assoc J.* 1978;119(9):1034-1039.
25. **Morisky DE, DeMuth NM, Field-Fass M, et al.** Evaluation of family health education to build social support for long-term control of high blood pressure. *Health Educ Q.* 1985;12(1):35-50.
26. **Kirscht JP, Kirscht JL, Rosenstock IM.** A test of interventions to increase adherence to hypertensive medical regimens. *Health Educ Q.* 1981;8(3):261-272.
27. **Logan AG, Milne BJ, Achber C, Campbell WP, Haynes RB.** Work-site treatment of hypertension by specially trained nurses. A controlled trial. *Lancet.* 1979;2(8153):1175-1178.
28. **Logan AG, Milne BJ, Flanagan PT, Haynes RB.** Clinical effectiveness and cost-effectiveness of monitoring blood-pressure of hypertensive employees at work. *Hypertension.* 1983;5(6):828-836.
29. **Sackett DL, Gibson ES, Taylor DW, et al.** Randomised clinical trial of strategies for improving medication compliance in primary hypertension. *Lancet.* 1975;1(7918):1205-1207.
30. **Lee JK, Grace KA, Taylor AJ.** Effect of a pharmacy care program on medication adherence and persistence, blood pressure, and low-density lipoprotein cholesterol: a randomized controlled trial. *JAMA.* 2006;296(21):2563-2571.
31. **Murray MD, Young J, Hoke S, et al.** Pharmacist intervention to improve medication adherence in heart failure: a randomized trial. *Ann Intern Med.* 2007;146(10):714-725.
32. **Blenkinsopp A, Phelan M, Bourne J, et al.** Extended adherence support by community pharmacists for patients with hypertension: a randomised controlled trial. *Int J Pharm Pract.* 2000;8(3):165-175.
33. **Vrijens B, Belmans A, Matthys K, de Klerk E, Lesaffre E.** Effect of intervention through a pharmaceutical care program on patient adherence with prescribed once-daily atorvastatin. *Pharmacoepidemiol Drug Saf.* 2006;15(2):115-121.
34. **Community Pharmacy Medicines Management Project Evaluation Team.** The MEDMAN study: a randomized controlled trial of community pharmacy-led medicines management for patients with coronary heart disease. *Fam Pract.* 2007;24(2):189-200.
35. **Bouvy ML, Heerdink ER, Urquhart J, Grobbee DE, Hoes AW, Leufkens HG.** Effect of a pharmacist-led intervention on diuretic compliance in heart failure patients: a randomized controlled study. *J Card Fail.* 2003;9(5):404-411.
36. **Ogedegbe G, Chaplin W, Schoenthaler A, et al.** A practice-based trial of motivational interviewing and adherence in hypertensive African Americans. *Am J Hypertens.* 2008;21(10):1137-1143.
37. **Haynes RB, Sackett DL, Gibson ES, et al.** Improvement of medication compliance in uncontrolled hypertension. *Lancet.* 1976;1(7972):1265-1268.
38. **Schroeder K, Fahey T, Hollinghurst S, Peters TJ.** Nurse-led adherence support in hypertension: a randomized controlled trial. *Fam Pract.* 2005;22(2):144-151.
39. **Rudd P, Miller NH, Kaufman J, et al.** Nurse management for hypertension. A systems approach. *Am J Hypertens.* 2004;17(10):921-927.
40. **Vivian EM.** Improving blood pressure control in a pharmacist-managed hypertension clinic. *Pharmacotherapy.* 2002;22(12):1533-1540.
41. **Phumipamorn S, Pongwecharak J, Soorapan S, Pattharachayakul S.** Effects of the pharmacist's input on glycaemic control and cardiovascular risks in Muslim diabetes. *Prim Care Diabetes.* 2008;2(1):31-37.
42. **Hunt JS, Siemenczuk J, Pape G, et al.** A randomized controlled trial of team-based care: impact of physician-pharmacist collaboration on uncontrolled hypertension. *J Gen Intern Med.* 2008;23(12):1966-1972.
43. **Taylor CT, Byrd DC, Krueger K.** Improving primary care in rural Alabama with a pharmacy initiative. *Am J Health Syst Pharm.* 2003;60(11):1123-1129.
44. **Hawkins DW, Fiedler FP, Douglas HL, Eschbach RC.** Evaluation of a clinical pharmacist in caring for hypertensive and diabetic patients. *Am J Hosp Pharm.* 1979;36(10):1321-1325.
45. **Odegard PS, Goo A, Hummel J, Williams KL, Gray SL.** Caring for poorly controlled diabetes mellitus: a randomized pharmacist intervention. *Ann Pharmacother.* 2005;39(3):433-440.
46. **Sookaneknun P, Richards RM, Sanguansersri J, Teerasut C.** Pharmacist involvement in primary care improves hypertensive patient clinical outcomes. *Ann Pharmacother.* 2004;38(12):2023-2028.
47. **Solomon DK, Portner TS, Bass GE, et al.** Clinical and economic outcomes in the hypertension and COPD arms of a multicenter outcomes study. *J Am Pharm Assoc (Wash).* 1998;38(5):574-585.
48. **Birtwhistle RV, Godwin MS, Delva MD, et al.** Randomised equivalence trial comparing three and six months of follow up of patients with hypertension by family practitioners. *BMJ.* 2004;328(7433):204.
49. **Yilmaz MB, Pinar M, Naharci I, et al.** Being well-informed about statin is associated with continuous adherence and reaching targets. *Cardiovasc Drugs Ther.* 2005;19(6):437-440.
50. **Avanzini F, Corsetti A, Maglione T, et al; Studio per una Terapia Antipertensiva Razionale Investigators (Study on Rational Antihypertensive Therapy, STAR).** Simple, shared guidelines raise the quality of antihypertensive treatment in routine care. *Am Heart J.* 2002;144(4):726-732.
51. **Tsuyuki RT, Fradette M, Johnson JA, et al.** A multicenter disease management program for hospitalized patients with heart failure. *J Card Fail.* 2004;10(6):473-480.
52. **Krantz MJ, Havranek EP, Haynes DK, Smith I, Bucher-Bartelson B, Long CS.** Inpatient initiation of beta-blockade plus nurse management in vulnerable heart failure patients: a randomized study. *J Card Fail.* 2008;14(4):303-309.
53. **Lopez Cabezas C, Falces Salvador C, Cubi Quadrada D, et al.** Randomised clinical trial of a postdischarge pharmaceutical care program vs regular follow-up in patients with heart failure [in English, Spanish]. *Fam Hosp.* 2006;30(6):328-342.
54. **Sadik A, Yousif M, McElnay JC.** Pharmaceutical care of patients with heart failure. *Br J Clin Pharmacol.* 2005;60(2):183-193.
55. **Varma S, McElnay JC, Hughes CM, Passmore AP, Varma M.** Pharmaceutical care of patients with congestive heart failure: interventions and outcomes. *Pharmacotherapy.* 1999;19(7):860-869.
56. **Edworthy SM, Baptie B, Galvin D, et al.** Effects of an enhanced secondary prevention program for patients with heart disease: a prospective randomized trial. *Can J Cardiol.* 2007;23(13):1066-1072.
57. **Curbow B, Bowie J, Garza MA, et al.** Community-based cancer screening programs in older populations: making progress but can we do better? *Prev Med.* 2004;38(6):676-693. ■