The Effectiveness of Medication Adherence Interventions among Patients with Coronary Artery Disease: A Meta-analysis

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Abstract

Background—Despite the known benefits of medication therapy for secondary prevention of coronary artery disease (CAD), many patients do not adhere to prescribed medication regimens. Medication nonadherence is associated with poor health outcomes and higher health care cost.

Objective—The purpose of this meta-analysis was to determine the overall effectiveness of interventions designed to improve medication adherence (MA) among adults with CAD. Additionally, sample, study design, and intervention characteristics were explored as potential moderators to intervention effectiveness.

Methods—Comprehensive search strategies facilitated identification of two-group, treatment versus control design studies testing MA interventions among patients with CAD. Data were independently extracted by two trained research specialists. Standardized mean difference effect sizes were calculated for eligible primary studies, adjusted for bias, then synthesized under a random effects model. Homogeneity of variance was explored using a conventional heterogeneity statistic. Exploratory moderator analyses were conducted using meta-analytic analogues for ANOVA and regression for dichotomous and continuous moderators, respectively.

Results—Twenty-four primary studies were included in this meta-analysis. The overall effect size of MA interventions, calculated from 18,839 participants, was 0.229 ($p<.001$). The most effective interventions utilized nurses as interventionists, initiated interventions in the inpatient setting, and informed providers of patients' medication adherence behaviors. MA interventions tested among older patients were more effective than those among younger patients. Interventions were equally effective regardless of number of intervention sessions, targeting MA behavior alone or with other behaviors, and the use of written instructions only.

Conclusions—Interventions to increase medication adherence among patients with CAD were modestly effective. Nurses can be instrumental in improving MA among these patients. Future

research is needed to investigate nurse-delivered MA interventions across varied clinical settings. Additionally, more research testing MA interventions among younger populations and more racially diverse groups is needed.

Keywords

medication adherence; patient compliance; coronary artery disease; meta-analysis

Introduction

Heart disease is the leading cause of death among adults in the United States.[1,2] Coronary artery disease (CAD), the most common form of heart disease, is responsible for 385,000 deaths and $108.9 billion in health care expenditures annually.[1,2] Secondary prevention for CAD is a multi-intervention approach involving therapeutic lifestyle changes and evidence-based medical therapies, such as prescribed medications. Between 1980 and 2000, these therapies have contributed to a 50% reduction in CAD-related deaths.[3] Research suggests the greatest contributor to this reduction is medications for secondary prevention of CAD.[3]

Unfortunately, medication nonadherence is highly prevalent.[4] Approximately one-third of patients who have had a myocardial infarction do not adhere to prescribed medication regimens.[5] Nonadherence is associated with increased risk of all-cause and cardiovascular mortality, revascularization procedures, hospitalization, and higher health care cost.[6–8] Effective interventions to improve medication adherence (MA) in this population are critically needed.

Efficacy of MA interventions varies.[9–14] Few systematic reviews have focused on MA interventions among CAD patients.[15–18] Prior reviews have been limited by narrow search strategies, unclear inclusion criteria, lack of a quantitative synthesis, or absent exploration of potential moderating variables.[16] To date, no current meta-analyses exist addressing MA intervention effectiveness among patients with CAD. Thus the overall effectiveness of MA interventions in this population is unclear; furthermore, the most effective types of interventions are yet unknown.

A meta-analysis and moderator analysis of MA interventions among CAD patients could promote efficiency in developing future interventions and provide clinicians with guidance to promote MA in clinical practice. The purpose of this systematic review and meta-analysis was to describe and quantify the overall effectiveness of the body of MA intervention research among CAD patients, and to explore potential moderators of intervention effectiveness. Additionally, we identified limitations in the extant research and suggested areas for future study.

The following research questions guided this study:

1. What is the overall effectiveness of MA interventions on MA outcomes among patients with CAD?

2. Does intervention effectiveness vary based on intervention, sample, or design characteristics?

Methods

This systematic review and meta-analysis was performed using standard meta-analysis techniques and PRISMA guidelines.[19, 20] This project was part of a larger parent study examining MA outcomes of MA interventions across multiple chronic and acute illnesses.

Search Strategies

We consulted an expert health sciences reference librarian to ensure comprehensive search strategies.[21] Databases searched included: MEDLINE, PubMED, PsychINFO, CINAHL, EBSCO, PQDT, Cochrane Central Trials Register, Cochrane Database of Systematic Reviews, IndMed, ERIC, International Pharmaceutical Abstracts, EBM Reviews - Database of Abstracts of Reviews of Effects, and Communication and Mass Media. Broad MeSH terms were used including: *patient compliance, medication adherence, drugs, prescription drugs, pharmaceutical preparations, generic, dosage, compliant, compliance, adherent, adherence, noncompliant, noncompliance, nonadherent, nonadherence, medication(s), regimen(s), prescription(s), prescribed, drug(s), pill(s), tablet(s), agent(s), improve, promote, enhance, encourage, foster, advocate, influence, incentive, ensure, remind, optimize, increase, impact, prevent, address, decrease.* Fifty-seven relevant journals were hand searched, and author searches and ancestry searches of prior reviews' bibliographies were conducted to identify additional potentially eligible studies.

Inclusion Criteria

We included 2-group, treatment versus control comparison studies testing interventions to increase MA in patients ≥ 18 years old with a diagnosis of CAD, defined by the primary studies. MA interventions are deliberate actions performed or directed by investigators to increase adherence to specified medication regimens. Examples include education, reminders, and special packaging. Studies with varied types of MA measurement (e.g., electronic monitoring devices, pharmacy refills, self-report) were included given the diversity of MA measures in this research area. Eligible studies needed to contain enough data to calculate an effect size (ES). The research team attempted to contact corresponding authors to obtain missing outcome data.

Data Extraction

To extract relevant data from primary studies, a coding strategy was developed from prior research and expert consultations. The codebook was developed through an iterative process and pilot tested. Data extracted included the primary study source, publication date, dissemination type (e.g., journal article, dissertation), presence of funding, participant demographics (e.g., age, gender, ethnicity, comorbidities), research methods, intervention details, and MA outcomes. Multiple descriptors of primary study research methods were coded, such as sample size, randomization, and intention-to-treat analyses. Method of MA measurement and follow-up interval were recorded. Varied intervention characteristics were coded, including content (e.g., problem solving, self-monitoring, goal setting), delivery (e.g., face-to-face, telephone), dose (e.g., length/number of sessions), and setting (e.g., clinic, home).

Included studies were independently coded by two extensively trained research specialists, then compared and discussed until consensus was reached. A doctorally-prepared senior research specialist supervised the coding process to ensure coding integrity, and reviewed all ES data. Questionable items were resolved in team meetings with the study principal investigator.

Data Analysis

All data were analyzed using Comprehensive Meta-Analysis Software.[22] Standardized mean difference effect sizes (*d*, ES) were calculated for each 2-group treatment versus control posttest comparison. The standardized mean difference ES between groups was calculated by dividing the difference between treatment and control group post-intervention means by the pooled standard deviation. Additional ES analyses were conducted within groups by subtracting the outcome scores from the baseline scores and dividing by the baseline standard deviation. ESs were weighted by the inverse of variance to account for sample size and adjust for bias, then synthesized using a random-effects model.[23] A random-effects model was chosen *a priori* given the expected within- and between-study variance across primary studies. Data were examined for possible outliers based on standardized residuals of each primary study's ES. Publication bias was examined by assessing the symmetry of a funnel plot constructed by plotting each primary study's standard error against its ES.[23]

Homogeneity of variance was tested using a conventional heterogeneity statistic (Q), to quantify observed heterogeneity across studies, and I^2, to determine the proportion of observed heterogeneity due to true differences in effects across studies.[23] Exploratory moderator analyses were used to examine possible associations between study characteristics and intervention effectiveness. Dichotomous variables were evaluated using subgroup analysis, and continuous variables were evaluated using meta-regression.[23]

Results

Twenty-four primary reports were eligible for analysis.[9–14,24–41] Additional coding information was found in 4 companion reports about the same primary studies.[42–45] Three primary study reports contained multiple comparison groups.[33,36,37] There were 28 treatment versus control group posttest comparisons, 9 treatment group pretest-posttest comparisons, and 6 control group pretest-posttest comparisons. Few smaller studies with negative findings were included, indicating evidence of publication bias.

Primary Study Characteristics

The primary studies included in this meta-analysis included 24 journal articles, 3 dissertations, and 1 presentation. Six studies were disseminated prior to 2000. Seventeen studies were supported by funding.

Primary study characteristics are presented in Table 1. Samples were majority male. The median of the mean age for participants was 62.9 years. Only 7 studies reported data on ethnicity. Of those, most subjects were Caucasian. Some studies reported additional chronic diseases among their subjects including: hypertension (*k*=17), undifferentiated diabetes (*k*=16), hyperlipidemia (*k*=12), heart failure (*k*=4), stroke (*k*=3), lung disease (*k*=3), renal

disease (k=2), osteoarthritis (k=1), asthma (k=1), atrial fibrillation (k=1), nephritic syndrome (k=1), thyroid disorder (k=1), and cerebral vascular disease (k=1).

Primary studies reported diverse methods. The median number of intervention sessions was two (k=17). The median number of days for MA intervention duration was 35 (k=23). Only one study reported intervention session duration. MA outcome data were collected a median of 124.5 days post-intervention (k=14). Studies reported diverse methods of collecting MA outcomes including pharmacy refill (k=7), self-report (k=18), biological measures (k=2), and pill counts (k=1).

Overall Effects of MA Interventions of MA Outcomes

Overall MA ESs are presented in Table 2. ESs were calculated for 28 treatment vs. control group comparisons containing 18,839 subjects. The overall ES for these comparisons was 0.229 (p<.001), indicating significant improvements in MA outcomes in the treatment over the control group (Figure 1). When the 3 largest sample studies were excluded, the ES for these comparisons demonstrated minimal change (d=0.269, p<.001). ESs were significantly heterogeneous.

We also calculated overall ESs for the 9 treatment group pre- vs. post-test comparisons and the 6 for control group pre- vs. post-test comparisons. While the former ES was positive (0.183) and the latter negative (-0.014), neither were statistically significant. Lack of statistical significance may reflect low power from the small number of comparisons.

Moderator Analyses

Continuous and dichotomous moderator analyses are displayed in Tables 3 and 4, respectively. Although all studies from the main analysis were examined for moderating variables, only those moderators reported for a sufficient number of comparisons were included in the analyses.

Intervention Moderators—Studies in which health care providers were given information about subjects' MA revealed a significantly greater ES (0.387) than when the providers were not given information on MA (0.151). An example of this type of intervention component could involve using a questionnaire on participants' baseline MA and barriers to MA.[24] Studies with nurse interventionists (0.428) reported significantly higher MA than studies without nurse interventionists (0.127). Studies with and without physician and pharmacist interventionists had similar ESs. Interventions started when participants were inpatients had significantly larger effects (0.590) than interventions that did not start with inpatients (0.141); however, there was little difference when the intervention was delivered at home versus in the clinic. With regards to the mode of intervention delivery, we saw no significant differences among telephone, written materials only, or face-to-face delivery. Interventions using mail delivery were less effective (0.060) than interventions without mail delivery interventions(0.292). There were several nonsignificant variables, including: utilization of theory, number of sessions, duration of intervention, time point for measuring outcome MA, goal setting, interventions delivered at home, interventions delivered in clinic, problem solving, succinct written instructions, any

written instructions, behavior target (MA or multiple behaviors), physician or pharmacist interventionists, telephone and face-to-face delivery, and written instructions only.

Report and Sample Moderators—Age of subjects had a significant positive slope (0.014), revealing that MA interventions led to greater adherence improvement in samples of older patients. Interventions were equally effective regardless of publication status, funding, and location. Other nonsignificant moderators included year of publication, percentage of women and underrepresented groups, and socioeconomic status (SES).

Design and Methods Moderators—Although sample size had a statistically significant negative slope, this finding is not clinically substantive. Other potential moderators related to design, such as blinding, allocation concealment, random assignment, and intention-to-treat analyses were not associated with MA effectiveness.

Discussion

Findings from this meta-analysis, the first of its kind, suggest interventions to increase MA among participants with CAD were significantly effective. These positive findings are similar to prior meta-analyses examining MA outcomes from MA interventions among underrepresented groups and from packaging intervention effects.[46,47] Although poor MA has been linked to negative health outcomes in patients with CAD,[4,6,7] consensus on the how much MA is needed to improve varied CAD-related outcomes is not yet clear. Prior research exists exploring MA and blood pressure outcomes[48, 49] and cardiovascular disease risk.[49] However, further research is needed to quantify the amount of MA needed to mitigate additional CAD-related outcomes. Moreover, the dose of MA intervention needed to change MA behavior among patients with CAD is yet to be determined. Due to the small number of comparisons employing similar measures of MA, we were unable to convert the ES to a clinical metric of adherence. Future MA intervention research among CAD patients should include explicit information regarding intervention dose.

Moderator findings

We found several interesting moderators. Interventions in which health care providers were given information regarding participants' MA were more effective than interventions without this component. Awareness of patients' MA behavior can motivate and guide providers to address issues related to MA. Clinicians working with patients with CAD should assess issues with or barriers to MA to identify the possible need to intervene. Future research might directly compare an intervention that provides patient MA status to health care providers to a similar intervention without this provision.

MA interventions delivered by nurses were especially effective. Nurses have considerable access to patients with CAD in outpatient settings, such as cardiac rehabilitation and clinics. Additionally, nurses working in the inpatient setting spend approximately 25%-37% of their time providing direct patient care and 11%-21% of their time in medication-related tasks.[50,51] In addition to substantial access to this patient population, nurses also have clinical skills to promote MA. For example, nurses have delivered efficacious MA interventions through counseling, [52] follow up communication, [27, 53, 54] and case

management.[55, 56] Nurses should play an active role in developing and implementing MA interventions among patients with CAD. Research exploring nursing interventions to increase MA among CAD patients could focus on testing or comparing specific intervention strategies such as education, counseling, and managing barriers. Specific nurse type and training were not clearly reported among studies, hindering the comparison of MA intervention effectiveness across different types of nurses. Future studies should explicitly identify types of nurses delivering MA interventions among patients with CAD.

MA interventions initiated in the inpatient setting were more effective. The inpatient setting may provide an opportunity for clinicians to inform patients and families about the importance of medications for secondary prevention of CAD, as well as strategies for MA. Moreover, the dire nature of hospitalization may influence patient and family receptivity to MA interventions. Most MA interventions initiated in the inpatient setting included follow up intervention content post-discharge. Continued reinforcement of MA post-discharge may positively affect MA outcomes. For those patients who may start medications outside of the hospital, interventions delivered at home or in the clinic were equally effective. Future research might directly compare MA interventions initiated in the inpatient setting to MA interventions initiated post hospitalization.

Regarding sample characteristics, only age appeared to impact intervention effectiveness. As the age of the sample increased, so did the intervention effectiveness. These findings support prior research related to statin MA and LDL goal attainment.[57,58] Chi and colleagues[57] postulated that older individuals are more likely to have multiple comorbidities and may be more attentive to prescribed medication regimens. Additional primary research is needed to identify effective MA interventions among younger populations with CAD. Furthermore, more primary research involving more diverse samples is needed. CAD-related deaths are higher among African-Americans than Caucasians and other groups.[2,59] Rates of MA for various chronic diseases also differ across race and ethnicity, with minority groups being less adherent to prescribed medications.[60,61] However, few primary studies included in this meta-analysis reported racially or ethnically diverse groups. Thus future primary research testing MA interventions among patients with CAD must strive to include minority groups to reduce this disparity.

We found some interesting nonsignificant moderators. Interventions focusing solely on MA were as effective as interventions that had multiple behavioral foci. Thus clinicians may take the opportunity to introduce strategies for MA while discussing other health behaviors with CAD patients. The use of only written material did not impact intervention effectiveness, suggesting providers should consider using more than this type of delivery when promoting MA among patients with CAD. Future MA intervention research among CAD patients should incorporate additional forms of intervention delivery beyond written materials. Number of intervention sessions did not appear to be a significant moderator. It is possible that even one or two intervention sessions may be effective in changing MA behavior among CAD patients. However, additional research testing or comparing various aspects of intervention dose could help identify the most effective dose needed to change MA behavior. We did not identify any specific intervention strategy that increased MA intervention

effectiveness; however, lack of statistical significance of these moderators may be related to the small number of comparisons.

MA interventions delivered by physicians or pharmacists were equally effective as interventions not delivered by these providers. Although these findings suggest involving these providers may not increase MA intervention effectiveness, the number of studies incorporating these types of interventionists was small. Future research could directly compare similar MA interventions among CAD patients delivered by different clinicians. Additional research may also explore variations in MA intervention delivery across diverse health care providers.

This meta-analysis was limited by some primary study characteristics. Although efforts were made to contact corresponding authors, some studies were excluded because critical data were missing from primary study reports. Primary study reporting limits generalizability of this study's findings to more diverse populations. Primary study quality is an important issue in meta-analysis work. Multiple strategies are recommended to manage primary study quality.[62,63] We used specific inclusion criteria to capture reports with more rigorous study designs, employed analysis techniques accounting for study heterogeneity, and explored study quality empirically through moderator analyses. Some publication bias was present. Smaller, negative studies are less likely to be published; therefore, access to these studies is limited. Despite extensive search strategies, capturing these relevant studies was a challenge.

Primary study reporting affected the ability to identify effective combinations of MA components. Several studies employed multiple intervention strategies; however, combinations of strategies were inconsistent. Thus determining the most effective combination of MA intervention strategies was not possible.

Measurement error within the primary studies could have introduced bias towards overestimation of MA intervention effects. Objective measures are the most sensitive and specific means of measuring MA;[64,65] however, most included studies utilized self-reported MA, which is known to overestimate patients' MA.[66] Future MA intervention research conducted among patients with CAD should consider using objective measures of MA to reduce bias.

Meta-analyses are observational studies. The moderator findings of this study are intended to promote additional exploration in this area of study. The scope of this meta-analysis is limited to MA among patients with CAD. Therefore, interpretation of these findings may not be possible among patients with other chronic illnesses or other forms of heart disease.

Conclusion

Medication management is an important aspect of secondary prevention for CAD. Nonadherence to prescribed medications for CAD has been linked with multiple poor outcomes. Findings from this meta-analysis suggest MA interventions among patients with CAD are effective, especially among older patients. Clinicians working with patients with CAD evaluate patients' MA behavior prior to initiating interventions to improve MA. Nurses are on the front lines of health behavior promotion among these patients and can be effective

MA interventionists. Future research is needed to explore MA interventions among younger populations and more racially diverse groups.

Acknowledgments

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Study name	Statistics for each study				Std diff in means and 95% CI
	Std diff in means	Standard error	Lower limit	Upper limit	
2012	0.516	0.228	0.069	0.962	
2012	0.140	0.164	-0.182	0.462	
2012	0.075	0.164	-0.245	0.396	
2012	-0.077	0.174	-0.418	0.265	
2011	0.383	0.694	-0.977	1.742	
2011	0.151	0.026	0.099	0.202	
2011	-0.411	0.369	-1.134	0.312	
2010	-0.021	0.139	-0.294	0.251	
2010	0.455	0.425	-0.378	1.288	
2009	0.598	0.142	0.319	0.876	
2008	0.382	0.812	-1.208	1.973	
2008	0.541	0.796	-1.019	2.100	
2008	-0.020	0.213	-0.438	0.397	
2008	0.114	0.195	-0.268	0.496	
2007	0.194	0.078	0.040	0.348	
2007	0.284	0.156	-0.021	0.589	
2006	0.143	0.381	-0.602	0.889	
2006	0.242	0.432	-0.605	1.089	
2005	0.375	0.158	0.065	0.685	
2004	0.979	0.193	0.600	1.358	
2004	0.132	0.057	0.019	0.244	
2001	0.059	0.042	-0.023	0.142	
2000	0.000	0.503	-0.986	0.986	
1998	0.424	0.077	0.274	0.574	
1990	-0.153	0.283	-0.708	0.402	
1988	0.739	0.387	-0.019	1.497	
1986	0.132	0.330	-0.515	0.780	
1985	2.521	0.585	1.374	3.668	
Summary Effect	0.229	0.047	0.138	0.321	

-4.00 -2.00 0.00 2.00 4.00

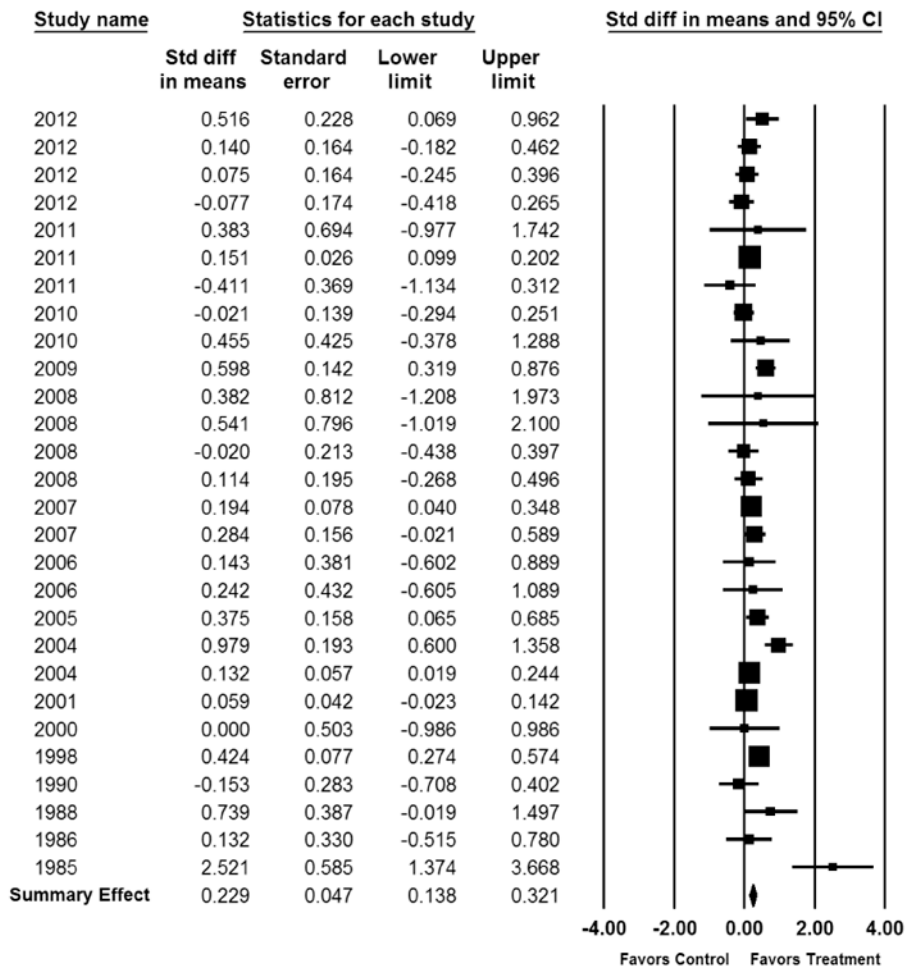Favors Control   Favors Treatment

Figure 1. Forest Plot of Main Effects

Forest plot of meta-analysis of two-group posttest comparisons of medication adherence outcomes listed by year of publication. Effect sizes calculated using a random effects model. Study weight is proportional to the area of each square.

Table 1

Characteristics of Primary Studies Included in Medication Adherence Meta-analyses

Characteristic	k	Min	Q_1	Median	Q_3	Max
Treatment group sample size	28	4	18.75	86.5	246.5	3635
Control group sample size	24	5	21	82	562	3010
Percentage attrition	23	0	0	4.545	14.646	65.282
Percentage female	23	0	25	40	51.05	67.4
Percentage underrepresented group subjects	7	7	24.1	48	90.4	92.9
Mean age (years)	21	53.7	58.4	62.9	64	72.22
Median number of intervention sessions	17	1	1	2	5	12
Median duration of interventions (days)	23	1	1	35	126	365
Median duration post-intervention for MA outcome data collection (days)	14	12	40.25	124.5	175.5	700

Note. k=number of comparisons in which characteristic was reported; Q_1=first quartile, Q_3=third quartile.

Table 2

Overall Effects of Medication Adherence Interventions among Patients with Coronary Artery Disease

Comparison	k	d	p (d)	95% Confidence interval	SE	Q	I²	p (Q)
Treatment vs. control groups at post-test[a]	28	0.229	<.001	0.138, 0.321	0.047	78.201	65.474	<.001
Treatment vs. control groups at post-test[b]	25	0.269	<.001	0.135, 0.403	0.068	65.384	63.294	<.001
Treatment group pre- vs. post-test	9	0.183	0.106	-0.039, 0.405	0.113	69.462	88.483	<.001
Control group pre- vs. post-test	6	-0.014	0.887	-0.208, 0.180	0.099	11.124	55.052	0.049

Note. k=number of comparisons; *d*=standardized mean difference effect size; SE=standard error; *Q*=conventional homogeneity statistic; *I²* =proportion of observed variance across effect size due to true differences in effects.

[a] all studies included

[b] three larger sample studies excluded

Table 3

Continuous Moderator Results

Moderator	k	B	SE	p
Report and Methods Moderators				
Year of publication	28	-0.005	0.004	0.205
Sample size	28	-0.000	0.000	0.004
Sample Attribute Moderators				
Age	21	0.014	0.004	0.001
Percent women	23	-0.000	0.002	0.968
Underrepresented groups	7	0.000	0.001	0.810
Intervention Feature Moderator				
Number of sessions	17	-0.013	0.013	0.304
Duration of intervention	23	-0.000	0.000	0.972
Time point for MA outcome data collection	14	-0.000	0.000	0.213

Note. k=number of comparisons; B=meta-regression coefficient (unstandardized); SE=standard error; *p* is value for B

Table 4

Dichotomous Moderator Results

Moderator	k	d	SE	Q_B	p
Report Moderators					
Publication status				1.267	0.260
Unpublished (e.g. dissertation, presentation)	4	0.724	0.474		
Published article	24	0.189	0.037		
Presence of funding for research				1.911	0.167
Unfunded	11	0.452	0.192		
Funded (any funding reported or acknowledged)	17	0.182	0.040		
Socioeconomic status				0.194	0.660
Not reported as low income	24	0.237	0.046		
Reported as low income	4	0.352	0.259		
Location				0.531	0.466
Not North America	7	0.380	0.125		
North America	21	0.182	0.045		
Research Methods Moderators					
Allocation to treatment and control groups				0.200	0.655
Not random assignment	8	0.199	0.068		
Random assignment	20	0.244	0.072		
Allocation concealment				1.222	0.269
Allocation not concealed	15	0.188	0.050		
Allocation concealed	13	0.319	0.108		
Theory				0.167	0.683
No theory	23	0.239	0.050		
Any theory	5	0.184	0.124		
Data collectors blinded				0.481	0.488
Data collectors not blinded	18	0.207	0.052		
Data collectors blinded	10	0.293	0.112		

Moderator	k	d	SE	Q_B	p
Intention-to-treat				0.000	0.997
No intention-to-treat	23	0.236	0.063		
Intention-to-treat	5	0.237	0.097		
Intervention Feature Moderators					
Goal Setting				0.095	0.758
No goal setting	23	0.227	0.050		
Goal setting	5	0.183	0.135		
Health care provider given information about MA				3.899	0.048
Health care provider NOT given information about MA	20	0.151	0.042		
Health care provider given information about MA	8	0.387	0.112		
Intervention delivered at home				0.676	0.411
Not at home	23	0.254	0.053		
At home	5	0.129	0.143		
Intervention delivered at clinic				0.705	0.401
Not at clinic	23	0.213	0.049		
At clinic	5	0.320	0.118		
Intervention started while subjects were inpatients				8.448	0.004
Not inpatients	19	0.141	0.037		
Inpatients	9	0.590	0.150		
Problem solving				0.307	0.580
No problem solving	22	0.245	0.054		
Problem solving	6	0.188	0.088		
Self-monitoring of medications				1.198	0.274
No self-monitoring	25	0.195	0.045		
Self-monitoring	3	0.492	0.267		
Succinct written instructions				1.820	0.177
No succinct written instructions	22	0.255	0.054		
Succinct written instructions	6	0.124	0.080		
Any written instructions				2.868	0.090

Moderator	k	d	SE	Q_B	p
No written instructions	19	0.287	0.065		
Any written instructions	9	0.149	0.049		
Behavior target				1.212	0.271
Multiple behaviors	11	0.306	0.109		
MA only	17	0.179	0.038		
Part of intervention delivered to providers				0.476	0.490
Not delivered to providers	24	0.213	0.053		
Delivered to providers	4	0.311	0.131		
Nurse interventionist				6.502	0.011
No nurse	18	0.127	0.020		
Any nurse	10	0.428	0.116		
Physician interventionist				0.397	0.529
No physician	21	0.223	0.050		
Physician	7	0.322	0.148		
Pharmacist interventionist				0.310	0.578
No pharmacist	21	0.240	0.056		
Pharmacist	7	0.193	0.062		
Mail delivery				10.845	0.001
No mail delivery	23	0.292	0.059		
Mail delivery	5	0.060	0.038		
Telephone delivery				0.701	0.403
No telephone delivery	14	0.192	0.065		
Telephone delivery	14	0.280	0.082		
Written materials ONLY				2.985	0.084
No written intervention	26	0.248	0.049		
Written intervention	2	0.008	0.130		
Face-to-face delivery				2.604	0.107
No face-to-face	7	0.143	0.048		
Face-to-face	21	0.288	0.076		

Note. k=number of comparisons; *d*=standardized mean difference effect size; SE=standard error; *QB*=sum of weighted sum of squares of subgroup means about overall mean; *p* is value for *QB*