

**Supplement 1. Summary of Results for Patient, Provider, and Systems Interventions**

<b>Clinical Condition</b>	<b>Type of Intervention</b> <b>Primary Outcome, Power</b>	<b>Strength of Evidence for Medication Adherence</b>	<b>Number of Studies; <i>n</i> of Individuals (<i>n</i> Analyzed) Followed by Results</b>	<b>Strength of Evidence for Other Outcomes</b>	<b>Number of Studies; <i>n</i> of Individuals (<i>n</i> Analyzed) Followed by Results</b>
Diabetes	Case management/ collaborative care (95-97)  0 of 3 studies powered for adherence as a primary outcome	Low SOE of benefit for medication adherence	3; 569 (501) Varied measures and magnitude	Low SOE of benefit for HbA1C	2; 240 (238)  1.2 percentage points difference between differences in groups
	Education with social support (98)  Powered for adherence as primary outcome	Insufficient for medication adherence	1; 199 (189) No stat sig difference	NA	NA
	Health coaching (99)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 56 (49) No stat sig difference	NA	NA
	Telephone counseling by pharmacist (100)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 232 (120) No stat sig difference	NA	NA
Hyperlipidemia	Collaborative Care (97)  Not powered for	Insufficient for medication adherence	1; 329 (117 on lipid- lowering meds) No sig diff between groups	NA	NA

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	adherence as primary outcome				
Hyperlipidemia	Decision Aids (101-103)  0 of 2 studies powered for adherence as primary outcome	Insufficient for medication adherence	2; 248 (98 + NR in 1 trial) Variable self-report measures with variable outcomes  1 of 2 RCTs with stat sig difference in adherence (102, 103). OR for missing no medication doses in past week: 3.4 (95% CI 1.5, 7.5)	Low for patient satisfaction	1; 98 (98)
Hyperlipidemia	Education and behavioral support (phone or mail) (104-108)  2 of 5 studies powered for adherence as a primary outcome (107, 108)	Low benefit for medication adherence	5; 18,492 (9,411 + NR in 1 trial) Variable measures with variable outcomes; 2 of 5 RCTs with stat sig difference in adherence  Higher medication adherence scale scores in intervention vs. control group at 6 months, 12 months, and 18 months, numbers NR (123)  Adjusted OR for MPR $\geq$ 80% over 6 months: 1.43, 90% CI 1.05-1.96) (108)  Adjusted OR for being in possession of a statin at 6 months: 1.64, 90% CI 1.19-2.26 (108)  Adjusted OR for statin prescribed	Insufficient	NA

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			at least every 30 days after refill date over 6 months :1.41, 90% CI 1.05-1.94) (108)		
Hyperlipidemia	Multicomponent (education face-to-face with pharmacist + blister packaging) (109)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 159 (159)  Difference in percentage points in adherence between groups for pills taken vs. prescribed over 6 months: 26.4  Difference in percentage points in adherence between groups for pills taken vs. prescribed over 6 months: 75.7  All medications over 6 months; adherence assessed at different frequencies between groups	Insufficient for LDL-C biomarker	1; 159 (135)  No stat sig difference in LDL-C between groups
Hypertension	Blister packaging (110)  Not powered for adherence as primary outcome	Low for benefit for medication adherence and persistence	1; 93 (85)  Difference in percentage points for mean proportion of medications taken over 12 months : 6  Difference in percentage points for refilling medications within 5 days of refill date (pharmacy refill) over 12 months: 14.3	Insufficient for SBP + DBP; angina, MI, or stroke	1; 93 (85)  No stat sig difference in change in SBP or DBP or in percentage of patients with reduced SBP at 6 or 12 months, or in percentage of patients with reduced DBP at 6 months, angina, MI, or stroke  Higher proportion of intervention vs control group with reduced DBP at 12 months: 29.8 percentage points
				Insufficient for health care	1; 93 (85)

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				utilization: ED visits + hospitalizations	No stat sig difference between groups for either outcome
Hypertension	Case management (111-113)  0 of 3 studies provided for adherence as primary outcome	Low for benefit for medication adherence	3; 516 (64 + NR in two studies)  Two of three RCTs with stat sig difference in adherence  Difference in between-group change in MEMS $\geq$ 80% adherence between baseline and 6 weeks: 31.3 percentage points(111)  Difference in MEMS adherence, mean over 6 months: 11.3 percentage points (112)	Low for benefit for SBP + DBP	2; 214 (64 + NR in one study)  Difference in SBP between groups at follow up between 6 weeks and 6 months: -8.5 to -14 mm Hg (range across studies)  Difference in DBP between groups at follow up between 6 weeks and 6 months: -3.1 to -9.2 mm Hg (range across studies)
Hypertension	Collaborative care (97, 114, 115)  0 of 3 powered for adherence as primary outcome	Low for no benefit for medication adherence	3; 1,194 (785)  No stat sig differences between groups	NA	NA
Hypertension	Education (face-to-face with pharmacist) (109, 116-118)  0 of 3 powered for adherence as	Low for benefit for medication adherence; insufficient for persistence	Adherence: 3; 348 (344)  Variable outcomes for adherence; 2 of 3 RCTs with stat sig difference in adherence:  Difference in percentage points in for pills taken vs. prescribed over	Moderate for benefit for SBP	2; 292 (268)  Change in mm Hg mean SBP between-group difference from 4 and 6 months: -6.4 to -8.9 (range)
				Insufficient for DBP	2; 292 (268)  Change in mm Hg mean DBP between-group difference from 4

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	primary outcome		6 months: 26.4(109)  Difference in percentage points for >80% adherence to all medications over 6 months: 75.7 (109)  Difference in between-group change in mean Morisky score between 4 and 6 months follow-up: 0.39 points (116, 117)  Persistence: 1; 56 (53)  No stat sig difference between groups refilling medications on time		and 6 months: -1.1 to -3mm (range)  1, 133 (NR)  No stat sig differences for sexual dysfunction, dizziness, and headaches  1; 133 (130)  Stat sig improvement in four of five questions  1; 133 (124)  0.08 fewer hospital visits in intervention group  1; 133 (124)  0.41 fewer visits in intervention group  1; 133 (124)  No stat sig difference
Hypertension	Education and behavioral support (telephone, mail, and/or video) (106, 119-124)  1 of 6 powered for adherence as primary outcome (124)	Low for benefit for medication adherence	6; 7,252 (5,405 + NR in two studies)  Multiple variable outcomes; three RCTs with stat sig difference in adherence  Difference in between-group change (percentage points) in pill count (taken vs. prescribed) between baseline to 6 months, adjusted for baseline age, sex and	Insufficient for SBP or DBP	1; 299 (267)  No stat sig difference between groups in change from baseline to 6 months

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			<p>adherence: 6 (122)</p> <p>No difference in adherence between groups at baseline and 6 months, but greater adherence in intervention vs. control group at 12 and 18 months; numbers NR (123)</p> <p>Absolute risk reduction in mean percent of days medications taken correctly over 12 months: 6.25 (124)</p>		

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Hypertension	Education with social support (98)  Powered for adherence as primary outcome	Insufficient for medication adherence	1; 199 (199) No stat sig differences between groups at 12 months	NA	NA
Hypertension	Risk communication (125)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 89 (89)  No stat sig difference between groups at 3 months	NA	NA
Heart failure	Access to medical records (126)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 107 (NR)  No stat sig difference at 6 or 12 months	NA	NA
Heart failure	Case management (127)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 156 (156)  Difference in percentage points in medication taken correctly at 30 days: 6.6 to 6.8 (range)  Difference in percentage points for proportion with >80% adherence at 30 days: 15.7 to 16.3 (range)  Difference in percentage points	Insufficient for all-cause hospital admission	1; 156 (156)  No significant difference in multiple measures of all-cause readmission

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			for proportion with >90% adherence at 30 days: 22.1 percent.		
Heart failure	Education and behavioral support (128)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 82 (82)  Significantly greater dose-count (percentage of doses taken vs. prescribed) from baseline to 2 months (numbers NR) and baseline to 9 months (numbers NR)	Low for benefit for cardiac event-free survival	1; 82 (82)  Hazard ratio for cardiac-related ED visits, hospitalizations, and death adjusted for covariates over 9 months: 4.223
Heart failure	Multicomponent pharmacist-led (129)  Study powered for adherence was primary outcome	Low for benefit for medication adherence	1; 314 (314 for MEMS caps, NR for MPR or self-report)	Insufficient for quality of life	1; 314 (NR) No stat sig difference
			Stat sig difference in adherence (MEMS,MPR, and self-report)	Low for benefit for patient satisfaction	1; 314 (NR) Difference of 0.3 between groups on 12-point validated questionnaire at 12 months
			Difference in percentage points for taking medication (MEMS) at 9 months: 10.9%	Low for benefit for all-cause ED visits and all-cause ED + hospitalizations	1; 314 (314) Difference of 0.52 mean all-cause ED visits and 0.69 mean all-cause ED + hospitalizations between groups over 12 months
			Difference in percentage points for medications taken within correct time frame (MEMS) over 9 months: 5.9%	Insufficient for health care utilization for all-cause hospitalization, CV-related and HF-related events, costs	1; 314 (314) No stat sig difference
			Difference in percentage points for MPR over 12 months: 4.2%		
			No stat sig difference for self-report		



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Heart failure	Reminder video and telephone calls (130)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 60 (50)  Difference in percentage points for video and phone intervention groups compared to control in percentage of pills taken over 8 weeks: 17 to 27 (range)	Insufficient for quality of life	1; 60 (42)  No stat sig difference
Myocardial infarction	Education and behavioral support (131)  Study powered for adherence as primary outcome	Low for benefit for medication adherence; insufficient for persistence	1; 907(836)  Percentage points mean increase in proportion of days covered per month over 9 months: 4.3%  Percentage points difference between groups of proportion with $\geq 80\%$ adherence over 9 months: 6  No stat sig difference for persistence	NA	NA
Asthma	Self-management (132-136)  Three of five studies powered for adherence as primary outcome(132, 133, 135)	Moderate for short-term benefit in medication adherence	5; 303 (300)  Difference in between-group change (percentage points) in adherence from baseline to 3 months to 1 year: 14 to 31 (range)	Insufficient for pulmonary function and inflammation markers	2; 152 (149)  No stat sig difference
				Insufficient for symptom improvement	5; 303 (300)  Varied measures and magnitude (inconsistent)
				Low for no benefit for quality of life	4; 248 (245)  Varied measures and magnitude (consistent)

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Asthma	Shared or clinical decision making (137)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 612 (612)  Difference in medication acquisition ratio for all asthma medications at year 1, adjusted for baseline continuous medication acquisition and balancing variables: 0.13 to 0.21	Low for benefit for pulmonary function	1; 612 (612)  Difference in FEV1 percentage points at year 1, adjusted for baseline percent predicted FEV1 and balancing variables: 2.7 to 3.2
				Low for benefit for symptom improvement	1; 612 (612)  Difference in mean equivalents of SABA canister equivalents acquired at 2 years between shared decision making and usual care: 1.6
				Low for benefit for quality of life	1; 612 (612)  Difference in subscale scores on 5-item Mini Asthma Quality of Life Questionnaire, at year 1, adjusted for baseline score and balancing variables: 0.28 to 0.39
				Low for benefit for health care utilization	1; 612 (612)  Difference of 0.36 to 0.37 fewer asthma-related visits per year, at year 1, adjusted for baseline asthma-related healthcare utilization and balancing variables

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Asthma or COPD	Pharmacist or physician access to patient adherence information (138, 139)  1 of 2 studies powered for adherence as a primary outcome (139)	Low for no benefit for medication adherence	2; 3,811 (3,596)  No stat sig difference	NA	NA
Depression	Case management (95, 96, 111, 140-142)  0 of 4 studies powered for adherence as a primary outcome	Moderate for benefit for medication adherence	4; 690 (617)  Difference in percentage points for adherence or filling prescriptions at 6-week followup: 9 to 15 (range across studies)	Moderate for benefit for symptom improvement	4; 688 (617) Between-group odds ratio of achieving remission at 12 weeks: 6.15 Between-group PHQ-9 score change from baseline to 12 weeks: 2.13 Difference in CES-D scale: 7.0 to 9.4 (range across studies) Mean difference in SCL-20 (0 to 4 range) scores between groups across 12 months: 0.08
				Insufficient for self-reported disability	1; 386 (315)  Varied measures, outcomes, time periods
Depression	Collaborative care (143-148)  0 of 5 studies	Moderate for benefit for medication adherence for telephone + in-person;	5; 921 (921)  Difference in percentage points for adequate dosage in the past 30 days: 16.5 to 40.3 (range across studies)	Low for benefit for symptom improvement for major depression of moderate	Severe depression: 2; 214 (214) Minor depression: 1; 149 (149) Moderate depression: 2; 156 (156) Major depression: 1; 79 (79)  Varied measures, outcomes, time

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	powered for adherence as a primary outcome	insufficient for telephone only; insufficient for depression + HIV patients	No stat sig difference for depression + HIV patients or telephone collaborative care only	depression; insufficient for severe or minor depression	periods
				Low for benefit for patient satisfaction with antidepressants	2; 370 (370) Difference in percentage points in those rating antidepressants as helping somewhat to a great deal: 6.0 to 24.8 (range across studies)
				Insufficient for health care utilization	3; 598 (598) Varied outcomes, time periods, and consistency
				Insufficient for costs	1; 228 (228) No stat sig difference
				Moderate for benefit for patient satisfaction with quality of care	3; 598 (598) Difference in percentage points in those rating quality of care as good to excellent: 5.1 to 32.5 (range across studies) at 3 to 4 months; 16 at 6 months
Depression	Telephone counseling and monitoring (149-151)  0 of 3 studies powered for	Insufficient for medication adherence	2; 270 (255)  No stat sig difference	NA	NA

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	adherence as a primary outcome				
Depression	Reminders to nonadherent patients and lists of nonadherent patients to providers (152)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 9,564 (9,564)  Difference in between-group change (percentage points) for adherence between baseline and 3 to 6 months; 1 to 3 (range across study)	NA	NA
Glaucoma	Multicomponent intervention (153)  Study powered for adherence as primary outcome	Low for benefit for medication adherence	1; 66 (66)  Difference in between-group change in adherence rate between 3 and 6 months: 0.13	Insufficient for intraocular pressure	1; 66 (66)  No stat sig difference
Multiple sclerosis (MS)	Telephone counseling and monitoring (154)  Study powered for adherence as primary outcome	Low for benefit for medication adherence	1; 435 (367)  Difference in between-group change (percentage points) of patients who discontinued use of MS therapy at follow up: 7.5	NA	NA
Musculoskeletal diseases	Decision aid (155)  Study powered for adherence as primary outcome	Insufficient for medication adherence, persistence, initiation of therapy	1; 100 (100)  Varied outcomes and measures	Insufficient for patient satisfaction	1; 100 (NR)  No stat sig difference
Musculoskeletal	Case management	Insufficient for	1; 127 (127)	NA	NA

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diseases	(156)  Study powered for adherence as primary outcome	medication adherence	No stat sig difference		
Musculoskeletal diseases	Virtual osteoporosis clinic (157)  Not powered for adherence as primary outcome	Low for benefit for medication adherence	1; 235 (211)  Difference in between-group change (percentage points) of women who filled osteoporosis medication prescription at 13 months from baseline: 23.7	Insufficient for patient satisfaction	1; 235 (211)  No stat sig difference
Musculoskeletal diseases	Telephone counseling and monitoring (158)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1; 2,097 (2,087)  Difference in between-group change (percentage points) of MPR during 12 months of following : 8	NA	NA
Multiple or unspecified chronic conditions	Case management (pharmacist-led) (159-161)  1 of 3 studies powered for adherence as primary outcome (159)	Low for no benefit for persistence	3; 3,307 (3269)  No stat sig difference	NA	NA

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Multiple or unspecified chronic conditions	Intensive interdisciplinary assessment followed by nurse-led case management (162)  Not powered for adherence as primary outcome	Insufficient for medication adherence	1,96 (75)  No stat sig difference	NA	NA

Abbreviations: CES-D scale = Center for Epidemiologic Studies-Depression scale; COPD = chronic obstructive pulmonary disease ; CI: confidence interval; CV = cardiovascular; DBP = diastolic blood pressure; ED = emergency department; FEV1 = forced expiratory volume at 1 minute; HF: heart failure; HIV: human immunodeficiency virus; MEMS = medication event monitoring system; MI = myocardial infarction; mm Hg = millimeter of mercury; MPR = medication possession ratio; NA = not applicable; NR = not reported; OR: odds ratio; RCT = randomized controlled trial; SABA = short-acting beta agonists. SBP = systolic blood pressure; SCL-20 = Hopkins Symptom Checklist-20; stat sig = statistically significant.