SUPPLEMENTARY MATERIALS (Online)

Appendix Table 1. Pharmacist Activities Other Than for Medication Adherence Frequently Reported in Included Studies

Pharmacist Activity Number of Studies Reporting Activity	**Description**
Patient Education (PE) n=20 studies	Most patient education was face to face with some providing supporting written and audiovisual materials. Content was education about the disease and risk factors; benefits of medication; the need to adhere to and continue medication regimen; self-care and monitoring particularly for diabetes.
Lifestyle counseling (LC) n=15 studies	Counseling other than for adherence was face to face or by phone. Content included dietary and lifestyle modifications such as exercise, salt intake, smoking cessation, and food choices.
Limited patient care (PC) n=11 studies	In most studies, pharmacists communicated recommended changes in medication to the prescribing provider. Pharmacist activity related to patient care was most often measuring blood pressure. In a few studies, the pharmacist could place laboratory orders related to lipid medication management or had delegated authority to modify medications. In a few studies with diabetes patients, the pharmacist performed exams of the feet and skin.

Resolution of medication or drug problems (DP)
n=27 studies
	Pharmacist activities related to medication were the most common across the included studies.[82]
	Interactions with patients were face to face or by phone. Communications with prescribing providers were mostly by electronic means (fax, e-mail, EMR) and less often by phone call or page.
	Activities including those related to patient adherence were:
	• Review of all current prescriptions and indications
	• Indication
	  ○ Determine appropriateness of medication
	  ○ Determine untreated indication
	• Effectiveness
	  ○ Identify dosing that is too low or ineffective medications
	• Safety

	○ Identify dosing that is too high ○ Determine medication interactions and other adverse events • Adherence ○ Collect information and assess causes of medication non-adherence and develop a plan for possible solutions • Monitoring ○ Monitor patient progress at follow-ups ○ Assess clinical outcomes against national guidelines and recommend related adjustments to medications
Goal setting (GS) n=13 studies	In studies where it was part of the protocol, goals for medication treatment and healthy behaviors were set collaboratively by patient, pharmacist, and prescribing physician. The goals would be shared and monitored against clinical indicators or behavioral outcomes including adherence at each follow-up. Often, the clinical goals were set based on national guidelines in currency at the time of the study.

Quality Assessment Tool for Estimates from Economic Review of Tailored Pharmacy-based Medication Adherence Interventions

The attached tool for quality assessment of economic evidence was developed for the scope and objective of this study, following methods developed by CDC and approved by the CPSTF for systematic economic reviews (see Supplemental Materials). Briefly, two raters used the tool to independently assign and later reconcile points which indicate limitations in the quality of the estimates for variables related to intervention cost, healthcare cost, QALY, and total cost per QALY gained. Each variable was scored as good, fair, or limited based on the total points (described below), and those that received a limited quality score were removed from further consideration and analysis. The quality assessment also assessed the estimates for fatal flaws, which are aspects of estimates that lead to misrepresentation of the true effectiveness, cost, or economic effects of the intervention.

Quality of Intervention Cost Estimate. Each intervention cost estimate was first scored for how well it captured the drivers of cost, where the drivers were pharmacist and other staff wages and benefits, the cost of patient education materials and adherence aids, and the cost of any additional interventions added to the pharmacy intervention. The cost estimate received an assessment of good, fair, or limited for capture of drivers if the total number of drivers not included in the estimate was 0-1, 2, or greater than 2, respectively. The cost estimate was then scored for appropriateness of measurement and methods of estimation, with points assigned for sample size of less than 50, data external to study, valuation based on non-local prices and conditions, intervention cost contaminated with other components such as healthcare, and any other aspect that may have impacted the cost of the intervention. The cost estimate received an assessment of good, fair, or limited for measurement and methods if the points totaled 0-2, 3, or ≥4, respectively. The final quality assigned to the cost estimate was the lower of the quality assessed based on capture of drivers and the quality based on appropriateness of measurement and methods.

Quality of Healthcare Cost Estimate. Each healthcare cost estimate was first scored for how well it captured the drivers of healthcare cost: outpatient visits, inpatient stays, ED visits, medications, and labs. The healthcare cost estimate received an assessment of good, fair, or limited for capture of drivers if the total number of drivers not included in the estimate was 0-1, 2-3, or ≥4, respectively. The cost estimate was then scored for appropriateness of measurement and methods of estimation, with points assigned for a patient pool that has mean age <50 years or >65 years, baseline clinical indicators close to normal, sample size of less than 50, biased selection of patients, intervention duration less than or equal to 6 months, not randomized, no control group, not a pre to post measure, significant baseline differences between intervention and control, costs unrelated to CVD or CVD risk factors, and valuation based on non-local prices and conditions. The healthcare cost estimate received an assessment of good, fair, or limited for measurement and methods if the points totaled 0-3, 4-7, or ≥8, respectively. The final quality assigned to the estimate was the lower of quality assessed based on capture of drivers and the quality based on appropriateness of measurement and methods.

Quality of QALY Estimates and Modeled Healthcare Cost Estimates. There are no components for QALY. Therefore, no assessment of quality based on capture of drivers is relevant for

QALY. For modeled healthcare cost, the estimate is assessed for capture of drivers: outpatient visits, inpatient stays, ED visits, medications, and labs. The healthcare cost estimate was assessed as good, fair, or limited for capture of drivers if the total number of drivers not included in the estimate was 0-1, 2-3, or ≥ 4, respectively. Each QALY and modeled healthcare cost estimate was scored for appropriateness of measurement and methods of estimation, with limitation points assigned on criteria similar to that for estimates of observed healthcare cost and additional criteria where the estimates are the result of modeling including: model inputs not drawn from trial or systematic review, model parameters not drawn from large longitudinal trials or systematic reviews, short model duration less than 5 years, models with non-standard structure or statistical properties, lack of sensitivity analysis, lack of discounting, no fade-out of intervention effect, or other shortfall. The QALY or modeled healthcare cost estimate received an assessment of good, fair, or limited for measurement and methods if the points totaled 0-3, 4-9, or ≥10, respectively. The final quality assigned to the estimate was the lower of quality assessed based on capture of drivers and the quality based on appropriateness of measurement and methods.

The quality assigned to estimates that are a combination of other estimates such as total cost which is intervention cost plus change in healthcare cost is the lower of the quality assigned to its intervention cost component and healthcare cost component.

Intervention Cost Estimates

Part 1. Intervention Cost Drivers
Consult the abstracted intervention narratives and intervention Methods sections to determine the components that are likely to be cost drivers. Compare the list of cost drivers to what the study explicitly states are included in intervention cost.

If you find there is missing information (i.e., a limitation) for any unaccounted cost drivers, enter "1" under the Limitation? column and the abbreviation under the Notes column. If your assessment is that the authors have adequately addressed the cost driver, enter "0" under the Limitation? column.

Cost Driver		**Limitation?**	**Notes**
Abbreviation	**Description**		
Pharmacist	Pharmacist wages		
Materials	• Patient education materials • Adherence aids (e.g., pill boxes, blister packs, calendars, etc)		
Communications	Web portals and communications infrastructure		
Additional intervention	Intervention over and above pharmacist medication adherence (e.g., team-based care, case management, disease management)		
Fatal Flaw	Describe (e.g., Reported estimate for intervention cost almost certainly excludes all or most of the components known to be delivered based on methods described in the study).		
TOTAL LIMITATIONS			
QUALITY GRADE		☐ Good (0-1) ☐ Fair (2) ☐ Limited (3-4)	

Part 2. Intervention Cost Measurement Shortfalls
If you find there is missing information (i.e., a limitation) for any measurement shortfalls, enter "1" under the Limitation? column and the abbreviation under the Notes column. If your assessment is that the authors have adequately addressed the measurement shortfall, enter "0" under the Limitation? column.

Shortfall		**Limitation?**	**Notes**
Abbreviation	**Description**		
Size	Small sample (<50 at baseline)		
Data Source	Appropriate data source (e.g., study records of time calendars and supplies procured)		
Valuation	Appropriate valuation based on local prices and conditions		
Healthcare Mixed	Intervention cost is mixed in with healthcare cost		
Other	Please name the limitation in the Notes column		
Fatal flaw	Describe (e.g., Inadequate information to derive intervention cost where an explicit estimate was not provided)		
Total limitations			
QUALITY GRADE		☐ Good (0-2) ☐ Fair (3) ☐ Limited (≥4)	

Healthcare Cost

Part 1. Healthcare Cost Drivers
Consult the abstracted intervention narratives and intervention Methods sections to determine the components that are likely to be cost drivers. Compare the list of cost drivers to what the study explicitly states are included in intervention cost.

If you find there is missing information (i.e., a limitation) for any unaccounted cost drivers, enter "1" under the Limitation? Column and any notes in the Notes column. If your assessment is that the authors have adequately addressed the cost driver, enter "0" under the Limitation? column.

Cost Driver		**Limitation?**	**Notes**
Abbreviation	**Description**		
Inpatient	Inpatient hospital stays		
Outpatient	• Outpatient visits with primary care provider • Outpatient visits with specialists		
ED	Emergency department visits		
Medication	Drugs and pharmaceuticals		
Labs	Laboratory tests and diagnostics		
Fatal Flaw	Describe (e.g., Reported estimate for healthcare cost almost certainly seriously underestimates or overestimates).		
TOTAL LIMITATIONS			
QUALITY GRADE		☐ Good (0-1) ☐ Fair (2-3) ☐ Limited (4-5)	

Part 2. Healthcare Cost Measurement Shortfalls
If you find there is missing information (i.e., a limitation) for the characteristics- reported in study based on information about how the measurements were made, enter "1" under the Limitation? column. If your assessment is that the authors have adequately addressed the limitation enter "0" under the Limitation? column.

Characteristic	Limitation?	Notes
Population		
Young (mean age <50 y) or very old (mean age > 65 y) population		
Baseline mean clinical indicators close to normal for study population (e.g. SBP/DBP < 140/90)		
Sampling and Analysis		
Small sample size (<50 at baseline)		
Selection bias (self-selection, convenience sample, etc.),		
Intervention Design and Time Follow-Up		
Duration: Short intervention length (≤6 months)		
Not randomized		
No comparison		
Post-only measure		
Significant differences between intervention and comparison groups		
Valuation		
Healthcare related to cardiovascular disease or cardiovascular risk factors		
Valuation based on local prices and conditions		
Fatal Flaw		
Describe (e.g., Conjecture that is not based on changes observed in trial or study)		
TOTAL LIMITATIONS		
QUALITY GRADE	☐ Good (0-3) ☐ Fair (4-7) ☐ Limited (8-10)	

QALY or Modeled Outcomes

QALY or Other Modeled Outcomes Measurement Shortfalls

If you find there is missing information (i.e., a limitation) for the characteristics- reported in study based on information about how the measurements were made, enter "1" under the Limitation? column. If your assessment is that the authors have adequately addressed the limitation enter "0" under the Limitation? column.

Characteristic	Limitation?	Notes
Modeled Population		
Young (mean age <50 y) or very old (mean age > 65 y) population		
Baseline mean clinical indicators close to normal for study population (e.g. SBP/DBP < 140/90)		
Model Input Values		
Inputs into model drawn from study or trial or systematic review (e.g., baseline characteristics, intervention effects)		
Model parameter values drawn from peer reviewed literature, large trials, or systematic reviews (e.g., probability of disease states and transition probabilities between states)		
Utility or disability weights drawn from literature or study based validated questionnaire for quality adjusted life year and disability adjusted life years		
Costs based on study records and local prices or based on healthcare resource prices from literature		
Model Characteristics		
Duration: Short intervention length (≤5 years)		
Appropriate methods (e.g., difference in difference, Markov model, individual simulation)		
Appropriate comparison (e.g., usual care)		
Appropriate sensitivity analysis (ROC curve, multiple factor simulations)		
Discounting (e.g., future values discounted at 3-5%)		
Appropriate fade-out of intervention effect		
Other		
Please name the limitation(s) in appropriate cell		
Fatal Flaw		
Describe the fatal flaw in the notes column (e.g., conjecture based on outcomes not from trial population or based on pathways that are not founded in evidence)		
TOTAL LIMITATIONS		
QUALITY GRADE	☐ Good (0-3) ☐ Fair (4-9) ☐ Limited (10-14)	