Economic Value of Pharmacist-Led Medication Reconciliation for Reducing Medication Errors After Hospital Discharge

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ABSTRACT

OBJECTIVES: Medication discrepancies at the time of hospital discharge are common and can harm patients. Medication reconciliation by pharmacists has been shown to prevent such discrepancies and the adverse drug events (ADEs) that can result from them. Our objective was to estimate the economic value of nontargeted and targeted medication reconciliation conducted by pharmacists and pharmacy technicians at hospital discharge versus usual care.

STUDY DESIGN: Discrete-event simulation model.

METHODS: We developed a discrete-event simulation model to prospectively model the incidence of drug-related events from a hospital payer's perspective. The model assumptions were based on data published in the peer-reviewed literature. Incidences of medication discrepancies, preventable ADEs, emergency department visits, rehospitalizations, costs, and net benefit were estimated.

RESULTS: The expected total cost of preventable ADEs was estimated to be $472 (95% credible interval [CI], $247-$778) per patient with usual care. Under the base-case assumption that medication reconciliation could reduce medication discrepancies by 52%, the cost of preventable ADEs could be reduced to $266 (95% CI, $150-$423), resulting in a net benefit of $206 (95% CI, $73-$373) per patient, after accounting for intervention costs. A medication reconciliation intervention that reduces medication discrepancies by at least 10% could cover the initial cost of intervention. Targeting medication reconciliation to high-risk individuals would achieve a higher net benefit than a nontargeted intervention only if the sensitivity and specificity of a screening tool were at least 90% and 70%, respectively.

CONCLUSIONS: Our study suggests that implementing a pharmacist-led medication reconciliation intervention at hospital discharge could be cost saving compared with usual care.

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Disruptions to, and changes in, a patient's outpatient medication regimen occur frequently during hospitalization. This often results in discrepancies between drugs prescribed at discharge and the medications outpatient providers believe that patients should be on.[1] Although the majority of such discrepancies do not have clinically important effects, their consequences can be profound. These events are defined as preventable adverse drug events (ADEs) because they are caused by medication discrepancies that could have been avoided. It is estimated that 2.4% to 4.1% of all hospital admissions are directly related to ADEs, and up to 69% of those ADEs are preventable.[2-5] There are other circumstances in which the presence of a medication discrepancy has not yet resulted in an ADE, but may still be costly and/or may expose patients to the risks of additional testing or monitoring.[6]

Medication reconciliation by pharmacists at hospital discharge is a possible strategy to reduce medication discrepancies and subsequent ADEs. Several systematic reviews have found that medication reconciliation significantly reduces the risk of medication discrepancies.[7-9] Despite this, not all studies evaluating the impact of medication reconciliation on health resource utilization (HRU) have found beneficial effects.[10-19] These findings naturally raise questions about the economic value of this intervention and how the balance between the costs and benefits of the intervention could be optimized by, for example, selectively targeting high-risk patients.

Accordingly, we conducted a simulation-based cost-benefit analysis to estimate and compare the economic value of 3 strategies at hospital discharge: a) usual care (no intervention), b) nontargeted medication reconciliation for all patients, and c) targeted medication reconciliation that uses a screening tool to identify patients at high risk of postdischarge ADEs.

METHODS

Overall Approach

We developed a 2-part discrete-event simulation to prospectively model the sequence of events that occur within the 30 days after

hospital discharge for a hypothetical cohort of patients who did, and did not, receive medication reconciliation. Consistent with the existing literature,[6] we categorized medication discrepancies that were associated with harm as preventable ADEs and those not associated with harm as "potential" ADEs. We categorized both preventable ADEs and potential ADEs into those that were (or were potentially) life-threatening, serious, or significant. Nonsignificant events were considered, by definition, to not be a medication discrepancy.

TAKE-AWAY POINTS

- Medication discrepancies at the time of hospital discharge are common and can harm patients.
- Little is known about the economic value of implementing medication reconciliation by pharmacists and whether this intervention is more cost-effective when targeted to those most at risk of medication discrepancies.
- A medication reconciliation intervention that reduces medication discrepancies by at least 10% could cover the initial cost of intervention.
- Our results suggest that, despite the use of relatively costly pharmacists and pharmacy technicians, the cost savings from avoided rehospitalizations would more than offset the cost of the intervention.

Our model first estimated the incidence of medication discrepancies, preventable ADEs, their associated major HRUs (ie, emergency department [ED] visits and rehospitalizations), and costs among patients who did not undergo reconciliation (**Figure 1** [A]). We then used the distribution of outcomes from the initial phase of the simulation to compare the impact of 3 interventions (Figure 1 [B]): a) a nontargeted pharmacist-led medication reconciliation intervention for all patients, b) a targeted pharmacist-led medication reconciliation intervention in which only patients at high risk of ADEs were intervened upon, and c) usual care (no intervention). Our modeling approach and structure have been explained in the **eAppendix** (eAppendices available at **www.ajmc.com**).

We used a cost-benefit analysis framework and conducted our analysis from the perspective of a hospital that was at risk for the added cost of any intervention and the savings from avoiding HRUs due to preventable ADEs. All costs were estimated in 2014 US dollars and, when necessary, unit costs were converted to 2014 prices using reported changes in the consumer price index.[20] Considering the short period of analysis, no discount rate was applied. All simulations were developed using Arena version 12.00 (Rockwell Automation Technologies, Inc, Milwaukee, Wisconsin).

Patient Characteristics

The characteristics of the simulated cohort were assumed to be similar to populations in the studies that were the basis of our assumptions about event probabilities (**Table 1**).[6] The model assumptions and event probabilities are based on data from the Pharmacist Intervention for Low Literacy in Cardiovascular Disease (PILL-CVD) study.[6] In this randomized clinical trial, 851 patients hospitalized with acute coronary syndromes or acute decompensated heart failure were randomized to receive either a pharmacist-assisted intervention (ie, medication reconciliation, inpatient pharmacist counseling, low-literacy adherence aids, and individualized telephone follow-up) or usual care after hospital discharge. Similar to the trial population, the simulated cohort was assumed to have an average age of 60 years, have a median 14 years of education, and to be 60% male. We assumed that approximately 10% of the hypothetical cohort had inadequate health literacy and 8.7% had marginal, and that 11.5% had some level of cognitive impairment. We also assumed that approximately 60% of patients were hospitalized with acute coronary syndrome, 30% with acute heart failure, and 10% with both diagnoses.

Estimates of Medication Discrepancies and Subsequent Events

The incidences of medication discrepancies, preventable ADEs, and potential ADEs for patients not undergoing medication reconciliation were estimated using the distribution of observed events in the control arm of the PILL-CVD study.[6] The distribution of events in the usual-care arm of PILL-CVD is summarized in **eAppendix Figure A**. In this study, 25 of the 125 (20%) patients with preventable ADEs were rehospitalized or visited an ED. Based on a case-by-case analysis of these patients by 1 study author (JLS), we determined that 24 of these ADEs were potentially amenable to medication reconciliation activities at the time of hospital discharge (as opposed to postdischarge activities, such as monitoring for ADEs).

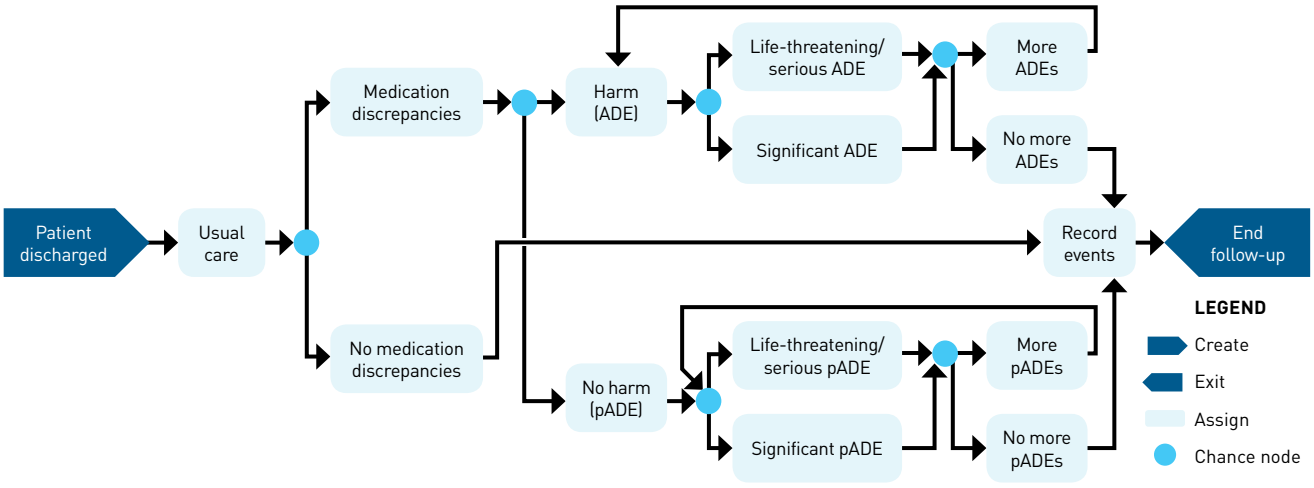
The proportion of patients who had rehospitalizations, ED visits, or both events, was based on the observed rates in this trial[6] and another large clinical trial.[17] In the base-case analysis, we assumed that the intervention could reduce the risk of rehospitalization due to preventable ADEs, amenable to medication reconciliation, by 52% (ie, a relative risk of 0.48). This was based on an average effectiveness rate of medication reconciliation observed in 4 published studies of at least moderate methodological quality.[11,14,15,21] The estimated effectiveness of the intervention may vary as a function of care setting, patient characteristics, composition of the healthcare team responsible for delivery of the intervention, and services that were bundled with medication reconciliation.[7,8] As a result, we varied our assumptions of effectiveness extensively in the sensitivity analysis.

Patient Targeting

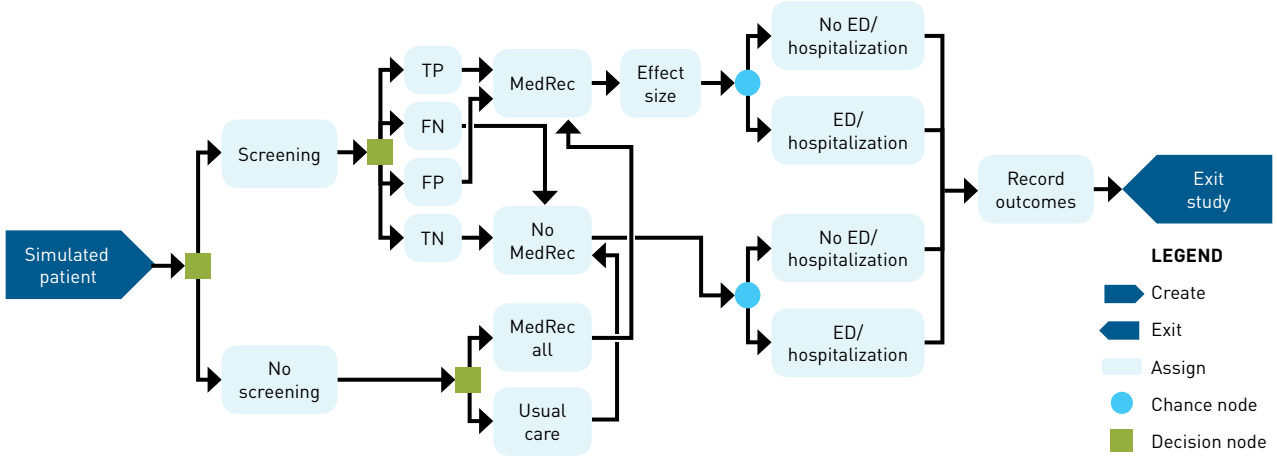
In order to estimate the impact of limiting medication reconciliation to high-risk patients (ie, those patients most likely to have a postdischarge ADE due to a medication discrepancy), we assumed that patients underwent screening with a tool that could predict, with some accuracy, the risk of ADEs based on the patient's characteristics at the time of hospital discharge. A perfect screening tool could exactly discriminate patients with and without preventable

FIGURE 1. Model Structure

A. Modeling the sequence of events in usual care strategy[a]



B. Modeling the impact of intervention on outcomes among patients simulated in part A[b]



ADE indicates an adverse drug event as a result of medication discrepancies; ED, emergency department visit; FN, false negative; FP, false positive; MedRec, medication reconciliation; pADE, a potential ADE as a result of medication discrepancies; PILL-CVD, Pharmacist Intervention for Low Literacy in Cardiovascular Disease study; TN, true negative; TP, true positive.

[a]Modeling the sequence of events within the 30 days after hospital discharge for a hypothetical cohort of patients in usual care strategy (ie, no medication reconciliation). Incidences of medication discrepancies for individual patients were modeled based on observed probabilities in the PILL-CVD clinical trial. Patients who experienced medication discrepancies either were harmed (ie, developed a preventable ADE) or were exposed to harms due to these discrepancies (ie, potential ADEs). The possibility of having more than 1 preventable ADE or potential ADE has been modeled. All event histories were recorded for individual patients to emulate the likelihood and distribution of events under the usual care arm of the PILL-CVD clinical trial.

[b]Modeling the impact of targeted and nontargeted intervention on outcomes among patients simulated in part A. Patient-specific incidences of events in part A were used as counterfactuals under usual care and for determining the true status of patients under targeted intervention (ie, whether they would have developed preventable ADEs under usual care). The model simulates the impact of medication reconciliation on the likelihood of reducing discrepancies and subsequent rehospitalizations and ED visits. Although all patients are assumed to receive medication reconciliation under a nontargeted intervention strategy, only those with TP and FP screening results underwent medication reconciliation. The model then calculated and recorded costs associated with intervention, rehospitalizations, and ED visits resulting only from preventable ADEs. The overall costs of usual care, nontargeted intervention for all patients, and targeted intervention were estimated and compared by aggregating individual patients' costs.

ADEs, based on the information available at discharge, and would only assign the former to receive the intervention.

Given the sensitivity and specificity of this tool, we assigned patients into 4 categories: a) true positive, who would have had a preventable ADE and were assigned to receive the intervention; b) false positive, who would not have had a preventable ADE but were assigned to the intervention; c) false negative, who would have had a preventable ADE but were not assigned to receive the intervention; and d) true negative, who would not have had a preventable ADE and were not assigned to receive the intervention. We assumed that the effectiveness of targeted interventions was similar to that of the nontargeted strategy, in which medication reconciliation was offered to all patients.

Costs

Average cost per rehospitalization was based on recent estimates by the Agency for Health Research and Quality.[22] The cost per ED visit was based on estimated charges in the same report, which were calculated by applying an estimated cost-to-charge ratio of 0.55.[23,24] A 3% penalty rate was applied to all rehospitalization costs to reflect the current policies for readmission payment adjusted amount.[25]

Intervention costs were calculated using estimated average pharmacist time per reconciliation[26] and average salary and benefit payments to pharmacists and pharmacy technicians.[27] We assumed that pharmacy technicians, rather than pharmacists, conducted 50% of medication reconciliation-related tasks (eg, taking medication histories) in order to reduce the intervention cost. Pharmacists were assumed to supervise technicians and do some of the tasks, like patient counseling or order review, themselves. This assumption was varied in the sensitivity analysis. We also assumed that a medication history conducted by a pharmacy technician under a pharmacist's supervision was as effective as that of one conducted by a pharmacist alone.[28-30]

TABLE 1. Model Parameters

	Base Case	Range	Citation
Proportion of patients with preventable ADEs	29.2%	Beta (125-303)	6
Proportion of patients with potential ADEs	30.8%	Beta (132-296)	6
Proportion of patients with preventable ADEs who also had potential ADEs	30.4%	Beta (38-87)	6
Probability that a preventable ADE is:			6
Life-threatening	2.9%	Beta (5-165)	6
Serious	14.1%	Beta (24-146)	6
Significant	82.9%	1 – beta (5-165) to beta (24-146)	6
Number of preventable ADEs per patient who had at least 1 preventable ADE			6
1	76%		
2	17%		
3	4%		
4	2%		
≥5	1%		
Probability of major resource utilization among patients with preventable ADEs	19.2%	Beta (25-100)	6
Percentage that require ED visit only	25.0%	Beta (6-18)	6
Percentage that require hospitalization only	29.2%	Beta (7-18)	6
Percentage that require hospitalization and ED visit	45.8%	Beta (11-14)	6
Relative risks of events in medication reconciliation versus usual care (no medication reconciliation)	0.48	(0-1)	Assumption
Sensitivity of screening tool for predicting preventable ADEs	70%	(10%-100%)	Assumption
Specificity of screening tool for predicting preventable ADEs	70%	(10%-100%)	Assumption
Mean cost per hospitalization	$10,000	± 20%	22
Median charge per ED visit	$713	± 20%	24
Cost-to-charge ratio for ED visits	0.55	209/383	23
Penalty for rehospitalization	3%		25
Mean pharmacist time per reconciliation (minutes)	46.2	± 50%	26
Mean annual salary of pharmacist	$120,850	± 20%	27
Mean annual salary of pharmacy technician	$30,370	± 20%	27
Overhead costs, including fringe and benefit	25%		Assumption

ADE indicates an adverse drug event occurring as a result of medication discrepancies; ED, emergency department.

Sensitivity Analysis

We performed extensive 1-way and 2-way sensitivity analyses to investigate the net benefit of medication reconciliation interventions under different assumptions for our model parameters, screening properties, and patients' characteristics. A probabilistic sensitivity analysis also was performed to examine distribution of our point estimates, given uncertainty of the model parameters, by varying all of our model parameters simultaneously.[31-33] We also reported credible intervals based on probabilistic sensitivity analyses that reflect uncertainty of simulated point estimates.

TABLE 2. Outcomes of Usual Care and Nontargeted Medication Reconciliation During the First 30 Days After Hospital Discharge, Assuming Different Effectiveness of Intervention[a]

Intervention	Usual Care	RR[b] = 0.48 (base case)	RR = 1	RR = 0.8	RR = 0.5	RR = 0
Number of ED visits caused by preventable ADEs (per 100 patients)	4.8	2.1	4.5	3.6	2.2	0.0
Number of hospitalizations caused by preventable ADEs (per 100 patients)	4.3	2.0	4.2	3.4	2.1	0.0
Number of interventions (per 100 patients)	0	100	100	100	100	100
Total cost per patient, $ (95% CI)	472 (247-778)	266 (150-423)	511 (285-814)	416 (234-651)	275 (153-436)	39 (7-73)
Net benefit, $ (95% CI)	ref	206 (73-373)	–39 (–101 to 27)	56 (–23 to 151)	197 (70-361)	432 (204-733)

ADE indicates an adverse drug event occurring as a result of medication discrepancies; CI, credible interval; ED, emergency department; ref, reference; RR, relative risk.
[a]Parentheses indicate 95% credible intervals from probabilistic sensitivity analyses estimated using Monte Carlo simulation.
[b]RR is relative risk of preventable ADEs in intervention versus usual care.

RESULTS

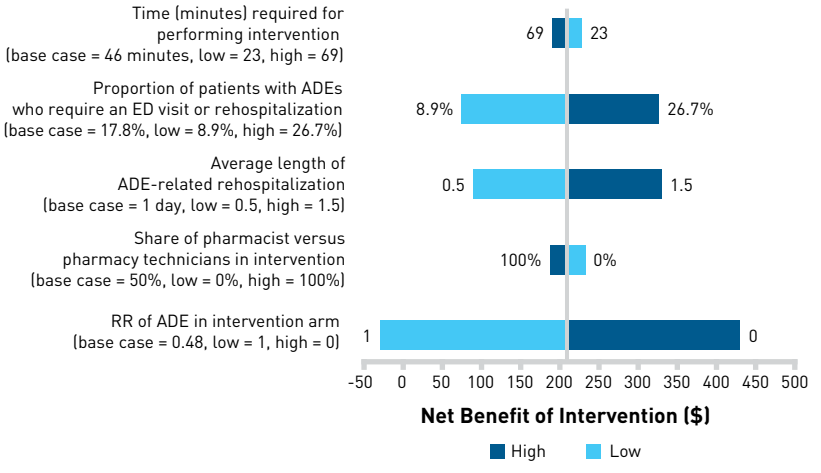
In a cohort of 10,000 patients not undergoing medication reconciliation, we estimated that 5090 would have at least 1 medication discrepancy within the first 30 days after hospital discharge. These medication errors would result in 3807 preventable ADEs and 5230 potential ADEs. Preventable ADEs would result in 421 rehospitalizations and 496 ED visits. Overall, the average cost of preventable ADEs was estimated to be $472 (95% credible interval [CI], $247-$778) per patient in the usual care strategy.

Medication Reconciliation for All Patients

Assuming that pharmacist-led medication reconciliation for all patients at hospital discharge could reduce medication errors by 52%, and therefore would reduce HRU due to preventable ADEs amenable to medication reconciliation by the same proportion, the number of rehospitalizations and ED visits related to preventable ADEs would be reduced to 199 and 215, respectively, with this strategy. This reduction in hospitalizations and ED visits would reduce the overall cost per patient to $266 (95% CI, $150-$423). This estimate includes the cost of medication reconciliation of approximately $39 per patient. Therefore, performing medication reconciliation for all patients at the time of hospital discharge would result in a significant net benefit of $206 (95% CI, $73-$373) per patient.

The impact of altering our assumptions about the effectiveness of medication reconciliation are presented in Table 2 and eAppendix Figure B. We found that the initial cost of the intervention would be more than offset by the savings from averted events as long as it reduced medication errors by at least 10%. The results of 1-way sensitivity analysis suggest that the net benefit is most sensitive to the effectiveness of intervention, the proportion of preventable ADEs that result in a rehospitalization or ED visit, and the average length of stay for patients who had an ADE-related rehospitalization (Figure 2). The results of our probabilistic sensitivity analysis are presented in eAppendix Figure C. We found that the uncertainty around net benefit ranges between –$2 and $577 per patient, with 99% of the simulated trials resulting in a positive net benefit.

FIGURE 2. One-Way Sensitivity Analyses Evaluating the Effect of Model Assumptions on Net Benefit of a Nontargeted Medication Reconciliation Intervention[a]



ADE indicates an adverse drug event as a result of medication discrepancies; RR, relative risk (of ADEs in the intervention arm versus usual care).
[a]Each bar shows changes in the magnitude of net benefit if a particular parameter in the model was varied in the specified range, holding every other parameter at its base case value. Only parameters with the largest influence on net benefit have been presented in this figure. The vertical line indicates the net benefit if all model parameters were set at their base-case values.

TABLE 3. Net Benefit ($) of Targeted Intervention Compared With No Intervention[a,b]

Specificity	Sensitivity									
	1	0.9	0.8	0.7	0.6	0.5	0.4	0.3	0.2	0.1
0.1	208	172	163	132	114	85	66	42	23	4
0.2	200	178	163	134	112	83	75	50	26	−11
0.3	204	177	162	144	117	95	82	51	13	−5
0.4	208	181	162	135	112	102	64	54	22	−1
0.5	209	187	155	143	112	91	67	44	21	2
0.6	222	194	185	156	127	102	75	57	30	6
0.7	220	200	184	146	125	103	83	60	37	2
0.8	218	206	174	153	127	104	86	60	37	22
0.9	224	199	179	149	135	114	86	63	38	20
1	232	200	179	157	137	115	82	61	44	11

[a]The net benefit ($) of the targeted intervention compared with no intervention for different assumptions for sensitivity and specificity of screening tool, assuming base-case effectiveness of intervention (relative risk = 0.48).
[b]The highlighted cells indicate combinations of sensitivity and specificity where the net benefit of the targeted intervention exceeds the net benefit of not targeting ($206).

Medication Reconciliation for Targeted Patients

The net benefit from targeting medication reconciliation under our base-case assumptions of 70% sensitivity and 70% specificity was $146 savings per patient, which was not superior to the savings from a nontargeted approach ($206 per patient). The impact of alternating our assumptions about sensitivity and specificity of the screening tool are presented in **Table 3** and **eAppendix Figure D**. We found that the net benefit could be as high as $232 per patient, if the specificity and sensitivity of a screening tool were 100%. The net benefit could exceed that which we obtained in the base-case analysis as long as the sensitivity and specificity of the screening tool were at least 90% and 70%, respectively. However, in general, improving the sensitivity of the screening tool has larger impact on net benefits than improving specificity. For example, a screening tool with 100% sensitivity resulted in a net benefit of $222 per patient even if the specificity was only 60%.

The added value of a targeted intervention increased as the effectiveness of the intervention decreased and the cost of intervention increased. For example, if medication reconciliation reduced the risk of medication discrepancy by 20% (rather than 52%) and is more expensive (eg, because it is performed by pharmacists rather than a combination of pharmacist technicians and pharmacists), then a targeted intervention is the preferred approach.

DISCUSSION

Although pharmacist-led medication reconciliation reduces medication errors that commonly occur after hospital discharge, its economic value has not been completely evaluated. We found that this intervention, when performed at the time of hospital discharge, reduced the cost of rehospitalizations and ED visits that resulted from medication discrepancies within 30 days after hospital discharge from $472 per patient to $266. This resulted in a net savings of $206 per patient, after accounting for the cost of the intervention. The magnitude of this savings could be increased if a screening tool, with very high sensitivity and modest specificity, was used to identify and target patients at higher risk of preventable postdischarge ADEs.

More than half of hospitalized patients are estimated to have 1 or more medication discrepancy after hospital discharge.[6,8] ADEs resulting from these discrepancies result in the rehospitalization of approximately 4% of discharged patients.[6] This highlights the opportunity for interventions that can prevent medication discrepancies to both improve quality and lower costs. Medication reconciliation at the time of hospital discharge involves a bundle of activities including patient counseling and communication with outpatient providers.

Although careful medication reconciliation at hospital discharge can potentially eliminate many discrepancies in discharge medication orders,[7,8] it, not surprisingly, has a more limited effect on other types of medication errors that occur during the postdischarge period. For example, patient misunderstanding of their medication regimen could lead to additional discrepancies after discharge.[10] Likely for this reason, reconciliation programs that include a telephone follow-up after discharge—along with other, more conventional features such as coordination with physicians, patient education, and transition coaching—have, in general, been more effective.[17,34]

Our results suggest that despite the use of relatively costly pharmacists and pharmacy technicians, the cost savings from avoided rehospitalizations would more than offset the cost of the intervention. This is consistent with the limited existing cost-effectiveness evidence.[35,36] The value of medication reconciliation could be increased if it were preferentially used for individuals at the highest risk of ADEs. This is consistent with the fact that many of the most effective medication reconciliation interventions reported in the literature are those that were targeted interventions, rather than administered to all patients.[18,19] Several studies have attempted to develop risk prediction models for hospital readmissions with acceptable accuracy.[37,38] However, these models tend to predict risk of all rehospitalizations in the first 30 days after discharge and, therefore, are not necessarily calibrated to predict the risk of readmission specifically resulting from medication errors.[1]

The estimates of costs and benefits of medication reconciliation in our study assume that those paying for medication reconciliation interventions are the same ones that share the savings from

reduced postdischarge HRUs. The extent to which this is true varies tremendously at present; however, it most certainly will increase dramatically in the near future. For example, in 2015, approximately 20% of Medicare payments are based on non–fee-for-service payment models. This share is expected to increase to 30% by 2016 and to 50% in 2018.[39] These models included bundled payments, in which providers are at risk for the cost of any readmissions occurring in the 30-to-90-day period after discharge.

Similarly, accountable care organizations put providers at risk for the total cost of care of the populations they serve; these incentives have encouraged providers to target readmissions as an opportunity to improve care and reduce costs. Moreover, Medicare has introduced readmission penalties broadly, and these penalties have led to much greater focus on readmission rates. As a whole, these payment models are critical to creating the business case for hospitals to invest in interventions such as mediation reconciliation.

Factors other than the intervention cost might limit the implementation of medication reconciliation. Pharmacists or other healthcare professionals conducting this intervention must have access to accurate and timely information about inpatient and outpatient mediations. As such, the availability of electronic health records[40] that can facilitate obtaining medication records from different points of care will directly affect the feasibility and success of medication reconciliation.[41] Patient-specific barriers, such as lower education level and language and other communication barriers, could limit the successful implementation of medication reconciliation in some healthcare settings.

Limitations

Our study should be viewed in light of its limitations. Only a handful of studies have shown the direct impact of medication reconciliation interventions on postdischarge HRU. As a result, our model was based on a chain of events whereby medication discrepancies lead to postdischarge ADEs and HRU, and on studies that show reductions in these discrepancies and in some of the downstream events. Although each link in the chain can be supported by data, we acknowledge that estimates of effectiveness on patient outcomes may be inaccurate. It is reassuring, however, that our results were largely unchanged in the extensive sensitivity analyses we conducted. In addition, the studies we used to derive our base-case estimates were based on specific patient populations, and thus may not be generalizable to all other patient groups or care settings.

CONCLUSIONS

Our study suggests that a pharmacist-led medication reconciliation can be a cost-saving strategy compared with usual care. The net benefit of this intervention could be enhanced using a highly sensitive screening tool for patients at high risk for postdischarge ADEs. Future studies should more directly make the link between interventions and reductions in postdischarge healthcare utilization in order to increase the precision of cost-benefit estimates.

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Authorship Information: Concept and design (TAB, SK, MN, JLS, WHS); acquisition of data (TAB, NKC, SK, MN, WHS); analysis and interpretation of data (TAB, NKC, SK, MN, JLS, WHS); drafting of the manuscript (NKC, MN); critical revision of the manuscript for important intellectual content (TAB, NKC, SK, MN, JLS, WHS); statistical analysis (MN); obtaining funding (NKC); and supervision (NKC).

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REFERENCES

1. Pippins JR, Gandhi TK, Hamann C, et al. Classifying and predicting errors of inpatient medication reconciliation. *J Gen Intern Med.* 2008;23(9):1414-1422. doi: 10.1007/s11606-008-0687-9.

2. von Laue NC, Schwappach DL, Koeck CM. The epidemiology of preventable adverse drug events: a review of the literature. *Wien Klin Wochenschr.* 2003;115(12):407-415.

3. Kongkaew C, Noyce PR, Ashcroft DM. Hospital admissions associated with adverse drug reactions: a systematic review of prospective observational studies. *Ann Pharmacother.* 2008;42(7):1017-1025. doi: 10.1345/aph.1L037.

4. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. The incidence and severity of adverse events affecting patients after discharge from the hospital. *Ann Intern Med.* 2003;138(3):161-167.

5. Forster AJ, Murff HJ, Peterson JF, Gandhi TK, Bates DW. Adverse drug events occurring following hospital discharge. *J Gen Intern Med.* 2005;20(4):317-323.

6. Kripalani S, Roumie CL, Dalal AK, et al; PILL-CVD (Pharmacist Intervention for Low Literacy in Cardiovascular Disease) Study Group. Effect of a pharmacist intervention on clinically important medication errors after hospital discharge: a randomized trial. *Ann Intern Med.* 2012;157(1):1-10. doi: 10.7326/0003-4819-157-1-201207030-00003.

7. Mueller SK, Sponsler KC, Kripalani S, Schnipper JL. Hospital-based medication reconciliation practices: a systematic review. *Arch Intern Med.* 2012;172(14):1057-1069. doi: 10.1001/archinternmed.2012.2246.

8. Lehnbom EC, Stewart MJ, Manias E, Westbrook JI. Impact of medication reconciliation and review on clinical outcomes. *Ann Pharmacother.* 2014;48(10):1298-1312. doi: 10.1177/1060028014543485.

9. Christensen M, Lundh A. Medication review in hospitalised patients to reduce morbidity and mortality. *Cochrane Database Syst Rev.* 2013;(2):CD008986. doi: 10.1002/14651858.CD008986.pub2.

10. Schnipper JL, Kirwin JL, Cotugno MC, et al. Role of pharmacist counseling in preventing adverse drug events after hospitalization. *Arch Intern Med.* 2006;166(5):565-571.

11. Walker PC, Bernstein SJ, Jones JN, et al. Impact of a pharmacist-facilitated hospital discharge program: a quasi-experimental study. *Arch Intern Med.* 2009;169(21):2003-2010. doi: 10.1001/archinternmed.2009.398.

12. Bolas H, Brookes K, Scott M, McElnay J. Evaluation of a hospital-based community liaison pharmacy service in Northern Ireland. *Pharm World Sci.* 2004;26(2):114-120.

13. Lisby M, Thomsen A, Nielsen LP, et al. The effect of systematic medication review in elderly patients admitted to an acute ward of internal medicine. *Basic Clin Pharmacol Toxicol.* 2010;106(5):422-427. doi: 10.1111/j.1742-7843.2009.00511.x.

14. Eggink RN, Lenderink AW, Widdershoven JW, van den Bemt PM. The effect of a clinical pharmacist discharge service on medication discrepancies in patients with heart failure. *Pharm World Sci.* 2010;32(6):759-766. doi: 10.1007/s11096-010-9433-6.

15. Kwan JL, Lo L, Sampson M, Shojania KG. Medication reconciliation during transitions of care as a patient safety strategy: a systematic review. *Ann Intern Med.* 2013;158(5, pt 2):397-403. doi: 10.7326/0003-4819-158-5-201303051-00006.

16. Nickerson A, MacKinnon NJ, Roberts N, Saulnier L. Drug-therapy problems, inconsistencies and omissions identified during a medication reconciliation and seamless care service. *Healthc Q.* 2005;(spec no 8):65-72.

17. Gillespie U, Alassaad A, Henrohn D, et al. A comprehensive pharmacist intervention to reduce morbidity in patients 80 years or older: a randomized controlled trial. *Arch Intern Med.* 2009;169(9):894-900. doi: 10.1001/archinternmed.2009.71.

18. Koehler BE, Richter KM, Youngblood L, et al. Reduction of 30-day postdischarge hospital readmission or emergency department (ED) visit rates in high-risk elderly medical patients through delivery of a targeted care bundle. *J Hosp Med.* 2009;4(4):211-218. doi: 10.1002/jhm.427.

19. Pal A, Babbott S, Wilkinson ST. Can the targeted use of a discharge pharmacist significantly decrease 30-day readmissions? *Hosp Pharm.* 2013;48(5):380-388. doi: 10.1310/hpj4805-380.

20. CPI inflation calculator [2014]. Bureau of Labor Statistics website. http://www.bls.gov/data/inflation_calculator.htm. Accessed June 2, 2015.

21. Bergkvist A, Midlov P, Hoglund P, Larsson L, Bondesson A, Eriksson T. Improved quality in the hospital discharge summary reduces medication errors—LIMM: Landskrona Integrated Medicines Management. *Eur J Clin Pharmacol.* 2009;65(10):1037-1046. doi: 10.1007/s00228-009-0680-1.

22. Pfuntner A, Wier LM, Steiner C. Costs for hospital stays in the United States, 2011. Healthcare Cost and Utilization Project website. https://www.hcup-us.ahrq.gov/reports/statbriefs/sb168-Hospital-Costs-United-States-2011.jsp. Published December 2013. Accessed June 20, 2015.

23. Williams RM. The costs of visits to emergency departments. *N Engl J Med.* 1996;334(10):642-646.

24. Medical Expenditure Panel Survey: table 6. emergency room services—mean and median expenses per person with expense and distribution of expenses by source of payment: United States, 2012. Agency for Healthcare Research and Quality website. http://bit.ly/2db645H. Accessed June 1, 2016.

25. Readmissions Reduction Program (HRRP). CMS website. http://www.cms.gov/Medicare/Medicare-Fee-for-Service-Payment/AcuteInpatientPPS/Readmissions-Reduction-Program.html. Accessed June 20, 2016.

26. Meguerditchian AN, Krotneva S, Reidel K, Huang A, Tamblyn R. Medication reconciliation at admission and discharge: a time and motion study. *BMC Health Serv Res.* 2013;13:485. doi: 10.1186/1472-6963-13-485.

27. Occupational employment and wages, May 2015. 29-1051 pharmacists. Bureau of Labor Statistics website. http://www.bls.gov/oes/current/oes291051.htm. Updated March 30, 2016. Accessed June 20, 2016.

28. Cooper JB, Lilliston M, Brooks D, Swords B. Experience with a pharmacy technician medication history program. *Am J Health Syst Pharm.* 2014;71(18):1567-1574. doi: 10.2146/ajhp130590.

29. Hart C, Price C, Graziose G, Grey J. A program using pharmacy technicians to collect medication histories in the emergency department. P T. 2015;40(1):56-61.

30. Johnston R, Saulnier L, Gould O. Best possible medication history in the emergency department: comparing pharmacy technicians and pharmacists. *Can J Hosp Pharm.* 2010;63(5):359-365.

31. Claxton K, Sculpher M, McCabe C, et al. Probabilistic sensitivity analysis for NICE technology assessment: not an optional extra. *Health Econ.* 2005;14(4):339-347.

32. Briggs AH. Handling uncertainty in cost-effectiveness models. *Pharmacoeconomics.* 2000;17(5):479-500.

33. Spiegelhalter DJ, Best NG. Bayesian approaches to multiple sources of evidence and uncertainty in complex cost-effectiveness modelling. *Stat Med.* 2003;22(23):3687-3709.

34. Jack BW, Chetty VK, Anthony D, et al. A reengineered hospital discharge program to decrease rehospitalization: a randomized trial. *Ann Intern Med.* 2009;150(3):178-187.

35. Karnon J, Campbell F, Czoski-Murray C. Model-based cost-effectiveness analysis of interventions aimed at preventing medication error at hospital admission (medicines reconciliation). *J Eval Clin Pract.* 2009;15(2):299-306. doi: 10.1111/j.1365-2753.2008.01000.x.

36. Feldman LS, Costa LL, Feroli ER Jr, et al. Nurse-pharmacist collaboration on medication reconciliation prevents potential harm. *J Hosp Med.* 2012;7(5):396-401. doi: 10.1002/jhm.1921.

37. Donze J, Aujesky D, Williams D, Schnipper JL. Potentially avoidable 30-day hospital readmissions in medical patients: derivation and validation of a prediction model. *JAMA Intern Med.* 2013;173(8):632-638. doi: 10.1001/jamainternmed.2013.3023.

38. Kansagara D, Englander H, Salanitro A, et al. Risk prediction models for hospital readmission: a systematic review. *JAMA.* 2011;306(15):1688-1698. doi: 10.1001/jama.2011.1515.

39. Cutler D. Payment reform is about to become a reality. News @ *JAMA* website. http://newsatjama.jama.com/2015/02/11/jama-forum-payment-reform-is-about-to-become-a-reality. Published February 11, 2015. Accessed April 30, 2015.

40. Poon EG, Blumenfeld B, Hamann C, et al. Design and implementation of an application and associated services to support interdisciplinary medication reconciliation efforts at an integrated healthcare delivery network. *J Am Med Inform Assoc.* 2006;13(6):581-592.

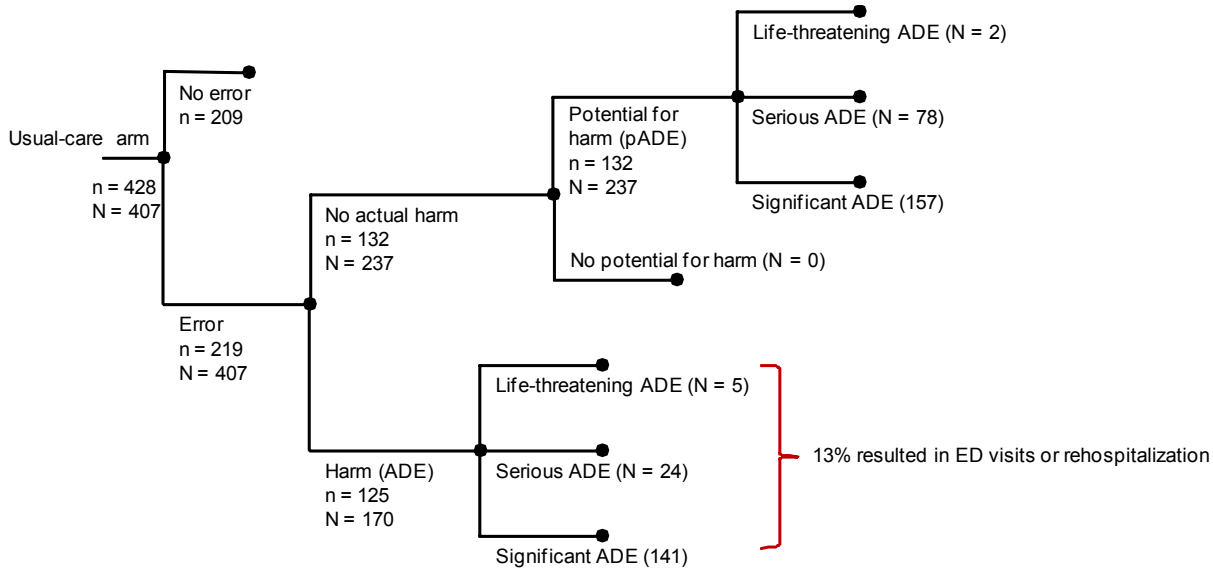
41. Schnipper JL, Hamann C, Ndumele CD, et al. Effect of an electronic medication reconciliation application and process redesign on potential adverse drug events: a cluster-randomized trial. *Arch Intern Med.* 2009;169(8):771-780. doi: 10.1001/archinternmed.2009.51. ■

eAppendix

Design and structure of the simulation model

We developed a discrete-event simulation (DES) model to simulate the distribution of events observed in the Pharmacist Intervention for Low Literacy in Cardiovascular Disease study (PILL-CVD) (a randomized control trial) and to estimate the health resource utilization (HRU) and spending associated with those events. We simulated the effect of targeted and nontargeted medication reconciliation interventions on overall costs, after accounting for the cost of the intervention itself. For this purpose, we first developed a model to prospectively simulate the chain of events that occurred within the 30 days after discharge from hospital in a cohort of hypothetical patients who did not receive medication reconciliation (ie, usual care) (Figure 1A). To do this, we created a hypothetical cohort of 10,000 patients and tracked them through their first 30 days after hospital discharge. All probabilities were based on event rates in the control arm of the PILL-CVD trial. The incidence of medication errors; potential adverse drug events (ADEs); preventable ADEs (significant, serious, and life-threatening); major HRUs (emergency department [ED] visits and rehospitalizations); and costs associated with those HRUs were derived from the peer-reviewed literature and were simulated and recorded for each patient.
In the second part of the simulation (Figure 1B), we used the distribution of events among the simulated cohort in the initial phase to compare 3 interventions: a) usual care (no intervention); b) a pharmacist-led medication reconciliation intervention for all patients; and c) a targeted pharmacist-led medication reconciliation intervention. To do this, we created identical clones of the cohort in the usual-care arm and their history of events (simulated in the initial phase) and assigned them to 1 of the 3 interventions. Conditional on our assumptions about the effectiveness of interventions that were derived from the peer-reviewed literature, the impact of interventions on number of medication errors, preventable ADEs, potential ADEs, rehospitalizations, ED visits, and overall costs were estimated and compared with the usual-care arm. We used cost-benefit analysis from a hospital payer's perspective in that the cost of intervention and savings resulting from avoiding HRUs due to preventable and potential ADEs were accounted for in the analysis. All the simulations were developed using Arena Version 12.00 (2007 Rockwell Automation Technologies, Inc, Milwaukee, Wisconsin).

Figure A. Number of Events During the First 30 Days After Hospital Discharge Among 428 Patients in the Usual Care Arm of the PILL-CVD Randomized Clinical Trial[a]



ADE indicates preventable adverse drug event; ED, emergency department; error, medication discrepancy; pADE, potential adverse drug event.

[a]In the Pharmacist Intervention for Low Literacy in Cardiovascular Disease study (PILL-CVD), a total of 25 major health resource utilizations (HRUs) (6 emergency department [ED] visits, 7 rehospitalizations, and 11 both ED visits and rehospitalizations) occurred among 125 patients who had at least 1 preventable adverse drug event (ADE) in the usual-care arm amenable to medication reconciliation. Overall, 170 preventable ADEs occurred among these 125 patients within the first 30 days of hospital discharge in the usual-care arm. Therefore, the ratio of HRU events to number of preventable ADEs was 14.7% (25/170 =14.7%), while the ratio of HRU events to number of patients with preventable ADEs was 17.8% (25/125 = 20%).

Figure B. Net Benefit of Medication Reconciliation for All Patients Versus Usual Care for Different Assumptions About Effectiveness

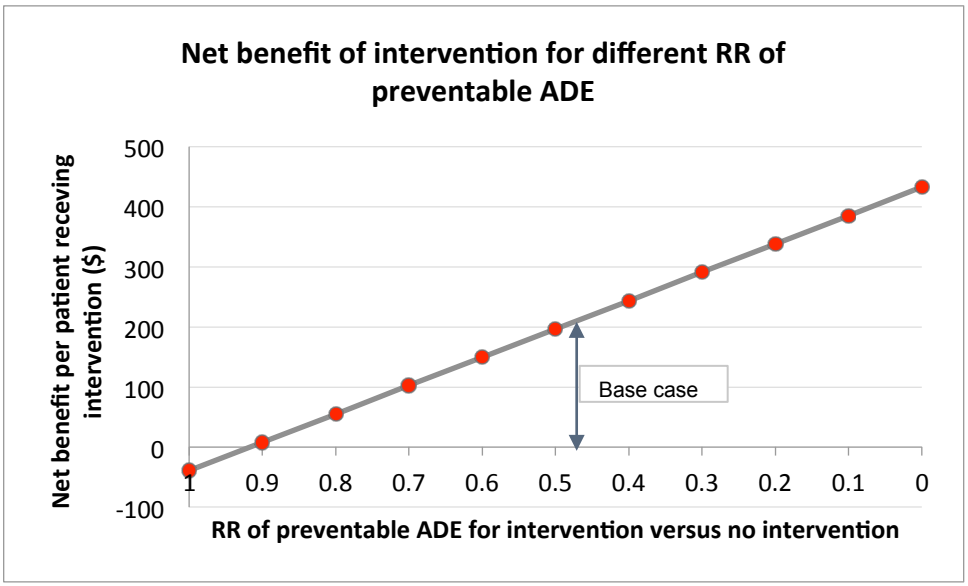
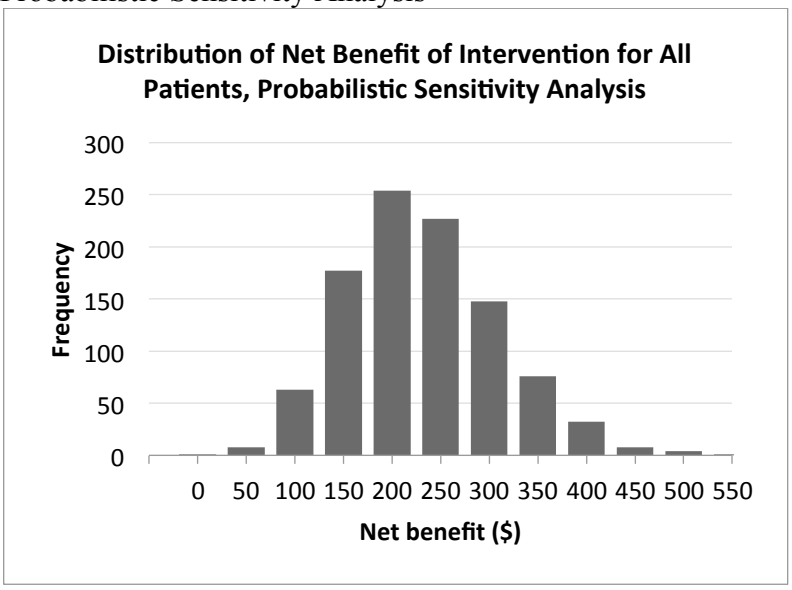


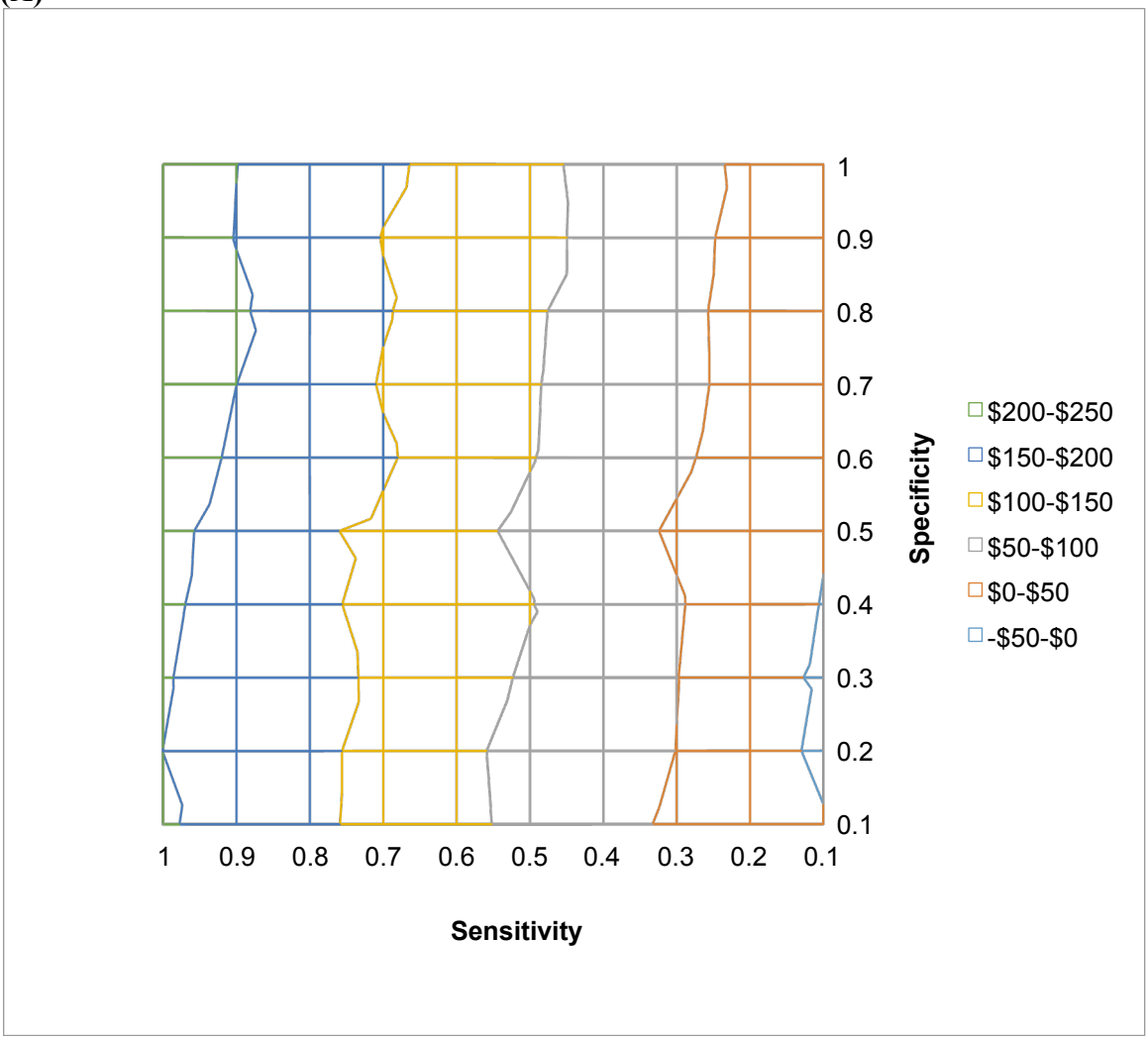
Figure C. Distribution of Net Benefit Under the Base-Case Scenario, Estimated Using Probabilistic Sensitivity Analysis[a]



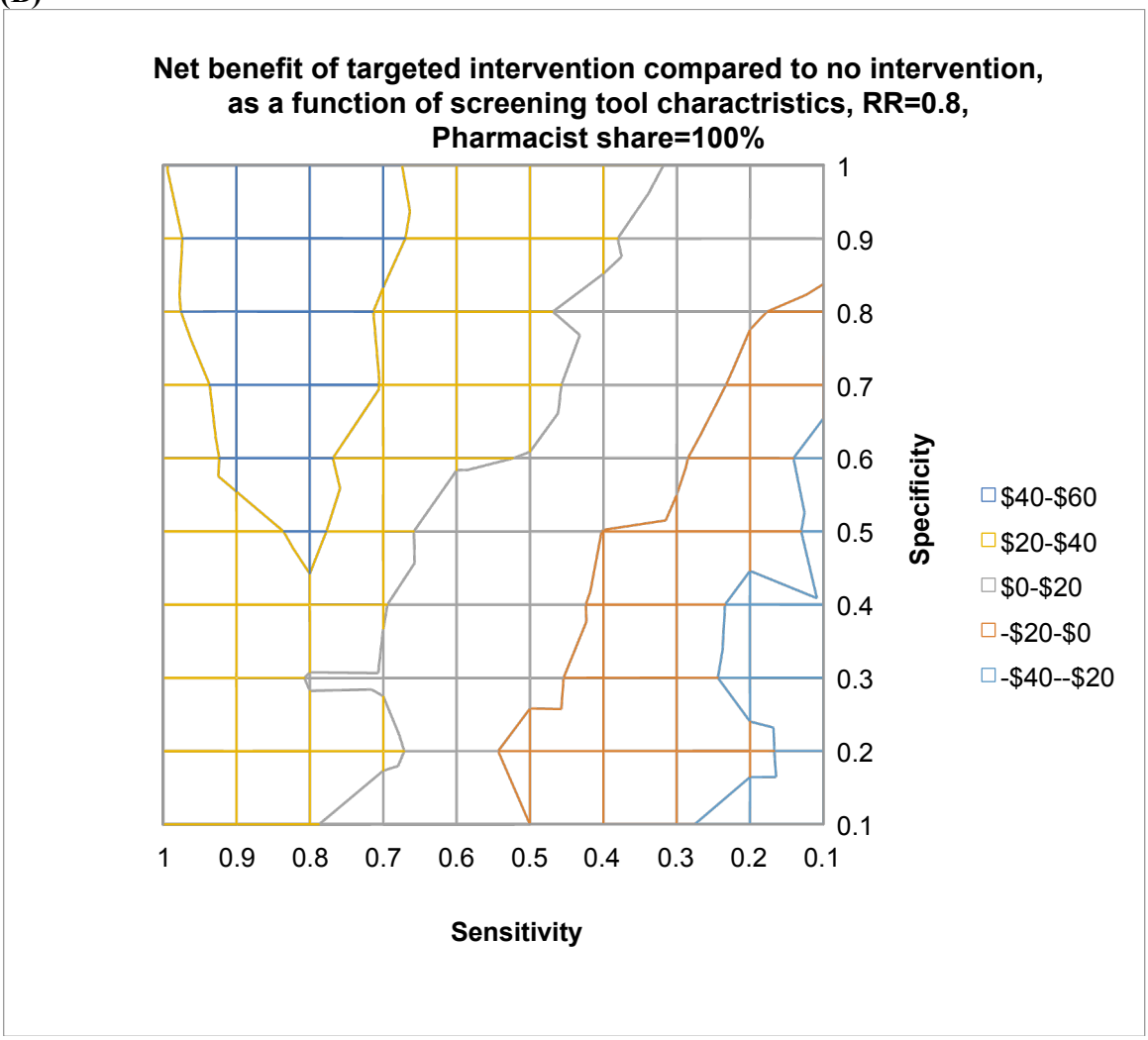
[a]This distribution represents the likelihood of true net benefit and how uncertain we are about the estimated net benefit ($206 per patient) given the uncertainty of our model parameters. For this probabilistic sensitivity analysis, a complete set of model parameters were drawn from their probability distribution and, conditional on that particular set of parameter values, expected net benefit was estimated by simulating outcomes in 10,000 patients. The process was repeated for 1000 distinct realizations of model parameters, and the distribution of net benefit for these 1000 runs has been shown in this Figure.

Figure D. Net Benefit of Targeted Intervention ($) Versus Usual Care for Different Assumptions for Sensitivity and Specificity of Screening Tool

(A)



(B)



(A) Under the base-case scenario that we assume, intervention can reduce discrepancies by 52% and pharmacist involvement was 50%.

(B) We assume that intervention can reduce discrepancies by 20% and that pharmacist involvement was 100%. Net benefit of nontargeted intervention compared with usual care was $30 per patient under this scenario.

These Figures show the expected net benefit of targeted intervention for a given sensitivity and specificity of the screening tool. For example, assuming that sensitivity and specificity of the screening tool both were 70%, the net benefit would be expected to be in the $100-$150 range under the base-case scenario.