Cost-Effectiveness Analysis of a Pharmacist-Led Medication Therapy Management Program: Hypertension Management

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ABSTRACT

Objectives: Uncontrolled hypertension is a common cause of cardiovascular disease, which is the deadliest and costliest chronic disease in the United States. Pharmacists are an accessible community healthcare resource and are equipped with clinical skills to improve the management of hypertension through medication therapy management (MTM). Nevertheless, current reimbursement models do not incentivize pharmacists to provide clinical services. We aim to investigate the cost-effectiveness of a pharmacist-led comprehensive MTM clinic compared with no clinic for 10-year primary prevention of stroke and cardiovascular disease events in patients with hypertension.

Methods: We built a semi-Markov model to evaluate the clinical and economic consequences of an MTM clinic compared with no MTM clinic, from the payer perspective. The model was populated with data from a recently published controlled observational study investigating the effectiveness of an MTM clinic. Methodology was guided using recommendations from the Second Panel on Cost-Effectiveness in Health and Medicine, including appropriate sensitivity analyses.

Results: Compared with no MTM clinic, the MTM clinic was cost-effective with an incremental cost-effectiveness ratio of $38,798 per quality-adjusted life year (QALY) gained. The incremental net monetary benefit was $993,294 considering a willingness-to-pay threshold of $100,000 per QALY. Health-benefit benchmarks at $100,000 per QALY and $150,000 per QALY translate to a 95% and 170% increase from current reimbursement rates for MTM services.

Conclusions: Our model shows current reimbursement rates for pharmacist-led MTM services may undervalue the benefit realized by US payers. New reimbursement models are needed to allow pharmacists to offer cost-effective clinical services.

Keywords: clinical, cost-effectiveness, economic, economic analysis, healthcare costs, medication management, medication therapy management, models, pharmaceutical services, pharmacotherapy, pharmacology.

Introduction

Cost-effectiveness analyses (CEA) have become an important tool to help decision makers better understand how to deliver healthcare efficiently. CEA have important limitations to consider when interpreting the results. For example, inputs for the CEA may be derived from heterogeneous populations or weak study designs or may require assumptions owing to unavailability of data. Additionally, evidence used in the model may not represent the nuance and complexities of the clinical setting. Nevertheless, these potential limitations are addressed or acknowledged and appropriate methodologies employed, CEA provide valuable information on the clinical and economic trade-offs resulting from the allocation of healthcare resources for a population.1

Nearly 50% of the US population has hypertension and about 10% have a history of coronary heart disease, heart failure, or stroke.2 This makes cardiovascular disease (CVD) the deadliest and costliest chronic disease in the United States. The average annual direct medical cost of CVD and stroke was over $210 billion from 2014 to 2015. The 2017 hypertension guideline revision increased the volume of patients with hypertension by lowering the threshold for being considered hypertensive to 130/70 mmHg.3 Uncontrolled hypertension causes target organ damage and significant disease burden on the community.4

Pharmacists are an important community medical resource and are frequently considered the most accessible primary healthcare provider.5 Easy accessibility positions pharmacists to improve healthcare efficiency and improve patient health, especially for a population with multiple and complex chronic conditions, such as hypertension and diabetes. Pharmacists use their training in medication education, motivational interviewing, adverse event monitoring, and medication and disease management during medication therapy management (MTM) visits to improve patient outcomes.6 Research surrounding MTM typically includes intermediate medication-related outcomes such as avoidance of drug-related adverse events, increased adherence,
and improvement of clinical outcomes. Nevertheless, longer-term outcomes, costs, and value of the program are not known.

Several studies investigating the effectiveness and economic impact of MTM services have reported medication-specific outcomes such as identification of subtherapeutic doses, non-adherence, and untreated indications. Many commonalities exist across MTM services; however, different policies and procedures across organizations create important heterogeneity in scope and intensity of services provided. Additionally, owing to the voluntary nature of receiving MTM services, study designs are prone to selection bias. Yet, research consistently reports real-world improved outcomes. Brenner et al. followed MTM patients and controls for 6 months after the MTM service and reported an increase in medical costs from preintervention to postintervention in the control group while the intervention group saw a slight decrease. The observational design and unadjusted baseline characteristics limit the ability to draw conclusions. The benefits of MTM are typically reported over short observational windows owing to lack of time and resources. Uncaptured long-term outcomes may be a significant limitation to the demonstration of value of MTM services. Our study addresses the gap in evidence between intermediate improvements in clinical outcomes and long-term benefits in health, quality of life, and economic efficiency by modeling the blood pressure-lowering effect of the MTM service to avoidance of CVD events. Current reimbursement models may not allow for pharmacists to devote their time to providing comprehensive and proactive MTM services because of a higher opportunity cost of dispensing prescriptions. Structured value assessment of specific pharmacist-led services is needed to substantiate reimbursement and demonstrate long-term value for money. Therefore, this research sets out to investigate the cost-effectiveness of a pharmacist-led comprehensive MTM clinic compared with no clinic for 10-year primary prevention of stroke and CVD events in patients with hypertension.

**Methods**

**Setting, Population, Perspective, and Threshold**

University of Illinois Health & Hospital System (UI-Health) offers a fully integrated pharmacist-led MTM clinic. The clinic deviates from traditional Centers for Medicare and Medicaid Services–reimbursed MTM services by providing proactive, comprehensive, monthly face-to-face visits to any patient in need of global medication and disease state assistance. The clinic operates out of UI-Health’s Outpatient Care Center with 3 residency trained clinical pharmacists providing longitudinal care that includes, but is not limited to, medication reconciliation, optimization of a personalized and evidence-based medication regimen, adverse event monitoring, adherence assistance, and care coordination. All visits are documented in the patient’s electronic medical record, and medication changes are made in collaboration with the patient’s providers. The clinic averages 200 patients and 12 visits per patient per year, including 160-minute initial visit and 11 30-minute follow up visits. Services provided at the UI-Health MTM clinic have evolved since its inception in 2004 and now offer elements of comprehensive medication management. Nevertheless, for consistency with the clinic’s official name and previous publications, it will be referred to as an MTM clinic in this paper.

Clinical-effectiveness inputs into the model are derived from a recent published study on UI-Health’s MTM clinic. The observation window for the study was from 2001 to 2011 and included 158 MTM clinic patients with diabetes or hypertension and 158 controls who were matched on age, sex, and comorbidities. The authors used a difference-in-difference analysis to investigate the mean change in A1C, diastolic blood pressure, systolic blood pressure (SBP), and emergency department and hospital admissions at 6 and 12 months. The MTM clinic patients experienced an 8.2-mmHg (P = .0018) decrease in SBP and a 0.63% (P = .0160) decrease in A1C at 12 months compared to controls. Patients who did not receive the MTM service experienced an increase in SBP over the 52-week observation period. The average age of patients included in the study was 70 years old, and 60% were female.

To determine whether the results are cost-effective, a willingness-to-pay (WTP) threshold of $100 000/QALY was chosen. Additional threshold analyses were performed at $50 000/QALY and $150 000/QALY to determine value-based reimbursement prices at those thresholds. Fixed WTP thresholds are used to make coverage decisions in some countries such as the United Kingdom and Thailand; however, a WTP threshold has not been developed in the United States for many reasons. The WHO does not take a stance on fixed WTP thresholds, but the Commission for Macroeconomics and Health suggest that dynamic thresholds ranging from 1 to 3 times the national gross domestic product per capita plus additional QALY gained may be reasonable. The US gross domestic product per capita was $62,795 in 2018, suggesting a WTP threshold between $60,000/QALY and $180,000/QALY may be acceptable in the United States. The Institute for Clinical and Economic Review uses a threshold range from $100,000 and $150,000/QALY to calculate the health-benefit benchmark price.

To assess the cost-effectiveness of a pharmacist-led MTM service, a semi-Markov model was developed using cohort simulation. A semi-Markov model was used to incorporate time-varying mortality. The population of interest included patients with hypertension and no history of prior CVD (primary prevention). The setting of this intervention was a community health center with pharmacy services or a community pharmacy that offers comprehensive MTM services. The model investigated a 10-year time horizon and a cycle length of 1 year and was performed from the payer perspective. Methodological aspects of the model were guided by the recommendations from the Second Panel on Cost-Effectiveness in Health and Medicine and the Consolidated Health Economic Evaluation Reporting Standards checklist was used to guide proper reporting.

**Model Structure**

The model structure was designed to capture the value of the SBP-lowering effect observed in the retrospective controlled cohort study from the UI-Health MTM clinic and to incorporate the capabilities of risk prediction equations to estimate likelihood of incident cardiovascular disease (Fig. 1). The average number of patients who attend the MTM clinic was 200, which was used as the size of the hypothetical cohorts. The model included 6 mutually exclusive health states (hypertension [primary prevention], stroke, myocardial infarction [MI], other [peripheral artery disease, angina, and transient ischemic attack], history of CVD [chronic CVD], and death) and 3 tunnel states (stroke recovery, MI recovery, and other recovery). The tunnel states were between the respective CVD event and recovery, and represented the nonacute status of patients who experienced a CVD event the previous year where healthcare utilization and quality of life were affected as the patient moved from the CVD event to a stable recovery phase. All patients entered the model in the primary prevention health state. Patients could then transition to 1 of the 3 cardiovascular event states (stroke, MI, other) or death, with transitions occurring up to once per year. Patients can transition
from a CVD event health state back into the same CVD event, into one of the other CVD events, to the recovery state, or to death. If the patient did not transition to a recurrent event, a different CVD event, or death they moved to a recovery state, which is specific to each CVD event. Once in the recovery state, patients transitioned to another CVD event, death, or history of CVD. The history of CVD represented a health state where the patient was stable from the event. Simulated patients still required increased attention to prevent recurrence and maintain quality of life. Lastly, patients could transition to another CVD event or death from the history of CVD state.

Function

The model was used to determine the total direct healthcare costs and total number of quality-adjusted life years (QALYs) accrued by the hypothetical cohorts of patients, MTM clinic and no MTM clinic. The costs and QALYs were discounted to represent their net present value at a rate of 3% per year. The life-table method was used to prevent overestimation and underestimation of patients in each cycle caused by all patients transitioning at the end of a cycle.

Transition Probabilities

The office-based Framingham Risk Equation was used to calculate the 10-year CVD event risk of the 2 cohorts, MTM cohort and control. The characteristics that were included in the nonlaboratory equation were age, diabetes, smoking status, total cholesterol, treatment for hypertension, body mass index, and SBP. Smoking status was not collected during the study and was missing. The missing smoking status for each patient was imputed by extrapolating their likelihood of smoking from sex-specific smoking prevalence in Illinois for 2018. The baseline patient characteristics from the UI-Health MTM study were entered into the Framingham Risk equation as being 8.2 mmHg lower, the mean reduction observed in the Moran et al study. Ten-year risks of CVD events were calculated, transformed to 1-year risks (to meet the 1-year cycle structure) using Fleurence and Hoolenbeak’s method. We assumed constant 1-year risks over the 10 years owing to lack of data to support time-varying risk. To test this assumption, we developed a scenario analysis with a linearly increasing risk of CVD events over the 10 years.

With the exception of general mortality rates, the remaining transition probabilities were identified in the literature referenced in Heart Disease and Stroke Statistics—2019 Update. The type of CVD event a patient transitions to from primary prevention was based on the proportion of patients with incident CVD who have a stroke, MI, or other (23%, 22%, and 55%, respectively). Transition probabilities to the same CVD event (eg, stroke to stroke) reflected 1-year recurrence estimates. Transition probabilities to other CVD events (eg, stroke to MI) were set to mimic the risk of moving to a respective event from the primary prevention health state. Transition probabilities moving from a CVD event to death were based on annual event-specific mortality rates. Transition probabilities to another CVD event from a recovery state represented the risk of recurrence 1 to 2 years post-CVD event and were calculated by transforming a 5-year risk of a recurrent event to a 2-year risk using methods described above. Transition probabilities from history of CVD to another event were calculated using the same method used for recurrence from the recovery states. Mortality rates for nonevent health states were obtained from United States life tables and were time-varying over 10 years based on the average age of the cohort.

Cost and Utility Inputs

The costs and utility values for each health state are listed in Table and were obtained from a thorough systematic literature review. The systematic literature review was conducted using PubMed and Embase and yielded 1895 studies for utility values and 825 studies for costs. Four coauthors screened titles,
SBP-lowering effect required to be cost-effective at $100 000/QALY. A fifth scenario analysis incorporated linearly increasing risk over the 10-year time horizon to test the assumption of constant CVD risk during the 10 years. Understanding adherence is challenge, we performed a sixth scenario analysis that investigated the cost-effectiveness if 50% of patients in the MTM cohort became fully nonadherent and experienced a full loss of effect after 1 year.

Results

One hundred and twenty patients were included in the cohort; 38 patients were excluded from the risk calculation because of a history of CVD. The 8.21-mmHg decrease in SBP experienced by the MTM cohort translated to a 3.3% decrease in 10-year cardiovascular event risk compared to the no MTM cohort (39.6% vs 42.9%) and a 0.46% decreased annual risk. The difference in risk between the MTM cohort and no MTM cohort was transformed into a risk ratio to prevent effectiveness estimates from converging during the 1-way sensitivity analysis. Base-case cost-effectiveness results are listed in Table 2. Under the base-case assumptions, our model estimated that each patient in the MTM cohort lived 0.02 years longer, experienced 0.09 more QALYs, and had 0.05 fewer CVD events compared with the no MTM cohort. MTM cohort incremental costs were $3214 compared with the no MTM cohort. At the clinic population level (200 patients) the MTM cohort lived 4.5 years longer, experienced 18 more QALYs, and had 10 fewer CVD events compared with the no MTM cohort. Incremental costs of the MTM cohort compared to no MTM cohort were $1104 022 but prevented $461232 in direct medical costs for a net cost of $642 790 over 10 years. The resulting incremental cost-effectiveness ratio (ICER) for the MTM service was $38 778 per QALY gained.

Upon 1-way sensitivity analysis (Fig. 2), the ICER was most sensitive to variance in the risk ratio of relative effectiveness between no MTM and MTM. The ICER varied from $4212/QALY to $133 000/QALY at the upper bound (1.234) and lower bound (0.992) ranges of the risk ratios, respectively. The ICER remained under the commonly cited WTP threshold of $100 000/QALY, with the exception of the lower-bound values of the risk ratio of having an initial CVD event. The utility estimate for primary prevention, risk ratio of relative effectiveness, proportion of CVD events that were MI, and cost of the history of CVD health state were the most sensitive parameters in the model. The utility estimate for primary prevention strongly dictated the quality-of-life benefit of preventing CVD events. The proportion of CVD events that are MI have a large impact, because the annual cost of treating an MI was greater than the other CVD events. The cost of the history of CVD state is a sensitive parameter, because most patients eventually end up in this health state. The scenario analysis incorporating increasing risk over 10 years increased the ICER to $66 711/QALY. The scenario analysis performed to investigate 50% adherence after year 1 in the MTM cohort resulted in an ICER of $27 407/QALY. The ICER was lower in the 50% adherence scenario analysis
Figure 2. Tornado diagram evaluating impact of model variables on incremental cost-effectiveness ratio.

Figure 3. Incremental cost-effectiveness acceptability curve for MTM clinic compared with no clinic.
because of the decreased costs on the MTM clinic, whereas the effectiveness was not affected as much because the first year of 100% adherence prevented patients from going down the cascade of CVD in later years.

The 10,000-iteration Monte Carlo simulation (Fig. 3) showed consistency with the deterministic base-case results. The MTM clinic was cost-effective 58% of the time, 88% of the time, and 96% of the time at WTP thresholds of $50,000/QALY, $100,000/QALY, and $150,000/QALY, respectively. The NMB was $993,294 at a WTP of $150,000/QALY, respectively. The value of MTM services has largely been confined to the reporting of intermediate clinical outcomes, such as adherence and medication-related quality measures. By modeling the long-term clinical and economic benefits, we showed the MTM service to be cost-effective, which may be used promote the expansion and reimbursement of pharmacist services.

To put coverage decisions into perspective, this intensive pharmacist-led MTM service can be compared to the cost-effectiveness of commonly covered hypertension medications and interventions. Angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers are recommended agents known to lower SBP by about 8 mmHg, similar to the MTM effectiveness at UI-Health. A recent systematic review of cost-effectiveness studies of antihypertensive medicines reviewed 76 studies, including angiotensin-converting enzyme inhibitors and angiotensin-receptor blockers. All reviewed studies included showed cost-effectiveness compared with a patient who does not visit the MTM clinic, when monitored, as seen in the UI-Health MTM clinic program, limiting continuity of care. The UI-Health MTM clinic is not currently reimbursed for their services and is financially able to provide these innovative services owing to support through the 340B program.

Results of the threshold analyses are listed in Table 4. Reimbursement rates for follow-up visits could be increased by 17%, from $60 to $70 per visit, and still be cost-effective at a $50,000/QALY gained threshold. Both initial and follow-up visit reimbursement rates could be increased by 95%, from $120 to $234 and from $60 to $117, and still be cost-effective at a $100,000/QALY gained threshold. To remain cost-effective at a $150,000/QALY threshold, initial and follow-up visit reimbursement could be increased by 170%, from $120 to $324 and from $60 to $162. These increases in reimbursements per visit translate to annual reimbursements of $644/patient/year, $1076/patient/year, and $1490/patient/year relating to $50,000/QALY, $100,000/QALY, and $150,000/QALY thresholds, respectively. Assuming current

### Table 3. Calibration of model findings with epidemiological literature.

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Model Findings</th>
<th>Epidemiology literature</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age adjusted prevalence of CVD</td>
<td>34%</td>
<td>37.96%</td>
</tr>
<tr>
<td>Proportion of deaths related to CVD events</td>
<td>30%</td>
<td>29%</td>
</tr>
<tr>
<td>Prevalence of stroke</td>
<td>8.125%</td>
<td>12.64%</td>
</tr>
<tr>
<td>Age adjusted incidence of new or recurrent Myocardial infarction (annual)</td>
<td>11.00 per 1000</td>
<td>10.95 per 1000</td>
</tr>
<tr>
<td>Prevalence of other (TIA, PAD, angina)</td>
<td>16.5%</td>
<td>16.34%</td>
</tr>
<tr>
<td>SBP lowering effect (8.2 mmHg) on stroke incidence</td>
<td>21%</td>
<td>41%</td>
</tr>
</tbody>
</table>

CVD indicates cardiovascular disease; PAD, peripheral artery disease; SBP, systolic blood pressure; TIA, transient ischemic attack.

### Table 4. Health benefit benchmarks – threshold analyses.

<table>
<thead>
<tr>
<th></th>
<th>$50,000 per QALY gained</th>
<th>$100,000 per QALY gained</th>
<th>$150,000 per QALY gained</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reimbursement per visit</td>
<td>$120 initial visit</td>
<td>$234 initial visit</td>
<td>$324 initial visit</td>
</tr>
<tr>
<td></td>
<td>$70 follow-up</td>
<td>$117 follow-up</td>
<td>$162 follow-up</td>
</tr>
<tr>
<td>Annual reimbursement per patient (“Netflix model”)</td>
<td>$644/patient/year</td>
<td>$1076/patient/year</td>
<td>$1490/patient/year</td>
</tr>
<tr>
<td>Reimbursement increase (%)</td>
<td>17</td>
<td>95</td>
<td>170</td>
</tr>
</tbody>
</table>

QALY indicates quality-adjusted life-year.
rates for lower SBP effects. Additionally, MTM providers can address uncertainty by standardizing processes and providing evidence to support the effectiveness of their clinic. Chain pharmacies may have an advantage because of standardized MTM operations. Nevertheless, health system pharmacies, academic centers, and clinics may be able to leverage their potential heightened clinical capabilities and ability to track outcomes via access to electronic health records.

Pharmacist-led services may be suitable candidates for outcomes-based reimbursement contracting by collecting intermediate outcomes, such as SBP during visits. Outcomes contracts could target clinical outcomes such as SBP or, for clinics with less resources, a utilization metric such as number of visits a year may be appropriate.

Another potential model for reimbursement is a payer licensing agreement (PLA), also referred to as a “Netflix model” of reimbursement. In a PLA, the payor licenses the service with the right to offer it to all patients who qualify for receiving the service. Simply put, a PLA is a membership-style reimbursement where the payor reimburses the MTM provider for an unlimited amount of MTM services for a year. For example, considering the MTM service was cost-effective at up to $1490 per patient per year, the payer would reimburse the MTM provider $1490 per patient and the patient would be eligible to receive the service as many times as needed during that year. This prevents barriers of access such as a rejected claim because a patient scheduled a visit too soon after the previous visit. Many patients with multiple chronic conditions have transportation or scheduling issues limiting their flexibility in scheduling visits. The Netflix model addresses these types of important barriers to access.

There are important limitations to this study. The population at UI-Health represents mainly underserved African Americans and Latin Americans, which may not be generalizable to other clinics. Additionally, the cohort used to develop the Framingham Risk Equation was mostly white. Nevertheless, literature has showed the equation to be valid in African Americans and Latin Americans. Smoking status was not documented in the UI-Health MTM clinical study, which is a parameter in the Framingham Risk Equation. Therefore, we had to impute the missing smoking status based on a distribution of smoking probability stratified by the state of Illinois and sex. Additionally, the population in the UI-Health MTM clinical study were elderly and had complex medical comorbidities, which can lead to uncertainty in risk estimations from the Framingham Risk Equation.

In addition to hypertension management, the pharmacist-led MTM visit includes other elements of care that are not included in the current cost-effectiveness model. We did not include other benefits observed in the UI-Health MTM clinic study, such as lower A1C, because they are not included in the Framingham equation. Therefore, this current evaluation underestimates the cost-effectiveness and proposed reimbursement rates. Had the model included other outcomes, the pharmacist-led MTM service would have demonstrated better cost-effectiveness. Therefore, the proposed reimbursement rates may be low estimates of cost-effective rates because benefits beyond SBP lowering were not included in the valuation; however, they are provided in the real-world clinic.

Conclusion

Our model suggests the pharmacist-led MTM clinic provided service is cost-effective from a US payer perspective for the management of hypertension. Pharmacists provide significant value to the health system in the form of avoidance of CVD events and improved quality of life. This model may be used to support reimbursement reform for pharmacist-provided services, allowing pharmacists to perform more clinical services.

Supplemental Material

Supplementary data associated with this article can be found in the online version at https://doi.org/10.1016/j.jval.2020.10.008.

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 Provision of study materials or patients: Tilton, Jun, Scott-Horton
Administrative, technical, or logistic support: Touchette
Supervision: Touchette

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