USC School of Pharmacy

Cost-Effectiveness Analysis of Non-Invasive Screening in patients with Diabetic Foot Ulcers

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Abstract

Introduction:

The prevalence of diabetic foot ulcers (DFU), one of the most common complications of diabetes, is rising fast along with the prevalence of diabetes. As a well-known risk factor of lower extremity amputation, diabetic foot ulcers are costly in pecuniary and nonpecuniary means. However, early screenings within low-risk diabetic foot ulcers patients are not recommended on clinical guidelines. We sought to find the cost-effectiveness of non-invasive screening test ankle-brachial index (ABI) and transcutaneous oxygen measurement (TcPo2) for diabetic foot ulcers to achieve better clinical outcomes.

Methods:

We used a hybrid model that combined decision tree with Markov modeling to evaluate the cost-effectiveness of ABI and TcPo2 for patients with diabetic foot ulcers. The hypothetical cohort aged 66 was evaluated annually until the endpoint. We calculated costs and quality-adjusted life-years (QALYs) based on the previous studies and further evaluated the incremental cost-effectiveness ratio (ICER) and incremental net monetary benefit (iNMB) with a $50,000 baseline willingness-to-pay threshold. We had one-way sensitivity analysis performed and produced tornado diagrams to evaluate the uncertainty of our key parameters. We had probabilistic sensitivity analysis performed and produced ICER planes and cost-effectiveness acceptability curves to summarize the impact of uncertainty on the results.

Results:

The total cost with the ABI screening test to diabetic foot ulcers increased by $16,814.01 on average per patient compared with the costs of no screening, but each of them gained 0.56 more QALYs in return. The ICER was $30,202.78 per QALY, and the iNMB was $11,021.20. The cost of screening with TcPo2 to diabetic foot ulcers patients increased by $53,479.21 on average per person compared to the costs of no screening, and QALYs increased by 2.18 in return. The ICER was $24,488.24 per QALY, and the iNMB was $55,714.44.

Conclusions:

Non-invasive screening tests are cost-effective using a $50,000 willingness-to-pay threshold. They can improve patients' quality of life with diabetic foot ulcers in a cost-effective way.

INTRODUCTION & METHODS

Diabetic foot ulcers are a common but deadly complication of diabetes mellitus. The epidemiological study had shown that about 15% of patients with diabetes suffer from diabetic foot ulcers each year[1], caused by a deep tissue lesion. DFU infection is the major risk factor for lower limb amputation, which carries a 40% mortality in one year, 35%-65% in three years, and 39%-80% in five years[2].

Accurate diagnosis of the severity of diabetic foot ulcers is an essential step in the DFU management regimen. Previous studies have shown that about 85% of DFU related amputations may be prevented with early diagnosis and appropriate treatments[3]. Unfortunately, non-invasive screening tests like ankle-brachial index (ABI) are not recommended to low-risk patients on clinical guidelines[4].

This study sought to identify a relationship between costs and effectiveness of non-invasive screening test ankle-brachial index and transcutaneous oxygen measurement (TcPo2) for patients with diabetic foot ulcers from a U.S. health care sector perspective.

A cost-effectiveness analysis was performed under the basic principles of the U.S. Public Health Service as outlined by Gold et al.[5], Neumann et al.[6], and utilized a hybrid model that combines a decision tree and Markov model, demonstrated in detail by Briggs et al.[7] This study compared health outcomes and costs from a U.S. health care sector perspective. No human subjects or patient data was involved in the analysis.

Study Population

The patient population of the analysis was set in the U.S. The prevalence of diabetic foot ulcers in the U.S. was set to be 13%[9] for the base-case analysis, and the total population of the U.S. in 2021 was around 330 million by the time it was recorded. As a result, the calculated diabetic foot ulcers population, around 43 million in the U.S., was used for the base-case analysis. Although diabetic foot ulcers can occur at any age, they are most prevalent in patients aged 45 and over. The analysis utilized the average age of diabetic foot ulcers patients, at 66, reported by Skrepnek et al.[10]

Utilities

The utility of the patient in each Markov state is displayed. Utilities for healthy patients in diabetic control, for patients with diabetic foot ulcers, and for amputees were set from Carrington et al[11]. These values were found consistent with major studies estimating the quality of life of relevant patient cohorts.

Utilities			
DF utility	0.6	Gamma	11
Minor amputation utility	0.7	Gamma	11
Major amputation utility	0.7	Gamma	11
Base utility	0.8	Gamma	11
Death	0	Fixed	11

Costs

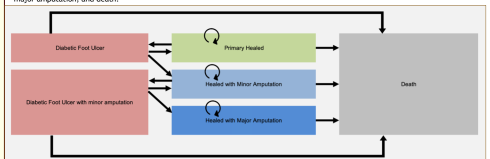
All costs were discounted by 3% and inflated to 2021 U.S. dollars. "DFU cost" refers to the total ulcer-related costs, including pharmacy costs, inpatient hospitalization costs, nursing facility charges, emergency department charges, outpatient office visit charges, and home therapy charges[12]. ABI and TcPo2 screening costs were confirmed with the Centers for Medicare and Medicaid Services Physician Fee Schedule. The cost of minor and major amputations was assumed to be of the foot and cost the same amount[13].

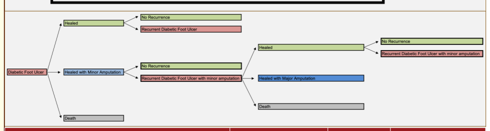
Costs			
ABI screening cost	$ 108	Gamma	15
TcPo2 screening cost	$ 223	Fixed	16
DFU cost	$ 22,259	Gamma	12
Minor amputation cost	$ 74,654	Gamma	13
Major amputation cost	$ 74,654	Gamma	13

METHODS cont. & RESULTS

Markov Model

The Markov model, programmed entirely in Microsoft Excel, had cycle lengths of 1 year and was simulated with a life-long time horizon. The information required in the Markov model was generated from the decision tree regarding whether to screen with one of our choices. If the screening was being performed, the model began with the initial screening event where patients were predicted to be healed, amputated, or dead according to the sensitivity and specificity reported in the meta-analysis by Wang et al.[8] For ABI, the sensitivity, and specificity for predicting healing was 48% and 52%, and for predicting lower-limb amputation was 52% and 73%. For TcPo2, the values were 72%, 86%, 75%, 58%, respectively. Since the predictability did not specify with non-healing diabetic foot ulcers, the non-healing diabetic foot ulcers patients were treated as immediate recurrence in the analysis. Also, to account for double amputees, the patients predicted to be in the amputated node the first time and having a recurrent diabetic foot ulcers in the same year would undergo another screening event and get predicted one more time. The Markov model has six health states: diabetic foot ulcers, diabetic foot ulcers with minor amputation, primary healed, healed with minor amputation, healed with major amputation, and death.





Transition probabilities	Value	Distribution	Source
Sensitivity of ABI predicting healing	48.0%	Uniform	8
Specificity of ABI predicting healing	52.0%	Uniform	8
Sensitivity of ABI predicting amputation	52.0%	Uniform	8
Specificity of ABI predicting amputation	73.0%	Uniform	8
ABI, Probability of DFU to Healed	13.0%		
ABI, Probability of DFU to Minor Amputation	22.3%		
ABI, Probability of DFU to Death	64.7%		
noABI, Probability of DFU to Healed	13.0%		
noABI, Probability of DFU to Minor Amputation	8.9%		
noABI, Probability of DFU to Death	78.1%		
Sensitivity of TcPo2 predicting healing	72.0%	Uniform	8
Specificity of TcPo2 predicting healing	86.0%	Uniform	8
Sensitivity of TcPo2 predicting amputation	75.0%	Uniform	8
Specificity of TcPo2 predicting amputation	58.0%	Uniform	8
TcPo2, Probability of DFU to Healed	43.5%		
TcPo2, Probability of DFU to Amputation	21.1%		
TcPo2, Probability of DFU to Death	35.5%		
noTcPo2, Probability of DFU to Healed	4.6%		
noTcPo2, Probability of DFU to Amputation	6.1%		
noTcPo2, Probability of DFU to Death	89.3%		
Probability, stayed in healed	60.0%		
Probability, recurrent DFU from healed	40.0%	Uniform	14

Outcomes

The model calculated the total cost for each patient entering each of the disease states until having a major amputation or death, whichever comes first. Total quality-adjusted life-years (QALYs) were also calculated for each patient. Model outcomes were reported as the difference in costs and QALYs, the incremental cost-effectiveness ratio (ICER), between screened and unscreened groups. Incremental net monetary benefits (iNMB) were also reported with the base-case willingness-to-pay threshold equals $50,000, which approximately equals U.S. gross domestic product per capita.

Sensitivity Analysis

One-way sensitivity analyses were performed and were ranked in a tornado diagram with the parameter that impacts the ICER or iNMB the most on the top of the diagram. For parameters that do not have reported confidence intervals, 20% mark up and down were calculated for the purpose of the analysis.

The model underwent 5,000 iterations of Monte Carlo simulation using the distribution suggested in table 1 for probabilistic sensitivity analysis to trace out the uncertainty. A cost-effectiveness acceptability curve was also constructed for both screening options, with willingness-to-pay thresholds increased from $0 to $150,000.

Results

Results for the base-case analysis showed that Diabetic foot ulcers patients who chose to have ABI screening were estimated to spend $16,814.01 more on average than diabetic foot ulcers patients with no screening, but they gained 0.56 more QALYs in return. The ICER was $30,202.78 per QALY. The iNMB was $11,021.20.

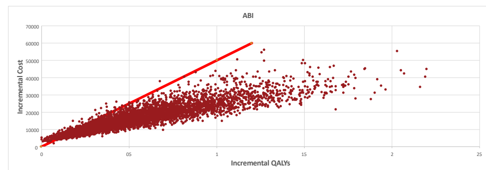
Diabetic foot ulcers patients who chose to have TcPo2 screening were estimated to spend $53,479.21 more on average than diabetic foot ulcers patients with no screening, and they gained 2.18 more QALYs in return. The ICER was $24,488.24 per QALY. The iNMB was $55,714.44.

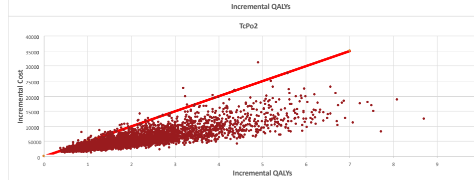
The ICER plane from probabilistic sensitivity analysis compared with and without ABI screening, with each dark-red mark representing a Monte Carlo simulation, 5,000 in total. 94% of iterations were cost-effective, with the willingness-to-pay threshold equaling $50,000, marked in the red line. ICER plane with and without TcPo2 screening, with 5,000 iterations in total, 98.6% were cost-effective with willingness-to-pay threshold equals $50,000.

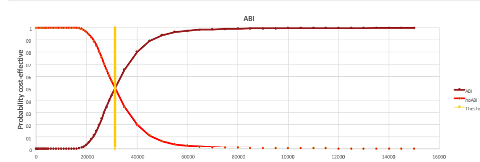
A tornado diagram that ranked the parameters impacting the ICER of with and without ABI the most is presented. The parameter that most influenced the ICER was prevalence of DFU, at the top of the diagram. ICER increased to $39,762.76 per QALY when the prevalence dropped to 8.3%. For iNMB, the tornado diagram showed that the specificity of ABI predicting amputation was the most influential. The iNMB increased to $23,257.62 if the specificity increased to 81%.

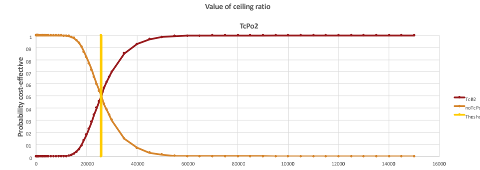
Similarly, tornado diagrams regarding ICER and iNMB for with and without TcPo2 were shown, respectively. The parameter that impacted ICER the most was the average cost of diabetic foot ulcers. The ICER increased to $37,083.52 per QALY if the cost increased to $46820.96. The parameter that impacted iNMB the most was the specificity of TcPo2 for predicting amputation, as well. The iNMB increased to $61,696.41 if the specificity increased to 64%.

The cost-effectiveness acceptability curves showed that screening with ABI was not cost-effective until the willingness-to-pay threshold increased to $31,300 per QALY, approximately; screening with TcPo2 was not cost-effective until the willingness-to-pay increased to $25,800 per QALY, approximately.









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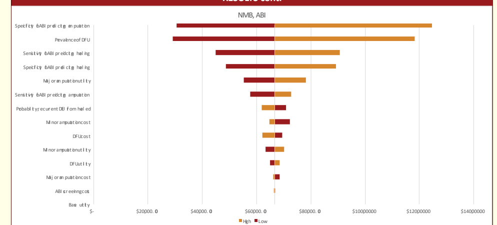

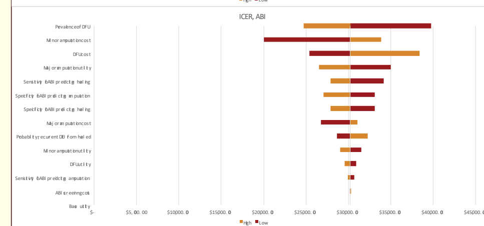

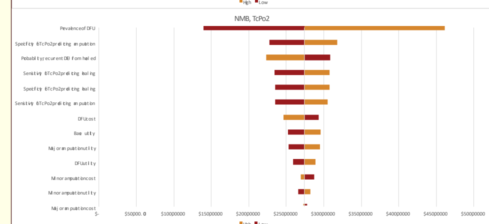

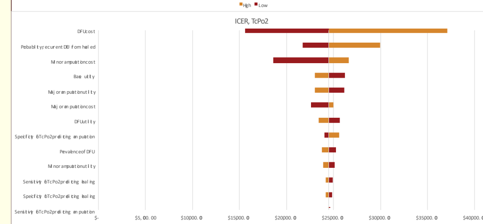

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