Predicted Costs and Outcomes From Reduced Vibration Detection in People With Diabetes in the U.S.

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OBJECTIVE — The ability to perceive vibration (vibration detection) has been shown to be a good predictor of the long-term complications of diabetic peripheral neuropathy (DPN). We aimed to estimate the predicted complications and costs for the U.S. health care system associated with reduced vibration detection (vibration perception threshold ≥25 V), estimated using a quantitative sensory testing device.

RESEARCH DESIGN AND METHODS — A Markov model was constructed for a hypothetical cohort of people with DPN. The model was run over a 10-year period using Monte Carlo simulations to estimate disease progression, predicted costs, and complications according to vibration detection levels.

RESULTS — The average individual with reduced vibration detection incurs approximately five times more direct medical costs for foot ulcer and amputations, yields 0.18 fewer quality-adjusted life-years, and lives for ~2 months less than an average individual with normal vibration detection.

CONCLUSIONS — The treatment of foot ulceration and amputation is time-consuming and expensive. If individuals with reduced vibration detection could be identified, then preventative care could be concentrated on those patients, potentially saving valuable resources and improving health outcomes.

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Approximately 15% of people with diabetes develop at least one foot ulcer during their lifetime (1–6). People with diabetes are 15 times more likely to have an amputation than those without (7). Diabetic foot ulceration and amputations cost U.S. health care payers $10.9 billion in 2001 (8). If at-risk groups could be identified and measures taken to prevent these complications, potentially large cost savings and improvements in health-related quality of life could result.

Diabetic peripheral neuropathy (DPN) increases the risk of foot ulcers and lower extremity amputation. Patients have an increased tendency to unrecognized damage through trauma and pressure. Reduced vibration detection is one of the first signs of polyneuropathy (9), and studies have shown it to be a good predictor of long-term complications of DPN (10–13). Vibration detection can be quantified using an electronic tuning fork that allows vibration to be adjusted depending on the voltage applied. The vibration perception threshold (VPT) is defined as the lowest voltage at which vibration can be detected. VPT has been shown to be a more accurate predictor of ulceration and amputation than three common clinical tests: foot sensation (using cotton wool), ankle reflexes, and vibration sensation (using a 128-Hz tuning fork), with test sensitivity and specificity of 70 and 72%, respectively (13). Moreover, VPT has been reported to have higher positive predictive value than both neuropathy disability score and Semmes-Weinstein monofilaments (14). Although sensory nerve fiber dysfunction is only one of many potential risk factors for diabetic foot ulcers, the ability to identify those with early markers for long-term complications should be of interest to clinicians. Moreover, forecasts of the financial burden associated with long-term complications are of key interest to healthcare financiers and policy makers. Our selection of VPT was based solely on the availability and strength of the published evidence.

In this study we aim to provide an estimate of the economic burden associated with reduced vibration detection and highlight the maximum potential benefits of screening and identifying an effective strategy for prevention of DPN complications. We draw on published evidence and advanced modeling techniques to predict the complications and costs to all U.S. health care payers for people with reduced compared with normal vibration detection. Mathematical modeling is a widely accepted technique for simulating the experiences of patient cohorts in the absence of sufficiently detailed long-term clinical data (15–18). Our model enables us to combine both clinical and economic data in order to estimate the burden of DPN complications in individuals with reduced vibration detection.

RESEARCH DESIGN AND METHODS

— We constructed a Markov model (19) of DPN progression in the U.S. The Markov model is an incidence-based approach to estimating resource use and associated costs and

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Abbreviations: DPN, diabetic peripheral neuropathy; QALY, quality-adjusted life-year; VPT, vibration perception threshold.

A table elsewhere in this issue shows conventional and Système International (SI) units and conversion factors for many substances.

Table 1—*Base case transitional parameter values and distributions*

	Base case value	Mean ± SD	Range	Source (ref.)
Event				
Annual rate of first foot ulceration for VPT ≥ 25 V	0.0495	0.049 ± 0.02	0–0.099	(11)
Annual rate of recurrent foot ulceration for VPT ≥ 25 V	0.1875	0.187 ± 0.08	0–0.375	(11)
Annual rate of first and recurrent foot ulceration for VPT < 25 V	0.0077 ± 0.0025* year	0.028 ± 0.01	0–0.065	(11)
Annual rate of amputation given ulceration	0.059	0.059 ± 0.02	0–0.1188	(21)
Proportion of foot ulcers healed within 12 months	0.694	0.69 ± 0.28	0.388–1	(20)
Utility with amputation	0.7	0.7 ± 0.02	0.65–0.75	(28)
Utility with foot ulceration	0.6	0.6 ± 0.02	0.55–0.65	(28)
Utility with good health	0.8	0.8 ± 0.02	0.75–0.85	(28)

Age-specific mortality rates*	Age (years)	Type 1 diabetic	Age (years)	Type 2 diabetic	(23,24)
	<50	0.013406	<35	0.01	
	55	0.044855	55	0.028	
	65	0.101843	70	0.058	
	>69	0.192797	>74	0.136	

*Linear interpolation was used to calculate age-specific rates between the ages given.

outcomes. Patients with diabetes begin with no ulceration and some remain ulcer free. Others progress to ulceration and remain in that state until healed or progress to amputation. Amputation is modeled as an acute event, and patients return to the equivalent of "healed" after amputation. Patients can die from all causes at any stage in the model. Mortality is dependent on age and DPN state.

Moving from one health state to another is dependent on transition probabilities. We estimated the proportion of patients with diabetes proceeding to each health state and identified the health service contacts and treatments provided at each stage. The outcomes of the model are costs, number of ulcers and amputations, duration of ulceration, life-years, and quality-adjusted life-years (QALYs) by vibration detection level.

Outcomes, rates, and transition probabilities

Rates of foot ulceration and amputation (the probability of healing and health state utility scores) were identified from the literature. The transitional probabilities used in the model and their sources are summarized in Table 1. Progression to ulceration is dependent on the level of vibration detection. We define reduced vibration detection to be a VPT test score of ≥25 V (11,12). The rate of progression to ulceration was taken from data presented in Young et al. (11). In their prospective study of 469 diabetic patients with no history of foot ulceration, <4% of patients with a VPT <25 V developed new ulcers versus almost 20% of those with a VPT ≥25 V. Moreover, no recurrent ulceration was reported in the group of patients with VPT <25 V, whereas 30 recurrent ulcers were reported in the group with VPT ≥25 V. Based on this data, we used an initial annual foot ulceration rate of 0.77% in the cohort with normal vibration detection (VPT <25 V). To control for between-group differences in the duration of diabetes, this rate was increased by 0.25% per annum. In the absence of data on recurrent ulcers for this group, we conservatively assumed that the probability of recurrent ulcers was identical to that for the first ulcer. Additionally, we used annual rates of 4.95 and 18.75%, respectively, for the first and recurrent foot ulceration in the cohort with reduced vibration detection (VPT ≥25 V) (11). These figures are conservative compared with those of Abbott et al. (12) who report a 7.2% incidence of first foot ulceration within 1 year for a sample of 1,035 patients with a VPT ≥25 V.

We modeled the duration of foot ulceration as the residual of the probabilities of healing, amputation, and death. The probability of a foot ulcer healing and the patient returning to a state of no ulceration is taken from Allenet et al. (20). This is the only published study that reports on a cohort of patients for 52 weeks. They estimated that 69.4% of patients receiving conventional treatment for first ulceration were healed within 52 weeks. Duration of ulceration is assumed to be independent of VPT score.

Holzer et al. (21) and Gonzalez and Oley (2) report an annual amputation incidence rate of 0.6% among people with diabetes. Moss et al. (22) reports foot ulceration prevalence rates of 9.5 and 10.5% among type 1 and type 2 diabetes, respectively. Using these data, we estimated a rate of 5.94% for progression from ulceration to amputation. Once patients have foot ulcers, they are equally likely to experience an amputation, regardless of their VPT score.

Mortality for the model is calculated using age-specific all-cause mortality rates for patients with diabetes. All-cause mortality rates for adults with type 1 and type 2 diabetes are based on Rossing et al. (23) and Geiss et al. (24), respectively (Table 1). Our model calculated the weighted average age-specific mortality rates based on proportions of diabetes type used in the model, taken from Young et al. (11), with 59.1% of the cohort type 2 diabetic and the remaining 40.9% type 1 diabetic. Foot ulceration and amputation have been shown to be associated with an increased risk of mortality among people with diabetes (25–27). We adjusted our mortality rates to account for these increases by assuming that the risk of death doubled after ulceration and quadrupled postamputation.

Utility scores were taken from Carrington et al. (28) (Table 1). The study

Table 2—*Health care costs used in the model*

	U.S. dollars, 2001	Proportion
Mean monthly cost		
Foot ulceration		
Not infected	$775.55	0.874
With cellulitis	$2,048.52	0.09
With osteomyelitis	$3,798.27	0.036
Weighted average cost	$999	
Total event cost		
Amputation		
Toe	$22,703	0.39
Foot	$42,673.04	0.12
Leg	$51,280.94	0.47
Weighted average cost	$38,077	

Source: Gordois et al. (8).

used a visual quality-of-life ladder to estimate the impact of diabetic foot ulceration and amputation on utility. Foot ulceration and amputation resulted in reported utility scores of 0.6 and 0.7, respectively. The diabetic control group returned a utility score of 0.8. Utility scores were multiplied by life-years to provide QALYs.

Costs used in the model

The cost data used in the model were estimated in a concurrent cost of illness study (8). We calculated the weighted average monthly cost of foot ulceration based on estimated costs and proportions of "not infected," "with cellulitis," and "with osteomyelitis." Similarly, we calculated the weighted average cost of amputation based on unit costs and proportions of toe, foot, and leg amputations (Table 2). To reflect a positive rate of time preference, costs and benefits were discounted to present values at a rate of 3% (29–31).

Estimation

The model was run over a 10-year time horizon with monthly cycles. We modeled the predicted costs and outcomes for both normal and reduced vibration detection cohorts using Monte Carlo simulations. The Monte Carlo approach simulates a random sample of patients with different rates of events (probabilities) drawn from predetermined distributions. This enabled us to account for uncertainties surrounding health state transition probabilities and utility scores. The main advantage of Monte Carlo simulation, over a basic expected value analysis, is that it allowed us to analyze the distributions of the costs and consequences and to define confidence intervals. The health state utility scores and transition probabilities were all characterized as symmetric triangular distributions (Table 1). This was appropriate for two reasons: minimum and maximum values are fixed, and the most likely value (mode) falls equally between the minimum and maximum.

RESULTS — From the 10,000 Monte Carlo simulations, the reduced vibration detection cohort experienced approximately three times more foot ulcers than the normal cohort (Table 3). This is explained by the higher probability of ulcers in the reduced vibration cohort. There is a greater relative share of recurrent ulcers (32%) in the cohort with reduced vibration detection compared with the normal cohort (5%), explained by the higher probability of recurrent ulcers. The reduced vibration cohort experienced approximately three and one-quarter times more amputations than the normal cohort. This is expected given that the probability of amputation is dependent on foot ulceration.

The mean time to first ulcer in the

Table 3—*Ulceration, amputation, and discounted mean costs and outcomes per person over 10 years*

	Full cohort		10% highest-cost subgroups	
Outcome	Normal vibration*	Reduced vibration†	Normal vibration*	Reduced vibration†
Total foot ulcers (*n*)	1,547	4,722	1,076	1,838
First ulcers (% total)	1,466 (95%)	3,219 (68%)	1,000 (93%)	1,000 (54%)
Recurrent ulcers (% total)	81 (5%)	1,503 (32%)	76 (7%)	838 (46%)
Mean time to first ulcer (years)	5.62 (5.48–5.76)	4.27 (4.17–4.37)	5.19 (5.02–5.35)	2.94 (2.81–3.08)
Mean duration of first ulcer (years)	1.01 (0.96–1.06)	1.11 (1.07–1.14)	1.37 (1.30–1.43)	1.89 (1.80–1.98)
Mean duration of recurrent ulcer (years)	0.92 (0.71–1.12)	1.03 (0.97–1.08)	0.97 (0.76–1.18)	1.41 (1.32–1.50)
Total amputations	97	314	97	314
Mean cost per person	$1,239 ($ 1,182–$1,297)	$6,188 ($ 5,926–$6,449)	$17,594 ($16,758–$18,430)	$40,796 ($39,909–$41,683)
Mean QALYs per person	5.69 (5.65–5.73)	5.51 (5.47–5.54)	5.96 (5.88–6.03)	5.59 (5.52–5.67)
Mean life-years per person	7.14 (7.10–7.19)	7.00 (6.95–7.05)	7.77 (7.68–7.87)	7.70 (7.61–7.80)

Data are means (95% CI) unless otherwise indicated. *VPT <25 V; †VPT ≥25 V.

Table 4—*Sensitivity analysis on reduced vibration cohort*

	Cost	QALYs	Life-years
Base model	$6,188	5.51	7.00
Annual rate of first foot ulceration			
+20%	$7,152 (15.6%)	5.47 (−0.7%)	6.97 (−0.4%)
−20%	$5,065 (−18.1%)	5.55 (0.8%)	7.04 (0.5%)
Annual rate of recurrent foot ulceration			
+20%	$6,413 (3.6%)	5.50 (−0.1%)	7.00 (0.0%)
−20%	$5,853 (−5.4%)	5.51 (0.1%)	7.00 (0.0%)
Proportion of foot ulcers healed within 12 months			
+20%	$5,569 (10%)	5.52 (0.2%)	7.00 (0.0%)
−20%	$6,963 (−12.5%)	5.49 (−0.3%)	6.99 (−0.1%)
Annual rate of amputation given ulceration			
+20%	$6,306 (1.9%)	5.51 (0%)	7.00 (0%)
−20%	$6,037 (2.4%)	5.51 (0%)	7.00 (0%)
Prevalence of type 1 diabetes			
7.5%	$6,531 (5.5%)	5.73 (4.1%)	7.29 (4.2%)
Discount rate			
5%	$5,585 (−9.7%)	5.07 (−7.9%)	6.65 (−5%)
0%	$7,255 (17.2%)	6.27 (13.9%)	7.98 (14%)

Data are discounted mean costs and outcomes (% change from base model) per person over 10 years.

reduced vibration cohort is ~15 months earlier than in the normal cohort, and the mean duration for recurrent ulcers was significantly lower than for first ulcers in both cohorts. This is surprising given that the probability of a foot ulcer healing is equal for first and recurrent ulcers. However, recurrent ulcers occur after first ulcers and therefore are more likely to be censored after 10 years of simulation. That is, some might be in a state of ulceration at the end of the 10-year period, and therefore the time in the ulcerated state is ended in the final period of the model rather than when the ulcer is healed. Similarly, the mean duration of ulcers in the normal cohort was significantly lower than that in the reduced vibration cohort. Individuals were more likely to experience foot ulcers toward the end of the 10-year simulation because the probability of foot ulceration increases with time in the normal vibration cohort. This censoring will underestimate the true mean duration (and costs) of ulcers in the normal vibration cohort.

The average individual with reduced vibration detection incurs approximately five times more costs for foot ulcers and amputations, yields 0.18 fewer QALYs, and lives for ~2 months less than an average individual with normal vibration detection (discounted) over 10 years. These differences were significant at the 1% level ($P < 0.0001$).

The 10% highest-cost subgroups have a shorter time to first ulcer, remain in ulceration longer, incur higher costs, and yield more QALYs and life-years than their full cohort counterparts. The main driver of these results is increased survival. An increase in average life-years results in additional QALYs and longer ulcer duration, resulting in higher costs. Furthermore, the 10% highest-cost subgroups contain all those individuals who required amputation. When comparing the differences between the two highest-cost subgroups with the differences between the full cohorts, the absolute difference in costs and QALYs was greater between the subgroups than the full cohorts. The reduced vibration subgroup yields 0.37 fewer QALYs ($P < 0.0001$) on average per person than the normal subgroup. This is a result of relatively longer ulcer duration in the reduced vibration subgroup, as time spent in ulceration yields lower utility scores. The difference in life-years between the subgroups was smaller than the difference between the full cohorts because the subgroups we selected were those with higher costs, which are associated with longevity and ulceration.

Sensitivity analysis

Sensitivity analysis was performed, varying each parameter by 20% above and below its "base case" expected value. To isolate the impact of varying the parameter from the inherent white noise of simulation, we used the same set of sample values for each distribution (32,33). The key drivers of costs in the reduced vibration detection cohort are the probability of first foot ulceration and the probability of healing (Table 4). The probability of recurrent ulceration has little effect on costs. However, recurrent ulceration can only follow first ulceration, and the duration of recurrent ulceration is censored. Varying the probability of amputation has a small effect on costs but leaves QALYs and life-years unchanged. The probability of first foot ulceration is the largest driver of QALYs and life-years, since transition to foot ulceration triggers a fall in the utility component of QALYs and doubles the risk of death. The second largest driver of QALYs is the duration of ulceration through the probability of healing. This is because time spent in ulceration has a negative impact on the utility component of QALYs. Analysis with proportion of the cohort with type 1 diabetes set at 7.5% [representative of the U.S. (34)] influences both costs and outcomes. This is because mortality rates are higher for type 1 diabetes. All results were sensitive to changes in the discount rate.

CONCLUSIONS — We estimated that the average individual with reduced vibration detection incurs approximately five times more foot ulcer and amputations costs, yields 0.18 fewer QALYs, and lives for ~2 months less than an average individual with normal vibration detection (discounted) over 10 years.

In a concurrent cost of illness study (8), we estimated that there are 5,522,500 people in the U.S. with diabetes who have DPN. Assuming that there is the same proportion of people with reduced vibration detection in the U.S. as reported by Young et al. (11), then there are ~2,378,600 people with reduced vibration detection. Multiplying this by the average cost per person ($6,188), we estimated that the long-term complications of DPN experienced by the population with reduced vibration detection will

cost all U.S. health care payers approximately $14.7 billion (discounted) over the next 10 years.

The treatment of diabetic foot ulceration and amputation is time-consuming and expensive. If appropriate at-risk groups could be identified by the use of VPT, resources could be concentrated on those patients. This could potentially save valuable resources and improve health outcomes. A recent study (35) showed that compliance with a preventative foot care program reduced the incidence of foot ulceration in individuals with reduced vibration detection. If all individuals with reduced vibration detection were identified and some new preventative strategy was available that reduced their risk of ulceration and amputation to levels experienced by those with normal vibration detection, this could save U.S. health care payers up to $11.8 billion and save 333,000 life-years and 428,000 QALYs (discounted) over the next 10 years.

This study is not without limitations. It is estimated that type 1 diabetes accounts for 5–10% of all cases of diabetes in the U.S. (34). However, the risk of foot ulceration for a given VPT level was drawn from a sample containing 40.9% of people with type 1 diabetes. Thus, people with type 1 diabetes are overrepresented in the model. This has implications for mortality and, therefore, both costs and QALYs because mortality rates for people with type 1 diabetes are higher than for those with type 2 diabetes. In the absence of separate studies of the predictive value of the VPT in type 1 and type 2 diabetic populations, it is not possible to overcome this limitation. Similarly, the model uses an initial age of 54 years. This is because the existing evidence on the predictive value of the VPT does not present evidence adjusted for age. Finally, the published evidence only has a maximum follow-up period of 4 years (11); we have projected future incidence of ulceration, assuming that the rates remain constant for 10 years.

We undertook a subgroup analysis of the 10% of individuals incurring the highest costs. Those in the reduced vibration cohort remained in ulceration for longer, had shorter time to first ulceration, incurred higher costs, and yielded fewer QALYs than those in the normal cohort. We can speculate that, given that the probability of foot ulceration increases with VPT score, those individuals incurring the highest costs may have higher VPT scores. Future research is needed on the costs and health consequences of individuals with extreme vibration detection levels. A future study might be designed to collect a minimum of individual level data on vibration detection, foot ulcers and amputations, and associated economic costs and health state utility scores over a long period (10 years) in patients with diabetes.

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