The healthcare costs of diabetic peripheral neuropathy in the UK

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ARTICLE POINTS

1 Diabetic peripheral neuropathy (DPN) is common among people with diabetes.

2 Complications such as foot ulceration and amputation incur relatively high and/or long-term costs.

3 A cost-of-illness study was undertaken to quantify the annual cost to the NHS of DPN in people with type 1 and type 2 diabetes.

4 The annual cost of DPN is estimated to be around £250 million in the UK.

5 Between 8% and 17% of the cost of diabetes is attributable to DPN.

KEY WORDS
- **Amputation**
- **Budget**
- **Costs**
- **Foot ulcer**
- **Diabetic peripheral neuropathy**

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Introduction

Up to 50% of people with diabetes have some degree of peripheral neuropathy, putting them at increased risk of foot ulceration, and up to 15% of all foot ulcers result in an amputation. This article descibes a prevalence and incidence-based cost-of-illness study undertaken to quantify the annual cost to the NHS of diabetic peripheral neuropathy among people with type 1 and type 2 diabetes in the UK. The robustness of the cost estimates was assessed by performing sensitivity analyses in which the rates of complications were varied.

Diabetic peripheral neuropathy (DPN) results in problematic and debilitating complications, which progress from underlying nerve dysfunction to loss of sensation and, eventually, nerve death, primarily in the lower extremities. It is estimated that 12–50% of people with diabetes have some degree of peripheral neuropathy (Nicolucci et al, 1996). Symptoms range from a slight numbness to severe pain in the feet, but many patients are asymptomatic.

Patients with DPN are at increased risk of foot ulceration. They are less likely to detect foot trauma, and breakages in the skin may become infected without treatment. Approximately 15% of people with diabetes develop at least one foot ulcer during their lifetime (Mancini and Ruotolo, 1997; NHS Centre for Reviews and Dissemination, 1999; Reiber et al, 1999; Boulton, 2000; Gonzalez and Oley, 2000; Kantor and Margolis, 2001; Spencer, 2002).

It has been estimated that 76% of ulcers are primarily neuropathic or neuroischaemic in origin (Walters et al, 1992). Deep foot ulcers may be accompanied by cellulitis (a subcutaneous inflammation of connective tissue) or osteomyelitis (infection in the bone), and a severely infected foot ulcer may lead to amputation of the toe, foot or leg. It is estimated that up to 15% of all foot ulcers result in an amputation (NHS Centre for Reviews and Dissemination, 1999).

In the UK, the care of people with diabetes (2–3% of the general population) accounts for 5% of total NHS resource use (Department of Health, 2001). The management of DPN and its complications is likely to form a large proportion of this total expenditure, because treatment is often resource intensive and long-term.

Aims

The aim of this cost-of-illness study was to quantify the annual healthcare costs associated with the management of symptomatic DPN, foot ulcers and lower limb amputations in the UK. Cost-of-illness studies inform decision makers about the expenditure that healthcare payers incur in the management of a disease, and how the management of each associated health state contributes to total cost. This offers an alternative perspective on the importance of a disease compared with other epidemiological indicators such as mortality and morbidity (Kernick, 2002).

Cost-of-illness studies can be used to identify funding priorities and inefficiencies. This information can be used by pressure groups when lobbying the Government for additional healthcare funding. It can also be used to identify priority areas for research, e.g. by industry when estimating the potential size of the market for new healthcare interventions.

Research methods

A prevalence-based model was constructed to estimate the annual cost of illness, and included chronic health states associated

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1 The number of people with diagnosed diabetes in the UK was estimated to be 1.4 million.

2 The proportions of people with type 1 diabetes (12%) and type 2 diabetes (88%) were estimated from the DARTS (2001) study.

3 The UK prevalence of diagnosed diabetes (2.3%) was estimated as the ratio of people in the UK with diagnosed diabetes to the UK population.

with DPN. This model was augmented with an incidence-based model and included acute events associated with the chronic health states (*Figure 1*).

The direct treatment costs of DPN and its complications were estimated from the perspective of the NHS. The NHS provides care that is free to the patient at the point of delivery, covers the major proportion of the UK population, and hence incurs the vast majority of healthcare costs. Mean costs in the UK were estimated and all results are reported in 2001 British pounds (£).

Health states of clinical and economic significance, and transitions between health states, were informed by the epidemiology of DPN. A clinically significant health state was defined as a chronic condition or acute event that is medically recognised as being a complication of DPN. An economically significant health state was defined as one that incurs costs in excess of those expected for a person with diabetes but without evidence of DPN.

Patients with diagnosed type 1 or type 2 diabetes may have symptomatic DPN (causing numbness or pain detected by the patient) or asymptomatic DPN (detected only by a diagnostic instrument). Patients with either symptomatic or asymptomatic DPN may have a foot ulcer, which may be accompanied by cellulitis or osteomyelitis.

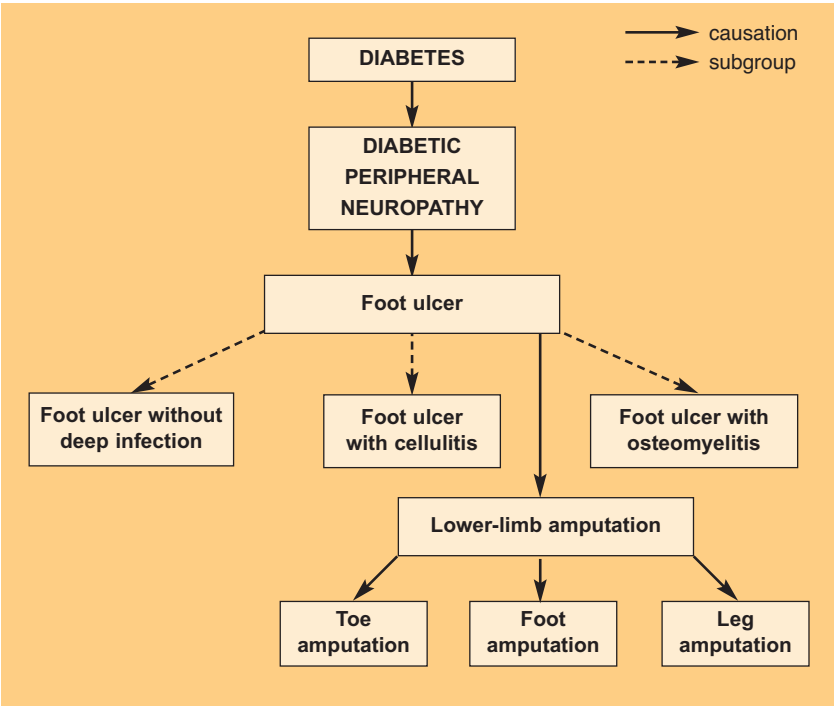

Figure 1. Health states and transitions in the cost-of-illness model.

Patients with foot ulcers may require a lower-limb amputation (toe, foot or leg) during the year as a result of severe infection (e.g. osteomyelitis).

People with undiagnosed diabetes were not included in the analysis since it is expected that complications occur only in diagnosed patients; at the latest, patients are diagnosed with diabetes at the same time as the complication.

Rates

The number of people with diagnosed diabetes in the UK was estimated to be 1.4 million (Diabetes UK, 2000). The proportions of people with diabetes having type 1 (12%) and type 2 (88%) variants were estimated from a study of the population of people with diabetes in Tayside, Scotland (DARTS, 2001). The UK prevalence of diagnosed diabetes (2.3%) was estimated as the ratio of people in the UK with diagnosed diabetes to the population of the UK (60 million; Office of National Statistics, 2002).

Prevalence and incidence rates of complications were derived from the literature and from local and national clinical databases. Foot ulcers may develop from DPN and/or ischaemia, and so the prevalence of foot ulceration was adjusted to include only foot ulcers that are neuropathic (primarily neuropathic or neuro-ischaemic) in origin (75.8% of all foot ulcers; *Table 1;* Walters et al, 1992).

National prevalence and incidence rates were estimated for the health states. Where data were available, rates were estimated separately for people with type 1 and type 2 diabetes. DPN and foot ulceration are longer-term conditions, and the rates of these complications are national prevalence rates. Lower-limb amputations are acute events, and the rates of these complications are national incidence rates.

The total annual costs of treating DPN and foot ulcers were estimated assuming that prevalence rates remain constant throughout a year. Constant prevalence does not require the same patients to remain in that health state throughout the year, but instead requires that at any point in time there are the same numbers of patients in that health state.

Table 1. Prevalence and incidence of diabetic peripheral neuropathy and its complications in the UK

Health state	Population	Estimated rate	References
		Prevalence	
Diabetic peripheral neuropathy	People with diabetes	22.70% (t1) 32.10% (t2)	Young et al, 1993
Neuropathic foot ulcer	People with diabetes	4.55%*	Walters et al, 1992 SIGN, 2001
No deep infection With cellulitis With osteomyelitis	People with diabetes and a foot ulcer	93.90% 1.95%† 4.15%†	Walters et al, 1992 Epling and Ball, 2002
		Incidence	
Lower-limb amputation	People with diabetes	0.80% (t1)‡ 0.17% (t2)‡	Office of National Statistics, 2002
Toe Foot Leg	Lower-limb amputees	53.5% 8.0% 38.5%	Department of Health, 2002b

t1 = type 1 diabetes; t2 = type 2 diabetes; SIGN = Scottish Intercollegiate Guidelines Network
* Estimated prevalence of foot ulceration = 6%; estimated proportion of foot ulcers being neuropathic = 75.8%.
† Estimated proportion of foot ulcers being Wagner Classification Grade 3 (deep ulcer with cellulitis, abscess formation or osteomyelitis) = 6.1%; estimated prevalence of osteomyelitis in patients with diabetes and severe foot ulcers = 68%. We assume that Grade 3 ulcers would be classed as 'severe'.
‡ Ratios of the annual numbers of amputations undergone by people with diabetes (England 2000–2001) to the estimated number of people with diabetes (2.3% of 50 million, England 2000). Cases were inpatient admissions with any OCPS4 code of X09 (amputation of leg), X10 (amputation of foot) or X11 (amputation of toe), and any diagnosis code of E10 (insulin-dependent diabetes mellitus) or E11 (non-insulin-dependent diabetes mellitus).

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1 The annual costs of DPN and foot ulceration are 52 times the mean weekly cost multiplied by the numbers of patients in the associated health state at any given time.

2 The annual costs of amputations are the costs of amputations times the annual numbers of amputations.

3 The total annual cost of managing DPN is the sum of these costs.

The products of the numbers of people with type 1 and type 2 diabetes and the national rates of complications were used to estimate the total numbers of people with diabetes who have DPN and a foot ulcer at a given point in time, or underwent an amputation during a year.

Costs

DPN and foot ulceration incur ongoing weekly costs. Mean weekly costs were the products of the mean weekly quantities of resources used and their respective unit costs. Amputations generally incur one-off costs, which were calculated as the products of the total quantities of resources used and their respective unit costs.

The annual costs of DPN and foot ulceration are 52 times the mean weekly cost multiplied by the numbers of patients in the associated health state at a given point in time. The annual costs of amputations were calculated as the products of the costs of amputations and the annual numbers of amputations. The total annual cost of managing DPN was the sum of these costs.

Management costs are presented in *Table 2*. Resource use was estimated from hospital episodes data (Department of Health, 2002b) and recommended practice in the *British National Formulary 43* (2002), and clinicians verified all assumptions. Unit costs were obtained from published drug tariffs, hospital episodes data and the literature (Netten and Curtis, 2001; Davis, 2001; *British National Formulary 43*, 2002; Department of Health, 2002c).

We estimated that 10% of patients with DPN would experience the painful, symptomatic variant and receive therapy (Backonja, 1999). Patients with asymptomatic or non-painful symptomatic DPN (symptoms of numbness and tingling) were assumed not to consult their GP, and hence not receive targeted therapy.

All patients with a foot ulcer were assumed to attend dermatology outpatient clinics for check-ups and wound dressing. It was assumed that 30% of all patients would receive a pair of surgical shoes. For patients unable to redress their wounds themselves (45% no deep infection; 75% with cellulitis; 85% with osteomyelitis) we assumed that a nurse home visit was required for each dressing between clinic appointments.

It was assumed that 50% of patients with a foot ulcer and osteomyelitis would

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1 The point estimates for parameters that are expected to have a substantial influence on the cost of illness were varied in a sensitivity analysis.

2 We estimated plausible upper and lower limits for these parameters to test the robustness of the cost-of-illness estimates to changes in prevalence and incidence rates and uncertainty around our baseline estimates.

require inpatient (dermatology) stay. The mean length of stay (12.3 days) was that for people having diabetes and admitted with a primary diagnosis of osteomyelitis in England (*British National Formulary 43*, 2002; Department of Health, 2002b).

We estimated the costs of inpatient stay for amputations as the products of inpatient lengths of stay for amputations (main operation) in England and the cost of a bed day. The cost of one bed day was calculated as the quotient of the mean cost per finished consultant episode (FCE) and the mean length of stay per FCE (Health Care Resource Group, Code Q15: amputations, elective inpatients) (*British National Formulary 43*, 2002; Department of Health, 2002b).

We assumed that 40% of foot amputees had their whole foot removed and received a prosthetic foot, that the remainder received surgical shoes following a partial foot amputation, and that all leg amputees received a prosthetic leg.

Sensitivity analysis

It is highly likely that there will be some difference between the estimated rate and the true rate of a complication, and cost-of-illness estimates may be sensitive to variations in these parameters. It is therefore good practice to estimate the range of costs within which the true cost of illness is expected to lie.

The point estimates for parameters that are expected to have a substantial influence on the cost of illness and/or which we were least certain about were varied in a sensitivity analysis. We estimated plausible upper and lower limits for these parameters. This tests the robustness of the cost-of-illness estimates to changes in prevalence and incidence rates and uncertainty around our baseline estimates.

DPN has no clear medical definition. As a result, different studies have used different criteria to define DPN; this has led to a wide variation in estimates of prevalence

Table 2. Costs of diabetic peripheral neuropathy and its complications in the UK

Health state	Estimated cost	References
	Mean weekly cost	
Painful symptomatic peripheral neuropathy	£3*	*British National Formulary 43*, 2002
Foot ulcer		
No deep infection	£59†	Netten and Curtis, 2001 *British National Formulary 43*, 2002
With cellulitis	£142†	Netten and Curtis, 2001 *British National Formulary 43*, 2002
With osteomyelitis	£264†	Netten and Curtis, 2001 *British National Formulary 43*, 2002 Department of Health, 2002b
	Total event cost	
Amputation		
Toe	£3 443‡	Department of Health, 2002b,c
Foot	£7 786‡	Department of Health, 2002b,c
Leg	£10 979‡	Davis, 2001 Department of Health, 2002b,c

Price year = 2001

* Amitriptyline (50 mg/day: median recommended dose).

† Mean number of weekly dressings: 3.5 (Melolin; no deep infection), 5.25 (Lyofoam; with cellulitis), and 7 (Lyofoam; with osteomyelitis). Mean numbers of weekly outpatient clinic attendances: 0.5 (no deep infection), 1 (with cellultis), 1.5 (with osteomyelitis). Surgical shoe cost: 1996 clinician estimate inflated to 2001 prices (Health Services Cost Index). Drugs received: amoxicillin (500 mg 3/day; 40% of patients with no deep infection), flucloxacillin (500 mg 4/day; all patients with a foot ulcer accompanied by cellulitis or osteomyelitis), and fusidic acid (750 mg 3/day; all patients with a foot ulcer accompanied by osteomyelitis). One dispensing fee included (total prescriptions in bands = 4000 and over).

‡ Inpatient lengths of stay (days): 15.0 (toe), 26.7 (foot) and 30.4 (leg).

Table 3. Annual costs of diabetic peripheral neuropathy and its complications in the UK

Health state	Type 1 diabetes		Type 2 diabetes		All diabetes	
	Patients	Annual cost (£ million)	Patients	Annual cost (£ million)	Patients	Annual cost (£ million)
Diabetes (type)*	167 300	–	1232 700	–	1400 000	–
DPN*	37 977	0.6	395 697	6.2	433 674	6.8
Foot ulcer: not infected*	7 145	21.7	52 643	160.1	59 788	181.9
Foot ulcer with cellulitis*	149	1.1	1 094	8.1	1 243	9.2
Foot ulcer with osteomyelitis*	316	4.3	2 326	31.9	2 641	36.3
Toe amputation†	541	1.9	850	2.9	1 391	4.8
Foot amputation†	81	0.6	127	1.0	208	1.6
Leg amputation†	389	4.3	612	6.7	1 000	11.0
Total annual cost	**–**	**34.5**	**–**	**217.0**	**–**	**251.5**

* Number of patients at a given point in time; † Number of new cases per year; DPN = Diabetic peripheral neuropathy

between studies. Our baseline point estimates were determined partly by the definitions used by the source study. We increased and reduced the prevalence rates of DPN by up to 50% in the sensitivity analysis.

It has been estimated that the prevalence of foot ulceration in people with diabetes in the UK is between 5% and 7% (Scottish Intercollegiate Guidelines Network (SIGN), 2001). The degree of error in our baseline estimate is therefore likely to be small. However, since treatment of foot ulcers can be long-term and weekly costs relatively high, small changes in the prevalence of foot ulceration and mix of severity (e.g. the proportions accompanied by infections) were expected to have a substantial impact on costs. In the sensitivity analysis, we increased and reduced the prevalence rates of foot ulceration by up to 50%, and varied the proportions of foot ulcers accompanied by cellulitis or osteomyelitis between 1% and 10% (i.e. the assumed minimum and maximum prevalence rates).

The literature suggests that the annual national incidence of lower-limb amputation is between 3 and 10 per 1000 people with diabetes. Although the degree of error in our baseline rate is likely to be small, we expect the total cost of DPN to be sensitive to small changes in the amputation rate because the associated procedure costs are high.

In the sensitivity analysis, we varied the incidence rates of amputations, holding constant the proportions of amputations by type. The highest annual incidence of amputation identified in a UK population was 10.1 per 1000 people with diabetes (Ward, 1995); we used this as our upper limit for the incidence rates of amputation and reduced rates by up to 50%.

Results

The estimated numbers of people with diagnosed diabetes in the UK were 0.17 million (type 1 diabetes), 1.23 million (type 2 diabetes) and 1.40 million in total (type 1 and type 2 diabetes). The total annual costs to the NHS of treating people with DPN and its associated complications were estimated to be £35 million (type 1 diabetes), £217 million (type 2 diabetes) and £252 million (type 1 and type 2 diabetes combined; *Table 3*).

Sensitivity analysis

The total annual cost of treating DPN and its complications was insensitive to changes in the prevalence of DPN and incidence of lower-limb amputation (*Table 4*). However,

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1 The total annual cost was very sensitive to changes in the overall prevalence of foot ulceration.

2 For every 10% increase (reduction) in the prevalence of foot ulceration, the total annual cost of DPN and its complications increased (decreased) by approximately 9%.

the total annual cost was very sensitive to changes in the overall prevalence of foot ulceration but less sensitive to changes in the proportions of foot ulcers accompanied by cellulitis or osteomyelitis. For every 10% increase (reduction) in the prevalence of foot ulceration, the total annual cost of DPN and its complications increased (decreased) by approximately 9%.

The total annual cost of DPN and its complications was nearly twice as sensitive to increases in the baseline proportions of foot ulcers accompanied by infections compared with decreases. For example, when the proportions of foot ulcers accompanied by cellulitis and osteomyelitis were 50% lower or higher than at baseline, the total annual cost of DPN and its complications was 6.9% lower and 12.7% higher, respectively.

When all parameters in the sensitivity analysis were set at their lowest rates (best scenario), the total annual costs of DPN and its complications were estimated to be approximately 54% lower (type 1 diabetes) and 55% lower (type 2 diabetes and type 1 and type 2 diabetes combined) than at baseline.

When all parameters in the sensitivity analysis were set at their highest rates (worst scenario), the total annual costs were estimated to be 78% (type 1 diabetes), 110% (type 2 diabetes) and 105% (all diabetes) higher than at baseline.

Conclusions

DPN is a common microvascular complication of diabetes. This study has attempted to quantify the direct healthcare costs of DPN and its complications. Approximately 2.3% of people in the UK have been diagnosed with diabetes, and an estimated 30% of these have some degree

Table 4. Results of the sensitivity analysis

Health state	Type 1 diabetes		Type 2 diabetes		All diabetes	
	Patients	Annual cost (£ million)	Patients	Annual cost (£ million)	Patients	Annual cost (£ million)
Prevalence of DPN						
Low estimate*	18 989	34.2	197 848	213.9	216 837	248.1
Baseline estimate*	37 977	34.5	395 697	217.0	433 674	251.5
High estimate*	56 966	34.8	593 545	220.1	650 511	254.9
Prevalence of foot ulceration						
Low estimate*	3 804	20.9	28 032	116.9	31 836	137.8
Baseline estimate*	7 609	34.5	56 063	217.0	63 672	251.5
High estimate*	11 413	48.1	84 095	317.1	95 508	365.2
Proportions of foot ulcers accompanied by cellulitis or osteomyelitis						
Low estimate*	76 (c) 76 (o)	31.6	561 (c) 561 (o)	195.8	637 (c) 637 (o)	227.5
Baseline estimate*	149 (c) 316 (o)	34.5	1 094 (c) 2 326 (o)	217.0	1 243 (c) 2 642 (o)	251.5
High estimate*	761 (c) 761 (o)	41.9	5 606 (c) 5 606 (o)	271.7	6 367 (c) 6 367 (o)	313.7
Incidence of lower-limb amputation						
Low estimate†	507	31.1	794	211.7	1 301	242.8
Baseline estimate†	1 015	34.5	1 588	217.0	2 603	251.5
High estimate†	1 281	36.3	9 437	269.5	10 718	305.8
Scenario analysis						
Best scenario	–	15.8	–	97.9	–	113.7
Baseline scenario	–	34.5	–	217.0	–	251.5
Worst scenario	–	61.4	–	454.8	–	516.1

Total annual cost of all complications. c = cellulitis; o = osteomyelitis; * Number of patients at a given point in time; † Number of new cases per year

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1 In the UK, the total annual cost of treating DPN and its complications was £252 million.

2 People with type 1 diabetes comprised 12% of all people with diabetes but accounted for 14% of the total annual cost of DPN and its complications.

3 Of the total annual cost of illness, 93.1% was attributable to the management of painful symptomatic DPN (2.7%) and foot ulceration (93.4%).

4 Amputations accounted for only 6.9% of the total annual cost of illness.

5 We estimate that, currently, £3 billion of NHS expenditure is attributable to diabetes (5% of total NHS expenditure in 2001–02).

of DPN. In the UK, the total annual cost of treating DPN and its complications was £252 million.

People with type 1 diabetes comprised 12% of all people with diabetes but accounted for 14% of the total annual cost of DPN and its complications, due to the relatively higher incidence of amputations among people with type 1 diabetes.

We estimated that 93.1% of the total annual cost of illness was attributable to the management of longer-term complications (painful symptomatic DPN [2.7%] and foot ulceration [90.4%]). Amputations incur one-off costs, are undergone by relatively few people with diabetes, and account for only 6.9% of the total annual cost of illness.

The annual cost of DPN and its complications was very sensitive to the prevalence of foot ulceration, which incurs relatively high long-term costs. Other health states either incur long-term but relatively inexpensive costs (painful symptomatic DPN), or require treatment that is resource intensive but short term (e.g. amputations). Higher and lower rates of these complications did not affect the total costs of illness to a substantial degree.

Our baseline cost of illness (£252 million) is dependent on various assumptions and subject to substantial uncertainty. However, the total annual cost of DPN complications is not expected to be more than 55% lower or 105% higher than the baseline estimate (£114–516 million). We estimate that, currently, £3 billion of NHS expenditure is attributable to diabetes (5% of total NHS expenditure in 2001–02 [£60 billion]; Department of Health, 2001, 2002a). Therefore, at least 8% and possibly up to 17% of total NHS expenditure on diabetes might be attributable to DPN.

We recognise that our analysis has several limitations. We have not included follow-up treatment for patients who have undergone an amputation, because of the lack of reliable data. However, our model does include the most clinically and economically significant health states and associated costs.

Data were obtained from regional and national databases (e.g. for the rates of amputations). The accuracy of our derived estimates is dependent on the accuracy of these datasets. In national hospital episode datasets, some patients with diabetes may not have been coded as having diabetes; we expect that some clinicians do not always complete all diagnoses codes for new admissions (Buxton et al, 1996).

Our estimates of prevalence and incidence are dependent on the quality of studies from which they are derived and these differ with respect to study populations, settings, analytical methods and clinical definitions. Selecting the most appropriate studies is problematic and inevitably requires trade-offs in accuracy between study factors (e.g. the appropriateness of the study sample and methods). For this reason, we performed sensitivity analyses on the least certain point estimates.

Finally, we have only estimated the direct medical costs of treating DPN and its complications. However, non-medical direct costs (e.g. travel costs) and productivity losses may be substantial for people with DPN. For example, patients may incur transport costs when attending outpatient appointments for foot ulceration treatment. Patients may require time away from work, either temporarily (e.g. during hospitalisation for osteomyelitis) or permanently (e.g. following a major amputation). Friends or relatives of patients may also incur costs if they accompany the patient to treatment sessions or cease paid employment to care for the patient.

Despite these limitations, we have attempted to quantify the annual cost of DPN and its complications among people with diabetes in the UK. We estimated that the NHS might incur a cost of up to £516 million. This could potentially be reduced by interventions to successfully treat DPN to prevent or delay its long-term complications. The development of such interventions by the healthcare industry may lead to substantial healthcare cost savings in the UK. ■

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