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Health-Economic Consequences of Diabetic Foot Lesions

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Diabetic foot complications result in huge costs for both society and the individual patients. Few reports on the health-economic consequences of diabetic foot infections have been published. In studies considering a wide societal perspective, costs of antibiotics were relatively low, whereas total costs for topical treatment were high relative to the total costs of foot infections. Total direct costs for healing of infected ulcers not requiring amputation are ~\$17,500 (in 1998 US dollars), whereas the costs for lower-extremity amputations are ~\$30,000–\$33,500 depending on the level of amputation. Prevention of foot ulcers and amputations by various methods, including patient education, proper footwear, and foot care, in patients at risk is cost effective or even cost saving. Awareness of the potential influence of reimbursement systems on prevention, management, and outcomes of diabetic foot lesions has increased. Despite methodological obstacles, modeling studies are needed in future health-economic evaluations to determine the cost effectiveness of various strategies.

In addition to causing suffering and morbidity, foot lesions in diabetic patients have substantial economic consequences. Several national and international consensus documents providing prevention and treatment recommendations have recently been published [1–3]. These recommendations would have various degrees of health-economic consequences. The costs of diabetic foot lesions are influenced by interventions to prevent the development of foot ulcers, by management strategies to shorten wound-healing time, by strategies to prevent amputation for patients with current ulcers, and by the management and care required by disability following amputations (table 1).

Before 1990, few studies addressed the economic impact of foot complications in patients with diabetes. Recently, however, a number of reports with various economic approaches have been published from different countries [4–15]. Relatively few studies discuss health economics, especially related to foot infections [16, 17]. In some reports, the costs of diabetic foot

complications are discussed generally, with the infected foot ulcer included as one of several ulcer types [5, 9].

The increased interest in investigations of the costs and health-economic issues of diabetic foot complications likely has several contributory factors. Diabetes is a chronic disease that requires a lifelong commitment of resources to prevent and treat complications. The disease affects an increasingly large number of people around the world, putting them at risk for disability and diminished quality of life. These strains on the health care budget occur at the same time that new, more expensive technologies and treatment options have become available. Here, we discuss the economic consequences of diabetic foot lesions and focus on the infectious aspects of this complication.

HEALTH ECONOMICS

Health economics has been defined as a science concerned with issues relating to the allocation of scarce resources to improve health [18]. Health-economic approaches may be descriptive, evaluative, or explanatory. The choice of a specific type of analysis depends on the purpose of a study and whether the consequences or outcomes between alternatives differ.

Descriptive studies of the costs of foot ulcers and amputations (cost of illness or cost of treatment) help

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Table 1. Resources potentially required for preventing and managing diabetic foot lesions.

Step	Components	Subcomponents	
1. Evaluation	Clinical examination (general/localized)	Laboratory tests Metabolic control of diabetes	
	Vascular assessment	Noninvasive testing Angiography	
	Diagnosing infection	Radiography, radionuclide scans, CT, MRI Bacterial culture Biopsy (for histology)	
	Social and educational issues	Living conditions Diet and nutritional status Education about diabetes and foot care Compliance with prevention and treatment strategies	
	Biomechanical issues	Walking pattern Foot dynamics	
2. Prevention	Screening for risk factors		
	Optimizing metabolic control		
	Educating patient and family		
	Chiroprapist or podiatrist care		
3. Medical treatment	Protective shoes		
	Antihyperglycemic agents		
	Granulocyte colony-stimulating factor		
	Cardiovascular agents, anticoagulants		
4. Surgical treatment	Oral and parenteral antibiotics		
	Vascular	Percutaneous transluminal angioplasty Reconstructive or bypass surgery	
5. Wound treatment	Orthopedic	Debridement Incision/drainage Revision/resection Minor/major amputation	
	Skin grafts		
	Appropriate dressings		
	Debridement (chemical, hydrotherapy, larval)		
	Topical growth factors		
	Human skin replacements		
	Tissue-engineering products		
	Topical antiseptics and antibiotics		
	6. Orthotic appliances	Shoes/insoles	
		Leg braces	
Total contact cast, aircast, other casts			
Prostheses			
7. Home care and social service	Wheelchair, crutches, walkers		
	Transportation (especially for medical care)		
	Meals and cleaning help		
	Disability accommodations for the home		

to make the economic consequences of the diabetic foot complication visible to decision-makers, health care providers, health professionals, and the patients and their support organizations. Results from studies could, therefore, have both clinical and policy implications. They can improve implementation of guidelines; serve as a basis for policy decisions regarding prevention, care, and treatment of diabetic foot lesions; and generate hypotheses for future intervention studies. Health-economic evaluations of various approaches to foot-ulcer care investigate which of several alternatives is most cost effective in treatment of the population included in the study.

Cost calculations must differentiate between the costs referable to foot complications and those for diabetic patients with foot ulcers that include treatment of non-foot-related disease and complications. This differentiation is especially important in the use of secondary data sources. One recent Swedish study showed that other conditions were reported as the primary diagnosis in >80% of the discharges, when diabetic foot complications were actually the main reason for inpatient treatment [19]. This demonstrates the risk of underestimation of the costs of diabetic foot lesions when analyses are based on primary diagnosis from secondary data sources. Underesti-

mation of costs for diabetes based on inpatient statistics or secondary databases has been observed in the United Kingdom as well [20, 21]. This probably occurs in health care systems without a direct connection between the diagnosis and economic compensation and may be less likely to occur in such countries as the United States, where the reimbursement system provides incentives for more accurately coded diagnoses [22].

HEALTH-ECONOMIC STUDIES

Costs of management and treatment. A number of studies of the economic consequences of diabetic foot ulceration and lower-extremity amputation have been published, but cost analyses based on prospectively followed patient populations are rare, as are reports focused on infected lesions (tables 2 and 3). Descriptions of costing and other methodological aspects are sometimes limited or missing, especially in the early studies. Costs reported from many studies are probably underestimated, because it is often unknown how, and to what degree, patients were treated before referral. The period before referral for foot ulcer treatment may represent patient and physician delay, as has been reported in several centers [32–35]. Delayed treatment and referral is frequently caused by failure to recognize the presence of infection and ischemia. This failure may be responsible for more proximal levels of amputation for patients whose limb was initially salvageable [35].

The total costs of a lower-extremity amputation include more than just inpatient care and surgery; outpatient visits and topical wound treatments, required until complete healing has been achieved, must be included as well. Costs of topical treatment and of inpatient stays have been found to be the most substantial costs in 2 Swedish studies [5, 17]. For many patients, the majority of topical-treatment costs occurred after an amputation had been done. In some published studies, it is uncertain whether topical treatment costs are included or not [8,

9, 11, 13], and this may explain some of the differences among study results.

Despite the different methods used, many studies confirm the substantial economic consequences of diabetic foot lesions [4, 5, 8, 10, 13, 15, 17, 27, 29]. Comparisons of results from various health-economic studies are complicated by differences in the study design (prospective vs. retrospective, primary vs. secondary data), patient populations, types of foot lesions, health care systems and settings, treatment practices, the time frame for analysis, the perspective of studies, reimbursement systems, and the countries included. In addition, some studies lack information about the year of costing [7, 14, 36], the monetary exchange rate, and the type of costs actually included. Other studies have included a mix of patients with and without diabetes [7, 10, 14, 28, 30]. Whether charges or costs were used also influenced study findings, and hospital costs may be only 70%–80% of charges billed [30].

Cost of deep foot infections. Health-economic reports on diabetic foot infections are limited. A Swedish study investigated costs for managing deep foot infections in 220 patients and categorized them according to clinical outcome [17]. Mean healing time for patients who did not need an amputation was 29 weeks; for those who required minor or major amputation, it was 52 weeks and 38 weeks, respectively (minor amputations required longer healing times than did major amputations). Total cost (in Swedish kronor [SEK] adjusted for inflation to 1998 prices and converted to US\$ by the 1998 exchange rate, US\$1 = SEK 7.95) for healing without amputation was \$17,554 per patient, whereas the corresponding cost for healing with minor amputation was \$33,540 and with major amputation was \$30,135. The cost for patients whose infections were unhealed at death was \$31,407. Topical treatment during outpatient care accounted for 51% of all costs and was the largest cost for all outcome groups except for patients who healed after

Table 2. Costs of treating foot ulcers not requiring amputation.

Reference	Country	No. of patients	Costs (year of costing)	1998 US\$ equivalent	Comments
Apelqvist et al. 1994 [5] ^a	Sweden	197	SEK 51,000 (1990)	8659	All ulcer types; total direct costs
Harrington et al. 2000 [8] ^b	USA	400,000	US\$3999–\$6278 (1996)	4238–6653	Inpatient and outpatient costs
Holzer et al. 1998 [9] ^b	USA	1846 ^c	US\$1929 (1992)	2452	Inpatient and outpatient costs; those aged >64 years excluded
Metha et al. 1999 [11] ^b	USA	5149	US\$900–\$2600 (1995)	993–2855	Private insurance charges; mean age, 51 years
Ragnarson Tennvall et al. 2000 [17] ^a	Sweden	88	SEK 136,600 (1997)	17,519	Deep foot infection; total direct costs
Ramsey et al. 1999 [13] ^b	USA	514 ^d	US\$27,987 (1995)	30,724	Including 2 years after diagnosis
Van Acker et al. 2000 [15] ^a	Belgium	120	US\$5227 (1993)	5658	Inpatient and outpatient costs

NOTE. For comparison of the results, costs were first adjusted for inflation to 1998 prices with a medical care index for Sweden and the United States and with the consumer price index for Belgium [23–26]. The Swedish currency was then converted to US\$ with the appropriate currency exchange rate for 1998 [23–26].

^a Based on data from observational studies.

^b Based on data from databases and other secondary sources.

^c No. of episodes.

^d Includes 80 amputations.

Table 3. Costs of lower-extremity amputations (all causes) in diabetic patients.

Reference	Country	No. of patients	Costs (year of costing)	1998 US\$ equivalent	Comments
Apelqvist et al. 1994 [5] ^a	Sweden	27	SEK 258,000 (1990)	43,800	All ulcer types; minor lower-extremity amputation; total direct costs
Apelqvist et al. 1994 [5] ^a	Sweden	50	SEK 390,000 (1990)	66,215	All ulcer types; major lower-extremity amputation; total direct costs
Ashry et al. 1998 [27] ^b	USA	5062	US\$27,930 (1991)	38,257	Hospital charges only
Cheshire et al. 1992 [28] ^a	UK	67	£ sterling 10,863 (1989)	25,706	Inpatient and outpatient costs (25% diabetics)
Eckman et al. 1995 [16] ^b	USA	NA	US\$28,539–\$29,458 (1993)	34,245–35,352	Inpatient and first-year costs
Gibbons et al. 1993 [29] ^b	USA	7	US\$18,341 (1990)	27,328	Inpatient care
Gupta et al. 1988 [30] ^a	USA	24	US\$27,225 (1978–1981)	79,495	Event and 3-year charges (83% diabetics)
Holzer et al. 1998 [9] ^b	USA	504 ^c	US\$15,792 (1992)	20,047	Gangrene/amputation, those aged >64 years excluded
van Houtum et al. 1995 [6] ^b	Netherlands	1575 ^d	NLG 28,433 (1992)	16,488	Hospital costs only
Johnson et al. 1995 [7] ^a	UK	23	£ sterling 12,476 (1992?)	24,701	6 months inpatient and outpatient costs (66% diabetics)
Palmer et al. 2000 [12] ^b	Switzerland	NA	CHF 35,271 (1996)	24,373	Event and first-year costs
Panayiotopoulos et al. 1997 [10] ^a	UK	20	£ sterling 15,500 (1994–95)	28,234	Inpatient and prostheses costs (46% diabetics)
Ragnarson Tennvall et al. 2000 [17] ^a	Sweden	77	SEK 261,000 (1997)	33,478	Deep infection; minor lower-extremity amputation; total direct costs
Ragnarson Tennvall et al. 2000 [17] ^a	Sweden	19	SEK 234,500 (1997)	30,083	Deep infection; major lower-extremity amputation; total direct costs
Singh et al. 1996 [14] ^a	UK	34	£ sterling 10,162 (1996?)	18,009	Event and first-year costs (44% diabetics)
Van Acker et al. 2000 [15] ^a	Belgium	7	US\$18,515 (1993)	19,996	Inpatient and outpatient costs; minor lower-extremity amputation
Van Acker et al. 2000 [15] ^a	Belgium	9	US\$41,984 (1993)	45,343	Inpatient and outpatient costs; major lower-extremity amputation

NOTE. For comparison of the results, costs were first adjusted for inflation to 1998 prices with a medical care index for Sweden and USA and with the consumer price index for the other countries and then transformed to US \$ with the appropriate currency exchange rate for 1998 [23–26, 31]. NA, not applicable; LEA, lower-extremity amputation; minor, amputation below the ankle; major, amputation above the ankle.

^a Based on data from observational studies.

^b Based on data from databases and other secondary sources.

^c No. of episodes.

^d No. of hospitalizations.

major amputation, for whom the inpatient costs dominated. The number of weeks between diagnosis of deep foot infection and healing and the number of surgical procedures were variables that explained 95% of the total costs. Costs of antibiotics accounted for <4% of the total costs.

In another Swedish study of diabetic patients with a foot ulcer, the average cost for all patients with an abscess or osteitis was US\$26,509, irrespective of the clinical outcome (costs in SEK adjusted for inflation to 1998 prices and converted to US\$ by the 1998 exchange rate) [5]. In that study, the costs of antibiotics were also low, representing just 2% of total costs. The average cost per ulcer episode for patients with osteomyelitis in an American study based on claims data was \$3980 (in 1992) [9]. In that study, all patients were <65 years of age, whereas in the 2 Swedish studies, many of the patients were older. Demographic differences between populations and the different methods of data collection might explain some of the differences in costs. Further, it is uncertain whether—and to what degree—outpatient management, such as topical-treat-

ment resource use and costs, was considered in the American study. Because of the methods for data collection, it was not possible to include costs until a specific end point in that study. In another American study, the authors claim that the cost of a minor amputation of an infected phalanx or metatarsal head, including a short hospitalization (3 days), is less than that for the more conservative approach of medical treatment with 6 weeks of intravenous antibiotics in the home [37]. These examples show that calculation of treatment costs is strongly influenced by the total time frame of observation and by whether patients are followed until a final end point.

In a study comparing resource use associated with diabetic foot infections for 3 European countries, the length of hospital stay was more than twice as long for patients in Germany than for those in Sweden and the United Kingdom [38]. Other major differences among the countries in management strategies, and thus in resource use, were the rates of amputation and vascular surgery and the use of antibiotics. In the United Kingdom, all patients were treated with intravenous antibiotics, compared

with only 58% in Sweden and 68% in Germany. The amputation rate was only 4% in the United Kingdom, compared with 16% and 17% in Germany and Sweden, respectively. The authors concluded that these differences could largely be explained by variations in access to inpatient and outpatient facilities, in patient selection, in patient characteristics, in reimbursement schemes, and in health care systems [38].

Cost of various types of foot ulcers. In the previously mentioned Swedish study, the total costs increased with the severity of the ulcer [5]. The average cost for patients with superficial ulcers, all of whom healed primarily without amputation, was US\$5098. For patients with gangrene, the most severe ulcer type, the average cost was US\$59,646 (costs in SEK adjusted for inflation to 1998 prices and converted to US\$). In this group of patients, the rate of amputation was 97%.

In a comparison of diabetes-related foot lesions among patients in the Netherlands and California [22], the duration of hospitalization was significantly longer in the Netherlands, whereas the incidence of lower-extremity amputation was higher in the United States. The authors suggested that these differences may be explained by differences in access to health care, health care financing, and reimbursement systems. In the Netherlands (as in many European countries), most people are ensured affordable governmental health care, whereas in the United States, costs are more often paid by the patient or by the patient's insurance company. If the cost of an amputation procedure is reimbursed but the costs of outpatient care are not, this may influence the rate of lower-extremity amputation.

Long-term costs. In addition to the short-term costs until an ulcer is completely healed, long-term costs for previously treated patients must be considered. These costs are especially high for patients who have undergone lower-extremity amputation, with a substantial part related to their increased need for home care and social services [4]. Long-term costs associated with amputations include prostheses, special footwear or other aids, rehabilitation, and costs related to any residual disability. The costs for home care and social services are highest among patients who have undergone major amputations [4]. Similarly, among patients with limb-threatening ischemia, another study found that the economic consequences of amputation were 10–40 times those of successful limb salvage [7].

Cost-effectiveness of prevention. Modeling studies of preventing foot complications have been limited to the effects of intensive insulin treatment to prevent the development of neuropathy [12, 39]. The potential economic benefits of preventing lower-extremity amputation have been discussed in a modeling study [40]. The cost effectiveness of preventing foot ulcers and amputations and the future costs of these complications were evaluated in a recent model simulation [41]. Prevention strategies, including patient education, foot care, and footwear interventions, were simulated in the model. Results showed that

providing all diabetic patients at risk for foot ulcers and amputations with optimal prevention would be a cost effective, or even cost saving, strategy [41]. This bolsters the recommendations from the international consensus documents.

Although prevention strategies cannot stop all ulcers, those that occur may be less severe with earlier initiation of appropriate care. A 1-year comprehensive prevention program, compared with standard care, resulted in a significant decrease in days affected by an ulcer, hospitalizations, foot surgery, and missed work days, in addition to fewer lower-extremity amputations [42]. This study demonstrates the potential economic and medical advantages if treatment delays could be limited.

Several reports have focused on the importance of patient compliance with prevention and treatment [43, 44]. Compliance may be influenced by several factors, including the degree to which expenses are covered for the patient. A report from Belgium concluded that incentives for prevention are low, from the patient's point of view, when the cost for prevention is paid by the patient and the cost for treatment is covered by the health care system [15].

Cost-effectiveness of topical treatment. Several problems can hinder cost-effectiveness analyses of topical treatments. A health-economic evaluation of topical treatment followed patients for 12 weeks and recorded resource use and outcomes [45]. Despite the relatively long follow-up period, only 17% of patients healed. This illustrates the problem of patients not being followed until a defined end point. Another problem illustrated by this study is the difficulty in choosing an alternative treatment for the evaluations. Three different topical dressings were used as standard treatment for comparison with the study dressing [45]. This reflects clinical practice, because the appropriate dressing differs during the healing process and no one of the standard dressings would be suitable for the whole time. Difficulty in choosing a relevant comparator for new dressings has resulted in the frequent use of saline dressings in clinical trials [46]. Although these may be an adequate control arm from a clinical viewpoint, they are not adequate for health-economic evaluations. Although the costs of saline dressings themselves are very low, the use of them is the most expensive treatment alternative because they require more frequent dressing changes and thus staff resources [47], and they are usually not typical of standard dressings for the whole healing time.

Dressings that require less frequent changes may be more cost effective, even if they are more expensive than other dressings [45]. This results from the sometimes overlooked costs of the staff performing outpatient dressing changes and the costs of staff or patient transportation. When patients or relatives perform dressing changes, there is also a cost related to their loss of work or leisure time. A more expensive treatment option may also lead to potential cost savings if it will result in a

shorter duration of hospitalization. This was shown in a British study, performed from the perspective of the hospital [48], in which diabetic patients with an infected foot ulcer were treated with or without the addition of granulocyte colony-stimulating factor (G-CSF) to standard care. Cost savings were shown in patients treated with G-CSF, because of earlier discharge from hospital. It is uncertain, however, whether or not this cost saving would occur if a wider societal perspective were taken or if resource use until a final end point were considered.

The problems with prospective health-economic studies of the diabetic foot (such as the long healing times and the need for different dressings in various phases of healing) are examples of reasons for the more frequent use of modeling studies during recent years. In some of these studies, new topical treatment technologies have been evaluated. Although these products are usually more expensive than standard dressings, they may be cost effective if they result in more effective or faster healing [49–51].

Other aspects of cost effectiveness. The cost effectiveness of different management approaches for diabetic patients with foot infections has been investigated in a US modeling study [16]. That study concluded that surgical debridement and a 10-week course of culture-guided oral antibiotic treatment may be as effective as and less costly than other alternatives, including more extensive diagnostic testing or immediate amputation. These types of analyses are, however, highly dependent on the performance characteristics attributed to various diagnostic tests and on presumed pretest probabilities for various diagnoses.

Other authors have argued that for osteomyelitis of the toe, a short course of antibiotic therapy and digit amputation is more cost effective than prolonged antibiotic therapy alone [52, 53]. One reason for the different conclusions is the use of different perspectives and a tendency not to consider certain costs, such as those that occur after a toe amputation. In a Swedish study, 76% of the total costs were incurred after amputations had been performed but before complete healing was achieved [5]. This was mainly attributable to costs for topical treatment after minor amputations.

METHODOLOGICAL AND PRACTICAL PROBLEMS IN HEALTH-ECONOMIC STUDIES

In some Swedish studies [5, 17], patients who underwent lower-extremity amputation were treated as inpatients by departments other than general or orthopedic surgery; thus, amputation costs and costs for postoperative treatment could be seriously underestimated if only wards connected to operating departments were considered. The tendency in published reports to limit cost analysis to inpatient care in the surgical departments rather than to a defined end point, such as complete healing or death, can be attributed to several factors. Sometimes the

analysis is done from the perspective of the surgical department, so other costs are seen as not relevant. Difficulty in obtaining resource-use data after hospital discharge limits the perspective in some cases. Similarly, a lack of understanding of diabetic foot disorders that leads to a belief that the problem is solved by amputation might contribute to incomplete analyses. To fully estimate the total direct short-term cost of foot ulcers and amputations, patients must be followed for resource use until a final end point, irrespective of where they are treated.

Databases and other secondary data sources. Few studies of diabetic foot lesions have been based on observational studies (tables 2 and 3) [5, 10, 14, 15, 17]. Recent studies describing the economic consequences of these problems have often been based on information from databases or claims data [6, 8, 9, 11, 13, 27]. Such studies make it more difficult to restrict the cost analysis to a single ulcer episode or to differentiate the various types of costs for different types of ulcers. The analyses are, however, often suitable for estimates of foot ulcer costs for large populations of diabetic patients during specified periods. The problems associated with cost analyses of diabetic foot lesions based on claims data or secondary sources are that some databases do not contain information about all types of resources used and that some databases are restricted to selected populations [11, 54], thus preventing extrapolation to larger groups.

Difficulties in performing health-economic studies. Cost-effectiveness analyses of management of diabetic foot lesions have many methodological difficulties in design and execution. Difficulties with conducting prospective randomized controlled studies of chronic wounds [55] include the extensive research resources necessitated by the long duration of wound healing and the heterogeneous nature of the patients, resulting in small subgroups. Furthermore, foot ulcers differ during the healing process; treatments in different phases make comparisons of strategies difficult. In addition, it may be difficult to perform blinded studies of topical treatments. The shortage of evidence regarding the management of diabetic foot disease [56–58] surely reflects the methodological challenges of performing such studies.

A direct comparison of cost analyses of primary healed foot ulcers and ulcers healed after amputation is inadvisable, because the 2 groups are usually not comparable for patient characteristics and background variables. Patients in the latter group often have more severe complications and comorbidities that probably will influence the outcome and resource use. Ethical reasons preclude randomization of treatment alternatives to solve this methodological problem. Amputations are undoubtedly a costly solution for society and result in serious disability for the patients. One reason for various incidences of lower-extremity amputation from different settings is different indications for amputations. In some Swedish studies [4, 5, 17],

strict criteria for amputation were used [59], and a nonhealing ulcer was not an indication for amputation. Other authors have reported the failure of a wound to heal, defined as no healing progress after 6 weeks, as an indication for amputation [60]. If the foot has an adequate vascular supply and no significant infection, a nonhealing plantar ulcer usually results from poor treatment and/or poor compliance [61].

Diabetic foot infections are one of the most costly foot complications because of their long healing time and often poor outcome. The large costs and poor quality of life associated with diabetic foot complications indicate that management strategies that speed healing and reduce the number of amputations could be cost effective. The chronic lifelong multifactorial problems associated with diabetes, the heterogeneous patient populations, the long duration of wound healing, the simultaneously occurring complications, the treatment by many specialists and professionals, and the complex causal relations are factors that complicate prospective health-economic studies of diabetic foot lesions. Health-economic evaluations in different types of settings would be valuable, but such studies are difficult to execute because of the risk that the treatment of patients may be altered by the study itself. The use of retrospectively collected resource-use data may better reflect actual clinical practice than would a prospective clinical trial. Other options are model simulations that include data from different sources, such as epidemiological information, outcome results from clinical trials, and local and national databases and registers.

CONCLUSIONS

The total costs of diabetic foot ulcers and amputations are high from both a short-term and a long-term perspective, and costs increase with ulcer severity. Topical wound treatments and inpatient care account for the largest fraction of costs over the time until complete healing. Important factors that influence the total costs and cost effectiveness of topical treatments and that have to be examined in health-economic analyses of the diabetic foot are costs of material, staff, and transportation; frequency of dressing changes; rate of healing; and final outcome.

The major costs for infected diabetic foot ulcers that healed after an amputation occur between amputation and complete healing and are mainly related to topical treatments. The costs of antibiotics are low in comparison with the total costs for treatment of diabetic foot infections. The total costs for treatment of deep foot infections are high, especially for patients who have undergone amputations. Total direct costs for healing of infected ulcers not requiring amputation are ~US\$17,500 (1998), whereas the costs for lower-extremity amputations are ~US\$30,000–\$33,500, depending on level of amputation. Prevention, including patient education, foot

care, and special footwear in accordance with present international recommendations, is cost effective or cost saving for all diabetic patients at high risk for foot ulcers and lower-extremity amputation.

A health-economic perspective of the diabetic foot implies consideration not only of the costs of the amputation procedure but also of the outcome of treatment, including quality of life, survival, and the possibility to save the limb. It is clear that amputation and its consequences result in very costly solutions, and approaches to saving the limb should therefore be the first choice.

References

1. American Diabetes Association. Consensus development conference on diabetic foot wound care. *Diabetes Care* **1999**; *22*:1354–60.
2. International Working Group on the Diabetic Foot. International consensus on the diabetic foot. Amsterdam: The International Working Group on the Diabetic Foot, **1999**.
3. Consensus statement. Foot problems of diabetics. Stockholm: Spri Publications, **1998**.
4. Apelqvist J, Ragnarson Tennvall G, Larsson J, Persson U. Long-term costs for foot ulcers in diabetic patients in a multidisciplinary setting. *Foot Ankle Int* **1995**; *16*:388–94.
5. Apelqvist J, Ragnarson Tennvall G, Persson U, Larsson J. Diabetic foot ulcers in a multidisciplinary setting: an economic analysis of primary healing and healing with amputation. *J Intern Med* **1994**; *235*:463–71.
6. van Houtum WH, Lavery LA, Harkless LB. The costs of diabetes-related lower extremity amputations in the Netherlands. *Diabet Med* **1995**; *12*:777–81.
7. Johnson BF, Evans L, Drury R, Datta D, Morris-Jones W, Beard JD. Surgery for limb threatening ischaemia: a reappraisal of the costs and benefits. *Eur J Vasc Endovasc Surg* **1995**; *9*:181–8.
8. Harrington C, Zagari MJ, Corea J, Klitenic J. A cost analysis of diabetic lower-extremity ulcers. *Diabetes Care* **2000**; *23*:1333–8.
9. Holtzer SES, Camerota A, Martens L, Cuerdon T, Crystal-Peters J, Zagari M. Cost and duration of care for lower extremity ulcers in patients with diabetes. *Clin Ther* **1998**; *20*:169–1.
10. Panayiotopoulos YP, Tyrell MR, Arnold FJL, Korzon-Burakowska A, Amiel SA, Taylor PR. Results and cost analysis of distal (crural/pedal) arterial revascularisation for limb salvage in diabetic and non-diabetic patients. *Diabet Med* **1997**; *14*:214–20.
11. Metha SS, Suzuki S, Glick HA, Schulman KA. Determining an episode of care using claims data. *Diabetic foot ulcer*. *Diabetes Care* **1999**; *22*: 1110–5.
12. Palmer AJ, Weiss C, Sendi PP, et al. The cost-effectiveness of different management strategies for type I diabetes: a Swiss perspective. *Diabetologia* **2000**; *43*:13–26.
13. Ramsey SD, Newton K, Blough D, et al. Incidence, outcomes, and cost of foot ulcers in patients with diabetes. *Diabetes Care* **1999**; *22*:382–7.
14. Singh S, Evans L, Datta D, Gaines P, Beard JD. The costs of managing lower limb-threatening ischaemia. *Eur J Vasc Endovasc Surg* **1996**; *12*: 359–62.
15. Van Acker K, Oleen-Burkey M, De Decker L, et al. Cost and resource utilization for prevention and treatment of foot lesions in a diabetic foot clinic in Belgium. *Diabetes Res Clin Pract* **2000**; *50*:87–95.
16. Eckman MH, Greenfield S, Mackey WC, et al. Foot infections in diabetic patients: decision and cost-effectiveness analyses. *JAMA* **1995**; *273*:712–20.
17. Ragnarson Tennvall G, Apelqvist J, Eneroth M. Costs of deep foot infections in patients with diabetes mellitus. *Pharmacoeconomics* **2000**; *18*:225–38.

18. Kobelt G. Health economics: an introduction to economic evaluation. London: Office of Health Economics, 1996.
19. Ragnarson Tennvall G, Apelqvist J. The inpatient care of patients with diabetes mellitus and foot ulcers: a validation study of the correspondence between medical records and the Swedish Inpatient Registry with the consequences for cost estimations. *J Intern Med* 2000; 248: 397–405.
20. Masson EA, MacFarlane IA, Power E, Wallymahmed M. An audit of the management and outcome of hospital inpatients with diabetes: resource planning implications for diabetes care team. *Diabet Med* 1992; 9:753–5.
21. Leslie PJ, Patrick AW, Hepburn DA, Scougal IJ, Frier BM. Hospital inpatient statistics underestimate the morbidity associated with diabetes mellitus. *Diabet Med* 1992; 9:379–85.
22. van Houtum WH, Lavery LA. Outcomes associated with diabetes-related amputations in the Netherlands and in the state of California, USA. *J Intern Med* 1996; 240:227–31.
23. US Bureau of Labor Statistics. Consumer price index, medical care. Vol 2000. Washington, DC: US Government Printing Office, 2000.
24. Landstingsförbundet. Statistisk årsbok för landsting 2000 [Statistical yearbook for county councils 2000] Stockholm: Landstingsförbundet (The Federation of County Councils), 2000.
25. Statistics Sweden. Statistical yearbook of Sweden, 2000. Stockholm: Statistics Sweden, 1999.
26. The Swedish Central Bank. Statistical yearbook 1998. Stockholm: The Swedish Central Bank, 1999.
27. Ashry HR, Lavery LA, Armstrong DG, Lavery DC, van Houtum WH. Cost of diabetes-related amputations in minorities. *J Foot Ankle Surg* 1998; 37:186–90.
28. Cheshire NJW, Wolfe JHN, Noone MA, Davies L, Drummond M. The economics of femorocrural reconstruction for critical leg ischemia with and without autologous vein. *J Vasc Surg* 1992; 15:167–75.
29. Gibbons GW, Marcaccio EJ, Burgess AM, et al. Improved quality of diabetic foot care, 1984 vs 1990: reduced length of stay and costs, insufficient reimbursement. *Arch Surg* 1993; 128:576–81.
30. Gupta SK, Veith FJ, Ascer E, White Flores SA, Gliedman ML. Cost factors in limb-threatening ischaemia due to infrainguinal arteriosclerosis. *Eur J Vasc Surg* 1988; 2:151–4.
31. Statistics Sweden. Statistical yearbook of Sweden, 1993. Stockholm: Statistics Sweden, 1992.
32. Jägeblad G, Apelqvist J, Nyberg P, Berger B. The diabetic foot: from ulcer to multidisciplinary team approach—a process analysis [abstract]. In: The diabetic foot, third international symposium, Noordwijkerhout, The Netherlands, 1999: 149.
33. Macfarlane RM, Jeffcoate WJ. Factors contributing to the presentation of diabetic foot ulcers. *Diabet Med* 1997; 14:867–70.
34. Mantey I, Foster AVM, Spencer S, Edmonds ME. Why do foot ulcers recur in diabetic patients? *Diabet Med* 1999; 16:245–9.
35. Mills JL, Beckett WC, Taylor SM. The diabetic foot: consequences of delayed treatment and referral. *South Med J* 1991; 84:970–4.
36. Bild DE, Selby JV, Sinnock P, Browner WS, Braveman P, Showstack JA. Lower-extremity amputation in people with diabetes. Epidemiology and prevention. *Diabetes Care* 1989; 12:24–31.
37. Hill SL, Holtzman GI, Buse R. The effects of peripheral vascular disease with osteomyelitis in the diabetic foot. *Am J Surg* 1999; 177:282–6.
38. Apelqvist J, Larsson J. What is the most effective way to reduce incidence of amputation in the diabetic foot? *Diabetes Metab Res Rev* 2000; 16(Suppl 1):S75–83.
39. Herman WH, Eastman RC. The effects of treatment on the direct costs of diabetes. *Diabetes Care* 1998; 21(Suppl 3):C19–24.
40. Ollendorf DA, Kotsanos JG, Wishner WJ, et al. Potential economic benefits of lower-extremity amputation prevention strategies in diabetes. *Diabetes Care* 1998; 21:1240–5.
41. Ragnarson Tennvall G, Apelqvist J. Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. *Diabetologia* 2001; 44:2077–87.
42. Patout CA, Birke JA, Horswell R, Williams D, Cerise FP. Effectiveness of a comprehensive diabetes lower-extremity amputation preventive program in a predominantly low-income African-American population. *Diabetes Care* 2000; 23:1339–42.
43. Armstrong DG, Harkless LB. Outcomes of preventative care in a diabetic foot specialty clinic. *J Foot Ankle Surg* 1998; 37:460–6.
44. McCabe CJ, Stevenson RC, Dolan AM. Evaluation of a diabetic foot screening and protection programme. *Diabet Med* 1998; 15:80–4.
45. Apelqvist J, Ragnarson Tennvall G. Cavity foot ulcers in diabetic patients: a comparative study of cadexomer iodine ointment and standard treatment; an economic analysis alongside a clinical trial. *Acta Derm Venereol* 1996; 76:231–5.
46. Margolis DJ, Kantor J, Berlin JA. Healing of diabetic neuropathic foot ulcers receiving standard treatment. *Diabetes Care* 1999; 22:692–5.
47. Apelqvist J, Ragnarson Tennvall G, Larsson J. Topical treatment of diabetic foot ulcers: an economic analysis of treatment alternatives and strategies. *Diabet Med* 1995; 12:123–8.
48. Edmonds M, Gough A, Solovera J, Standaert B. Filgrastim in the treatment of infected diabetic foot ulcers: retrospective cost analysis of a phase II randomised clinical trial. *Clinical Drug Investigation* 1999; 17:275–86.
49. Ghatnekar O, Persson U, Willis M, Ödegaard K. Cost effectiveness of becaplermin in the treatment of diabetic foot ulcers in four European countries. *Pharmacoeconomics* 2001; 19:767–78.
50. Allenet B, Parée F, Lebrun T, et al. Cost-effectiveness modeling of Dermagraft for the treatment of diabetic foot ulcers in the French context. *Diabetes Metab* 2000; 26:125–32.
51. Persson U, Willis M, Ödegaard K, Apelqvist J. The cost-effectiveness of treating diabetic lower extremity ulcers with becaplermin (Regranex): a core model with an application using Swedish cost data. *Value in Health* 2000; 3(Suppl 1):S39–46.
52. Benton GS, Kerstein MD. Cost effectiveness of early digit amputation in the patient with diabetes. *Surg Gynecol Obstet* 1985; 161:523–4.
53. Kerstein MD, Welter V, Gathan V, Roberts AB. Toe amputation in the diabetic patient. *Surgery* 1997; 122:546–7.
54. Birnbaum HG, Cremieux PY, Greenberg PE, LeLorier J, Ostrander J, Vendetti L. Using healthcare claims data for outcomes research and pharmacoeconomic analyses. *Pharmacoeconomics* 1999; 16:1–8.
55. Glover JL, Weingarten MS, Buchbinder DS, Poucher RL, Deitrick GA, Fylling CP. A 4-year outcome-based retrospective study of wound healing and limb salvage in patients with chronic wounds. *Adv Wound Care* 1997; 10:33–8.
56. Complications of diabetes: screening for retinopathy. Management of foot ulcers. Vol 5 York, UK: University of York, National Health Service Centre for Reviews and Dissemination, 1999.
57. Mason J, O’Keeffe C, McIntosh A, Hutchinson A, Booth A, Young RJ. A systematic review of foot ulcer in patients with type 2 diabetes mellitus. I: prevention. *Diabet Med* 1999; 16:801–12.
58. Connor H. Diabetic foot disease: where is the evidence? *Diabet Med* 1999; 16:799–800.
59. Larsson J, Apelqvist J, Agardh CD, Stenström A. Decreasing incidence of major amputation in diabetic patients: a consequence of a multidisciplinary foot care team approach? *Diabet Med* 1995; 12:770–6.
60. Pecoraro RE, Reiber GE, Burgess EM. Pathways to diabetic limb amputation: basis for prevention. *Diabetes Care* 1990; 13:513–21.
61. Cavanagh PR, Ulbrecht JS, Caputo GM. The non-healing diabetic foot wound: fact or fiction? *Ostomy Wound Manage* 1998; 44(Suppl 3A): 6S–12S.