

Diabetic foot ulcers: Evidence, cost and management



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The diabetic foot constitutes a tremendous challenge for people with diabetes, care givers and the health care system (Boulton et al, 2005). The International Working Group consensus document was a milestone in the recognition of the important consequences of the diabetic foot (International Working Group on the Diabetic Foot, 1999). Since then, there have been a substantial number of consensus documents, position statements, reviews and an impressive number of original papers.

Now is the time to consider the present situation and future developments as we eagerly await the birth of the second international consensus document expected at the *5th International Symposium on the Diabetic Foot*, to be held in Noordwijkerhout, the Netherlands, later this year.

In 2001, a cost-utility analysis of the prevention of diabetes-related foot ulcers and amputations was published (Ragnarson-Tennvall and Apelqvist, 2001). In this model simulation involving people with diabetes, optimal prevention according to international consensus recommendations (patient education, foot care and appropriate footwear) was compared with actual prevention and standard care in a Swedish population. The results from the study showed that if all people at risk of diabetic foot ulcers and amputations were provided with adequate prevention and multidisciplinary management when first presenting with an ulcer, this strategy would be highly cost effective or even cost saving.

These findings were supported by similar model simulations that found the approach cost effective when incidence of ulcer or amputation was reduced by 25–42% (Ortegon et al, 2004; Rauner et al, 2004). The conclusions from these studies were that the management of the diabetic foot according to present guidelines would result in improved survival and a reduced number of diabetic foot complications. In addition, it would be cost effective or even cost saving compared to standard care. These and other studies also stated the importance and

the influence of health care organisations and reimbursement in prevention and management of the diabetic foot ulcer (Boulton et al, 2005; Ragnarson-Tennvall and Apelqvist, 2004).

These papers not only had a substantial influence on increasing awareness among policy makers, care givers and health care organisations but also an increased interest from the pharmaceutical industry. Thus, cost-effectiveness analysis of local wound treatment was born.

In recent years, a number of reports have reported on the cost-effectiveness of different new technologies and dressings used for the local treatment of diabetic foot ulcers. Although many of these products are more expensive compared with standard treatments, the use of them may be cost effective if they result in less frequent dressing changes or more effective and faster healing with a lower probability of amputation.

It is important to be aware that a treatment could be cost effective in one group of patients or for one type of ulcers but not in another. An intervention could also be cost effective when used in one setting or country but not in another.

Large clinical studies describing the typical clinical presentation of diabetic foot ulcers and factors related to outcome were limited at the time of the consensus document. Today, the Eurodiale study (Prompers et al, 2007) along with other large cohort studies have given us a deeper understanding of the factors related to outcome and healing time in cases of diabetic foot ulceration (Apelqvist, 1998; Beckert et al, 2006; Jeffcoate et al, 2006; Margolis et al, 2000; Treece et al, 2004). According to results of these studies, which come from mostly European cohorts, the severity of diabetic foot ulcers at presentation is greater than previously reported: more than 50% with infection (with >50% of these being of neuroischaemic origin) and as many as one-third with both peripheral artery disease and infection. They report that non-plantar foot ulcers are now more common than plantar ulcers – especially in people with severe

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diabetes – and serious comorbidities increase significantly with increasing severity of foot disease (Margolis et al, 2000; Margolis et al, 2002; Margolis et al, 2003). However the trend in all these studies is a successive improvement in healing rate (50–60% at 20 weeks, >75% at one year). With the present knowledge and the development of more advanced technologies in wound healing we should be able to design more selective intervention studies based on the type, site, cause and condition of the wound as well as comorbidity and use more wound-specific ‘biomarkers’ for outcomes rather than the simplistic ‘intact skin’ as a primary end point (Oyibo et al, 2001; Zimny et al, 2004).

Signs of peripheral artery disease can be found in more than half of all people with a foot ulcer (European cohort of Prompers et al, 2007). Given the uncertainties of history and clinical examination, more objective measurements of skin perfusion are frequently needed. These non-invasive vascular tests can be used for predicting wound healing in diabetic foot ulcers and the need for revascularisation (Norgren et al, 2007). Studies performed on neuroischaemic and ischaemic ulcers show an improved intervention rate as well healing rate and an increased awareness of angioplasty as a method to achieve healing in a diabetic foot ulcer (Faglia et al, 2002; Adam et al, 2005; Jacqueminet et al, 2005). However we still have a limited number of interventional studies for neuroischaemic and ischaemic ulcers compared to studies investigating topical wound treatment in the neuropathic ulcer.

Infection is seldom the direct cause of an ulcer. However, once an ulcer is complicated by an infection, the risk for subsequent amputation is greatly increased (Armstrong et al, 1998). In the present Eurodiale study more than 50% of participants with a foot ulcer received antibiotics at admission to a diabetic foot clinic. Furthermore, 25–75% of the study participants at various centres were considered to have a wound infection

at time of admission. This finding is especially disturbing in a time of multiresistant microbes and the debate surrounding ‘bioburden’ and ‘biofilms’. However the choice of antimicrobial treatment is empiric and most studies of antibiotics in diabetic foot infection involve skin infections only and not ulcers with superficial or deep infection.

Recent research has emphasised the importance of psychological factors in the development of diabetic foot ulcers. Studies have shown that perceptions of the individual’s own risks based on symptoms and their own belief of the efficacy of self care can affect foot care practice and patient concordance.

There is a substantial amount of new information and knowledge waiting to be recognised and implemented in daily practice. However these findings indicate the need for not only interventional studies but also prospective data collection studies in selected patient cohorts. The recent studies have shown that the diabetic foot community now is mature enough to perform large, multicentre cohort, interventional studies on the same level and quality as in other areas of medicine. ■

Adam DJ, Beard JD, Cleveland T et al (2005) Bypass versus angioplasty in severe ischaemia of the leg (BASIL): multicentre, randomised controlled trial. *Lancet* **366**: 1925–34

Apelqvist J (1998) Wound healing in diabetes. Outcome and costs. *Clinics in Podiatric Medicine and Surgery* **15**: 21–39

Armstrong DG, Lavery LA, Harkless LB (1998) Validation of a diabetic wound classification system. The contribution of depth, infection, and ischemia to risk of amputation. *Diabetes Care* **21**: 855–9

Beckert S, Witte M, Wicke C et al (2006) A new wound-based severity score for diabetic foot ulcers. *Diabetes Care* **29**: 988–92

Boulton AJM, Vileikyte L, Ragnarson-Tennvall, Apelqvist A (2005) The global burden of diabetic foot disease. *Lancet* **366**: 1719–24

Faglia E, Mantero M, Caminiti M et al (2002) Extensive use of peripheral angioplasty, particularly infrapopliteal, in the treatment of ischaemic diabetic foot ulcers: clinical results of a multicentric study of 221 consecutive diabetic subjects. *Journal of Internal Medicine* **252**: 225–32

International Working Group on the Diabetic Foot (1999) *International Consensus on the Diabetic Foot*. IDF, Brussels

Jacqueminet S, Hartemann-Heurtier A, Izzillo R et al (2005) Percutaneous transluminal angioplasty in severe diabetic foot ischemia: outcomes and prognostic factors. *Diabetes and Metabolism* **31**: 370–5

Jeffcoate WJ, Chipchase SY, Ince P, Game FL (2006) Assessing the outcome of the management of diabetic foot ulcers using ulcer-related and person-related measures. *Diabetes Care* **29**: 1784–7

Margolis DJ, Kantor J, Santanna J et al (2000) Risk factors for delayed healing of neuropathic diabetic foot ulcers: a pooled analysis. *Archives of Dermatology* **136**: 1531–5

Margolis DJ, Allen-Taylor L, Hoffstad O, Berlin JA (2002) Diabetic neuropathic foot ulcers: the association of wound size, wound duration and wound grade on healing. *Diabetes Care* **25**: 1835–9

Margolis DJ, Gelfand JM, Hoffstad O, Berlin JA (2003) Surrogate end points for the treatment of diabetic neuropathic foot ulcers. *Diabetes Care* **26**: 1696–700

Norgren L, Hiatt WR, Dormandy JA et al (2007) Inter-Society Consensus for the Management of Peripheral Arterial Disease (TASC II). *Journal of Vascular Surgery* **45**: S5–67

Ortegon MM, Redekop WK, Niessen LW (2004) Cost-effectiveness of prevention and treatment of the diabetic foot. *Diabetes Care* **27**: 901–7

Oyibo SO, Jude EB, Tarawneh I et al (2001) The effects of ulcer size and site, patient’s age, sex and type and duration of diabetes on the outcome of diabetic foot ulcers. *Diabetic Medicine* **18**: 133–8

Prompers L, Huijberts M, Apelqvist J et al (2007) High prevalence of ischaemia, infection and serious comorbidity in patients with diabetic foot disease in Europe. Baseline results from the Eurodiale study. *Diabetologia* **50**: 18–25

Ragnarson-Tennvall G, Apelqvist J (2001) Prevention of diabetes-related foot ulcers and amputations: a cost-utility analysis based on Markov model simulations. *Diabetologia* **44**: 2077–87

Ragnarson-Tennvall G, Apelqvist J (2004) Health-economic consequences of diabetic foot lesions. *Clinical Infectious Diseases* **39**: S132–9

Rauner MS, Heidenberger K, Pesendorfer E-M (2004) Using a Markov model to evaluate the cost-effectiveness of diabetic foot prevention strategies in Austria. *Proceedings of the International Conference on Health Sciences Simulation* 18–22 January 2004, San Diego, California, USA

Treece KA, Macfarlane RM, Pound N et al (2004) Validation of a system of foot ulcer classification in diabetes mellitus. *Diabetic Medicine* **21**: 987–91

Zimny S, Schatz H, Pfohl M (2004) The effects of ulcer size on the wound radius reductions and healing times in neuropathic diabetic foot ulcers. *Experimental and Clinical Endocrinology & Diabetes* **112**: 191–4