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Effective Health Care

Bulletin on the effectiveness of health service interventions for decision makers

This bulletin discusses the effectiveness of screening for diabetic retinopathy and interventions for foot ulcers in people with diabetes.

Complications of diabetes:

Screening for retinopathy
Management of foot ulcers

- Over a million people in the United Kingdom have diabetes of which the majority have Type 2 (non-insulin dependent) diabetes.
- Diabetic retinopathy is the most common cause of blindness in people of working age in industrialised countries. Up to 40% of people have some retinopathy when Type 2 diabetes is first diagnosed.
- In its early stages, retinopathy causes no symptoms, but it can be detected by examination of the back of the eye. It has been estimated that comprehensive screening and treatment for diabetic retinopathy could prevent 260 new cases of blindness every year.
- Screening can be effectively provided by trained and accredited optometrists or by retinal photographers in a variety of locations. Screening needs to be efficiently organised at a local level to ensure adequate population coverage.
- 15% of people with diabetes develop foot ulcers associated with nerve damage (neuropathy), lack of blood supply (ischaemia), or both. Serious infection originating in a diabetic ulcer is the most common reason for amputation apart from trauma.
- Multidisciplinary interventions, such as education to increase patients' knowledge about foot care, podiatry, and therapeutic shoes, can improve the condition of the feet and help to reduce ulcer and amputation rates.
- Various treatments are used for diabetic foot ulcers, but evidence for their effectiveness is generally poor.

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A. Introduction

This bulletin is based on two systematic reviews undertaken to inform National Clinical Practice Guidelines for Type 2 diabetes.[2,59] The text is divided into two main sections, the first dealing with screening for diabetic retinopathy, and the second with prevention and treatment of diabetic foot ulcers.

Two of the most common specific complications of diabetes are problems with feet, particularly persistent ulcers, and visual problems caused by retinopathy. The underlying cause of both problems appears to be chronically elevated blood glucose levels. The population at risk is large and growing. Around 2% of the UK population are believed to have diabetes, of whom perhaps 200,000 have Type 1 (insulin dependent) diabetes, and more than a million have Type 2 (non-insulin dependent) diabetes.[1]

B. Retinopathy

This section is based mainly on a systematic review of the effectiveness of different screening methods for diabetic retinopathy.[2] See Appendix 1 for information on the review methodology.

B.1 Background Diabetic retinopathy is the leading cause of blindness in people of working age in industrialised countries.[3] Twenty years after diagnosis, almost all of those with Type 1 diabetes and 60% with Type 2 diabetes will have some degree of retinopathy.[4] British screening studies suggest that around 5–10% have sight-threatening retinopathy,[5–9] and up to 40% of people with newly diagnosed Type 2 diabetes have some retinopathy.

In diabetic retinopathy, small blood vessels in the retina (back of the eye) become blocked, swollen or leaky, causing oedema (swelling), and new, fragile vessels grow haphazardly in the retina. This process can continue for years without causing visual symptoms or visual impairment; during this period, retinopathy can only be detected by eye examination. If it is left untreated, bleeding and scarring will lead to progressive loss of vision.

The condition is treated by laser photo-coagulation. Large trials have shown that this type of treatment can prevent blindness if it is given before significant visual loss has occurred.[10,11] Meta-analysis of studies of screening, followed by treatment of sight-threatening retinopathy, shows a high level of effectiveness.[12,13] This cuts the frequency of severe visual loss or blindness among people with diabetes to less than half the level found among untreated controls (relative risk 0.39, 95% CI 0.28 to 0.55).

B.2 Screening for retinopathy If diabetic retinopathy is to be detected and treated before it becomes sight-threatening, regular examination of the eyes is necessary. Retinopathy fulfils all the World Health Organisation's criteria for a screening programme: it is an important public health problem, there are diagnostic procedures and adequate screening tests by which it can be identified, and there is an effective treatment. It can also be highly cost-effective, both in terms of long-term health gains and money saved by prevention of visual impairment. Indeed, US studies suggest that the cost of screening and subsequent treatment can be lower than the cost of dealing with the blindness that could be expected without screening.[14–16]

It has been estimated that systematic screening for diabetic retinopathy could prevent about 260 new cases of blindness per year among people aged under 70 in England and Wales.[17] Nevertheless, there is wide variability in screening services in England and Wales, both in coverage and methods used. A survey found that over 40% of screening programmes included fewer than half of the people known to have diabetes in the areas they served, and 18 hospitals, covering a population of 2.5 million, had no systematic screening programmes at all for their areas.[18] There was also wide variation in protocols for referral to specialists and in waiting times for people with sight-threatening retinopathy.

B.3 Effectiveness of retinal screening Twenty studies were included in the review. Nine were carried out in the UK,[10,11,19–25] six in the US,[26–31] two in the Netherlands,[32,33] one each in New Zealand,[34] the West Indies,[35] and Egypt.[36]

Table 1 Screening methods used for diabetic retinopathy.

Screening Tool (method type)	Varieties	'Gold standard'	Comment
Ophthalmoscope (ophthalmoscopy)	Direct, Indirect	Slit-lamp biomicroscopy	An ophthalmoscope allows the user to see into the eye. Ophthalmoscopy is routinely used by GPs and high-street opticians
Retinal (fundus) camera (retinal photography)	Digital, 33mm, polaroid; mobile or fixed	Multiple (usually 5 or 7) field stereo photography	These are specialised cameras, used to produce colour photographs of the retina. Digital cameras require less flash and allow the picture to be viewed on a computer screen

Screening methods The effectiveness of screening for prevention of blindness depends on the method used, the competence of the screener, the screening interval, and organisational or other factors which affect the uptake of screening.

There are two main types of screening method, ophthalmoscopy and retinal photography. These may be further subdivided (see Table 1). Either method is currently used with or without mydriasis (dilation of the pupils with eye drops).

Direct ophthalmoscopy provides a limited field of view of the retina; indirect ophthalmoscopy allows a wider view and is therefore more sensitive. Photographs can be taken with a variety of special cameras, which may be digital or may use polaroid or 35mm film. Both ophthalmoscopy and retinal photography can be carried out with or without mydriasis. These methods have been assessed under a variety of conditions, as used by a range of professional groups.

Figures for sensitivity (proportion of people with the target disorder in whom the test result is positive) and specificity (proportion of people without the target disorder in whom the test result is negative) reported in UK studies are summarised in Table 2. It should be noted that few methods meet criteria proposed by the British Diabetic Association for effective screening (>80% sensitivity, >95% specificity, <5% technical failure rate).[37]

These studies used a variety of reference standards. These could produce slightly different results, so the figures quoted may not be directly comparable.

Retinal photography Retinal photography allows the screening process to be separated from assessment and provides lasting records of patients' retinas. It can be carried out in a range of settings, from clinics to mobile converted vans; the photographs can then be assessed by suitably trained readers.[38]

In most screening studies, photography is carried out after mydriasis. This significantly improves the quality of the photographs and increases the sensitivity of screening; one study reported that mydriasis improved sensitivity from 61% to 81%.[27] However, the camera flash is less comfortable for the patient after mydriasis (flash rated 'comfortable' by 80% rather than 90%) and temporary visual impairment may render some patients unable to drive safely or read small print for several hours after treatment.[39] Digital cameras require less intense flash, which causes less discomfort.[24]

Some retinal photographs are unclear and cannot be assessed. The reported rate for this form of technical failure ranges from 3.7% to 22%;[21,27,36] it is less frequent when mydriasis is used. There may be further improvement with digital systems.

Ophthalmoscopy In most studies of screening using ophthalmoscopy alone, direct ophthalmoscopes were used.[10,11,22,23,27,30,32,34] The sensitivity of this method was often found to be low even in the hands of experts, although specificity was high, usually 90–100% (see Table 2). This means that when retinopathy is detected, the result is likely to be correct.

A New Zealand study found that hospital diabetologists achieved good results with ophthalmoscopy, with sensitivities of 70% for any retinopathy and 80–90% for sight-threatening retinopathy.[34] However, poor results have also been reported in this situation. A London study of an individual diabetologist reported 27% sensitivity for detection of serious retinopathy.[20] Despite evidence of highly variable accuracy, ophthalmoscopy by consultants or junior physicians in hospital clinics has been the most widely used screening method.[38]

When GPs use ophthalmoscopy, sensitivity is often reported to be poor, ranging from 33% for any retinopathy to 67% for sight-threatening retinopathy.[11] Specificity is usually high (75–100%). Widely varying results have been reported for opticians and ophthalmologists.[10,22,26,27,29,31,35] In the largest UK study, opticians were no more accurate than GPs, with 48% sensitivity for sight-threatening retinopathy.[11]

An important reason for the lack of sensitivity of the direct ophthalmoscope is that it offers a small field of view. This instrument is now rarely used by ophthalmologists; its place has been taken by the slit-lamp biomicroscope and hand-held lens, which offers a much wider field of view.

A recent London study of optometrists, accredited after specialist training, found much higher levels of accuracy.[19] Participants used mydriasis but it is not clear what type of ophthalmoscope was used. The positive predictive value (PPV) for referable eye disease was 79% (i.e. 79% of patients referred had retinopathy requiring treatment) and the negative predictive value (NPV) was 100% (no cases were missed). Sensitivity and specificity levels (Table 2) met the criteria quoted earlier.[37]

Combined ophthalmoscopy and retinal photography
Ophthalmoscopy and retinal photography may be regarded as complementary. Ophthalmoscopy allows examination of parts of the retina which do not normally appear in photographs, whilst photography produces a lasting record which can be used for quality assurance without recalling the patient. Used together, these two methods can provide a high degree of accuracy in the hands of ophthalmologists or optometrists,[10,24,40] but reported

Table 2 Screening for diabetic retinopathy in the UK (all studies included people with Type 1 and Type 2 diabetes). Studies in alphabetical order by name of first author.

First author, date.	Screening method	Screener	Number screened (if stated)	Severity of retinopathy	Sensitivity (%, 95% CI)	Specificity (%, 95% CI if reported)	Comparison ('gold standard')	Comments
Burnett, 1998[19]	Ophthalmoscopy: no details given	Optometrists	536	Referable	100	94 (90–98)	Ophthalmoscopy by ophthalmologist	Screeners (community optometrists) trained & accredited, paid £20 for each examination
Buxton, 1991[11]	Direct ophthalmoscopy Polaroid camera, no mydriasis	GP Optician Hospital doctor Ophthalmologist in GP practice or hospital clinic, photos read by ophthalmologist	2350 307 416 2799	Sight-threatening Sight-threatening	53 (44–62) 48 (26–70) 67 (50–84) 56 (49–72)	91 (90–92) 94 (92–97) 96 (94–98) 97 (96–98)	Ophthalmoscopy by trained clinical assistant	Cost-effectiveness studies based on same data[48,49] 5% of photos unusable, 90% 'assessable'
Forrest, 1987[20]	Ophthalmoscopy	Diabetologist Nurse Diabetologist Nurse	282	Any Sight-threatening	51 (35–68) 50 27 55	99 (97–100) 99 99 92	Five field stereoscopic fundus photography	Confidence intervals reported only for diabetologist, any retinopathy
Gibbins, 1994[21]	35mm camera, mydriasis	GP	143	Any Proliferative	87 (66–97) 100	77 (70–85) 96 (92–99)	Same photos assessed by ophthalmologist	Sensitivity based on 'good quality' photos (78% of total)
Gibbins, 1998[22]	Direct ophthalmoscopy 35mm camera, mydriasis	GP Optician GP Optician GP Optometrist Diabetologist GP Optometrist Diabetologist	613 in first phase of study 644 in second phase	Any Sight-threatening Any Sight-threatening	63 (56–69) 74 (67–81) 66 (54–77) 82 (68–92) 79 (74–85) 88 (83–93) 73 (66–79) 87 (77–94) 91 (79–87) 89 (79–95)	75 (70–80) 80 (75–85) 94 (91–96) 90 (87–93) 73 (68–79) 68 (62–74) 93 (89–96) 85 (81–88) 83 (79–87) 91 (88–94)	Photos assessed by trained graders Same photos assessed by trained graders	
Harding, 1995[23]	Direct ophthalmoscopy 35mm camera, mydriasis	Ophthalmologist in GP practices Ophthalmological clinical assistant, GP practice	358	Sight-threatening	65 (51–79) 89 (80–98)	97 (95–99) 86 (82–90)	Slit lamp bio-microscopy by retinal specialist	14% of photos 'unobtainable'
O'Hare, 1996[10]	Direct ophthalmoscopy Direct ophthalmoscopy plus photo with mydriasis	Optician GP Optician	 517 493	Referable	73 60 88	93 98 99	Ophthalmoscopy by ophthalmologist	Only opticians using both methods achieve BDA criteria
Taylor, 1999[24]	Polaroid camera Digital camera Polaroid plus ophthalmoscopy	District retinal screener	197 534 unclear	Any Referable Any Referable Any Referable	72 (66–78) 90 (86–94) 74 (68–80) 85 (80–90) 92 (86–98) 95 (91–99)	88 (85–91) 97 (95–99) 96 (94–98) 98 (96–100) 92 (86–98) 97 (95–99)	Seven field stereo photography (118 patients, randomly selected)	Results for referable retinopathy consistently meet BDA criteria. Patients preferred digital; 2.6% discomfort versus 17% with polaroid
Williams, 1986[25]	35mm or polaroid camera, no mydriasis	Ophthalmological clinical assistant	62	Any	96 (88–99)	98 (87–100)	Ophthalmoscopy by ophthalmologist	Unusually high levels of accuracy – but a small study

sensitivity falls below acceptable levels when screening is carried out by GPs.[10,11]

B.4 Who should screen, and where? There is wide variation in sensitivity of screening by different professional groups (Table 2). In general, it appears that more experienced professionals such as specialist ophthalmologists are likely to be more accurate, whatever the method used. Consistently good results have been reported in US studies of trained graders assessing photographs in specialist centres.[25,27,29]

In the UK, retinal photography in mobile screening units may offer a practical and effective option.[23,38,41] However, the level of training required to operate the camera has not been clearly defined, and considerable experience is likely to be required to read the photographs accurately.

Whatever screening method is used, quality control is essential. An independent service for quality assurance of retinal photographs is available from the Retinopathy Grading Centre at Imperial College School of Medicine in London (fax 0181 383 2182).

A report from Shropshire describes an effective community-based service launched in 1996.[42] The screeners are NHS registered optometrists, trained by the local diabetes service and paid for each screening report submitted. Patients are referred for screening by GPs; almost 8,000 – 90% of the target population – have been screened; 10% were referred, of whom 20% received laser treatment. When screening by optometrists was compared with retinal photography, minor differences were found in 4.4% of cases but there was no disagreement about action required.

More information, including training details and the referral protocol, is available from the Clinical Audit Manager at Royal Shrewsbury NHS Trust, phone/fax 01743 261118.

B.5 Frequency of screening Population studies suggest that people without retinopathy are very unlikely to develop sight-threatening disease within four years, but those who have some retinopathy are at risk.[43–45] However, these studies were of predominantly white people; the population in many parts of Britain might show a different risk pattern. Particularly rapid disease progression can occur in some groups, notably pregnant women.

A US study modelled outcomes and costs for eight strategies, including routine screening every two to four years and re-screening for those with retinopathy at six month to two year intervals.[14] All these strategies produced benefits which outweighed costs, but a six month screening interval for those with background retinopathy saved the most person-years of sight.

One and two year intervals have been compared in Iceland.[45] Although a two year interval was sufficient for people without retinopathy, it led to more practical problems than annual screening.

The consensus among expert groups in Europe is that yearly screening is appropriate.[37,46] The Chronic Disease Management Programme (CDMP) for diabetes in primary care requires a full review of the patients' health, including their eyes, at least annually.

B.6 Costs and cost-effectiveness Any system of screening requires initial investment in equipment, training and administration and will have ongoing organisation and personnel costs. The capital costs of setting up a screening programme for diabetic retinopathy might include the cost of fundus cameras (about £14,000 for polaroid equipment, £28,000 for digital cameras and associated computer) and vans for mobile screening units.[47] Other costs include establishing effective call/recall and quality assurance systems.

Cost-effectiveness studies have been carried out using data from the UK[48,49] and the US.[28] None of these studies include all the costs of screening programmes and they do not allow conclusions to be drawn on the relative cost-effectiveness of different screening methods, but they do suggest how cost-effectiveness might be maximised.

Greater test sensitivity improves cost-effectiveness, which falls markedly when sensitivity drops below 40%.[14]

The costs per patient are generally low when screening is carried out as part of a routine review. For example, reported costs for GPs using ophthalmoscopy during a routine review were a mere £9 per patient, or £273 per true positive case of sight-threatening retinopathy identified (based on a mean sensitivity of 53%).[49] Although the greatest levels of cost-effectiveness were reported for screening in primary care, this did not offer the level of effectiveness specified by the British Diabetic Association. This study reported higher costs for retinal photography.[49] The cost per true positive was £497 when ophthalmologists read photographs taken in general practice settings, but £1,178 when the photograph was taken in a hospital. This difference reflects more frequent use of the mobile camera in general practice, resulting in lower per capita costs.

Mobile screening, using a van equipped with a fundus camera, has been proposed as an effective and inexpensive option. Reported costs are £10–£13 per patient screened and just over £1,000 per patient requiring laser treatment.[12,38] This included the salary of the photographer, depreciation and running costs for van and camera, and costs of film and processing.[8]

Screening by accredited optometrists in London was reported to cost £12.62 per case (including training and quality audit costs), plus a £20 fee to the optometrist.[19] The cost per case identified (2.3% of patients screened) was £581.

The potential costs of failure to offer effective screening should be weighed against the costs of providing such a service. These could include not only the cost of looking after people with avoidable blindness, but also litigation costs if such people were to pursue legal action against the Health Authority for negligence.

B.7 Recommendations for policy

- There is adequate evidence that screening should be provided for all people with diabetes who are not being treated for retinopathy.
- The service needs to be organised efficiently at a local level to ensure adequate population coverage.
- Screening can be provided effectively by accredited optometrists, reimbursed on a per capita basis, or by mobile retinal photography, operating in a variety of locations as necessary.
- The evidence is insufficient to make specific recommendations on the best method of screening; this may vary according to local circumstances.
- Training should be provided for screeners.
- Quality control systems are essential.

B.8 Recommendations for research Further research is required on the following issues:

- The best and most cost-effective way(s) of organising screening.
- Screening intervals.

C. Foot problems associated with diabetes

At some time in their life, 15% of people with diabetes develop foot ulcers associated with peripheral neuropathy (nerve damage) and/or ischaemia (lack of blood supply).[50] Neuropathy leads to loss of sensation and muscular control, and can cause a variety of other abnormalities and symptoms such as pain. This may occur at the same time as ischaemia. In a local population study of 1,077 patients with diabetes, 7.4% had foot ulcers or had experienced them; 40% of these were neuropathic, 24% ischaemic, and 36% mixed.[51] Recurrence rates for diabetic foot ulcers are 35–40% over three years and 70% over five years.[52]

These ulcers can have serious consequences. They are highly susceptible to infection, which may spread rapidly, causing overwhelming tissue destruction.[53] 5–15% of people with diabetic foot ulcers require lower extremity amputation, usually because of gangrene; foot ulcers precede 85% of amputations in people with diabetes in the US. [54,55] Up to two-thirds of non-traumatic amputations in the US are in people with diabetes whose ulcers have progressed to gangrene.[56]

Foot ulcers are one of the most costly aspects of treatment of diabetes.[57] They also put a heavy load on community services, since most patients are treated in the community and district nurses may visit up to three times a week.[58]

C.1 Review methodology A systematic review evaluating the effectiveness of interventions specifically intended for treatment or prevention of diabetic foot ulcers was used to inform this part of the bulletin.[59] The review methodology is described in Appendix 2.

C.2 Prevention It is possible to identify feet at risk of neuropathic ulceration by checking for loss of sensitivity to touch or vibration.[60-62] Plastic filaments (monofilaments) offer a cheap, effective and convenient means for assessing neuropathy.[63,64]

A large randomised controlled trial (RCT) (n=2,001) in a Liverpool diabetic clinic demonstrated that amputation rates among people at high risk of ulcers could be significantly reduced by a foot protection programme.[65] Patients with Type 2 diabetes and foot deformities, history of foot ulceration, significant vascular or neuropathic disease were randomised to the intervention – weekly clinics providing chiropody, hygiene, hosiery, protective shoes and education – or usual care. At two years, the ulcer rate in the intervention group was non-significantly reduced, to 2.4%, compared with 3.5% in the 'usual care' group (p=0.14). Amputations, however, were reduced three-fold, with seven in the intervention group and 23 among controls (p<0.04).

Education and podiatry (specialist foot care) may improve knowledge of foot care, and in some studies led to improvements in the condition of the feet.[66–72] These studies were of additional educational sessions over 6 to 18 months, usually provided by nurses or podiatrists, at the patient's home or in clinics. They included instruction on the importance of blood glucose control, inspecting the feet, foot hygiene, footwear, and dealing with fungal infections, calluses and injuries to the skin.

One study reported significantly reduced ulcer rates in high-risk patients.[69] Patients who had ulcers or had undergone amputation were randomised to a one-off hour-long class (intervention group, n=103), or ' usual care' (control, n=100). The intervention group was shown slides of infected feet and amputations, and given a

simple check-list of foot-care instructions. After one year, there were eight ulcers and seven amputations in the intervention group, compared with 26 ulcers and 21 amputations among controls (p=0.005 and 0.025 for each outcome, respectively).

C.3 Footwear interventions

Callus formation often precedes the development of neuropathic ulcers.[50] Callus tends to form at pressure points in ill-fitting shoes, compounded by effects of neuropathy on patterns of weight-bearing. These problems can be reduced through provision of orthoses – usually custom-made insoles designed to redistribute weight on the foot – and/or therapeutic shoes. One study (n=69) found that therapeutic shoes with custom-made insoles could reduce ulcers in people at high risk; the relapse or new ulcer rate at one year was 28% in the intervention group, compared with 58% among those who continued to wear their own shoes (p=0.009).[73] A very small trial (n=20) found that orthoses (without special shoes) reduced callus over a year, but the benefit was not significantly greater than that of podiatry.[74]

C.4 Effectiveness of treatment

Total contact casting. This involves the use of a plaster cast to re-distribute weight over the foot. A study of 40 patients with ulcers on the soles of the feet (plantar ulcers) reported that casting led to faster healing than conventional treatment (42 versus 65 days).[75]

Antibiotics. Systemic antibiotics are regarded as part of standard treatment for invasive infections associated with diabetic foot ulcers. Four randomised studies were identified. A double-blind study comparing amoxycillin/clavulanic acid with placebo (n=44) found no benefit. Thirty two percent of patients with less serious ulcers given antibiotics had closed lesions within 20 days, compared with 50% of those given placebo.[76] RCTs including patients with more serious foot infections such as osteomyelitis demonstrated no significant differences between the following: clindamycin versus cephalexin (n=56);[77] imipenem/cilastatin versus ampicillin/sulbactam (n=93);[78] ofloxacin versus ampicillin/sulbactam/clavulanate (n=88).[79]

Growth factors.* These are substances derived from human tissue which can stimulate growth. Five RCTs, with patient numbers ranging from 13 to 382, found that three types of growth factor (CT-102, RGDpm, and rhPDGF) helped uninfected ulcers to heal significantly faster.[80–84] A pilot study using rbFGF found no benefit.[85] No adverse effects were reported in any of these trials.

Granulocyte-colony stimulating factor (G-CSF).* G-CSF can enhance ability to fight infection. In a trial involving 40 people with diabetes and severely infected feet, all treated with antibiotics, G-CSF reduced infection significantly.[86] After a week, 21% in the G-CSF group had healed ulcers, compared with none in the placebo group. Four in the placebo group required surgery, compared with none in the G-CSF group.

Human dermal replacement. This is a product composed of human skin cells, cultured onto an absorbable mesh. Three publications were identified, all originating from Advanced Tissue Sciences Inc. (USA), describing randomised studies of human dermal replacement. Two concerned the same multi-centre study (n=281),[87,88] whilst the third described an earlier pilot study (n=50).[89] Whilst these studies suggest benefit, their results should be viewed with caution because there was differential loss to follow-up (22% of the group receiving cultured human dermis, 11% of controls in the larger study) and no intention to treat analysis. Further research is required to assess the efficacy of cultured human dermis.

Ketanserin.* Two trials of 2% ketanserin ointment, which is believed to improve local blood supply, were identified; one (n=140) included only patients with Type 2 diabetes,[90] the other (n=299) included 45 patients with diabetes.[91] Both suggest that topical ketanserin may enhance healing. A study of oral ketanserin (n=45) found no significant effect.[92]

Prostaglandins. A trial using a prostaglandin analogue, iloprost*,[93,94] and one of prostaglandin E_1**,[95] suggest that prostaglandins may improve healing of ischaemic diabetic ulcers. However, these were particularly poor studies; outcome measures were subjective, assessment was not blind, and baseline characteristics and results were poorly reported.

Other topical agents.* Small RCTs have reported benefits for a variety of substances. One RCT found that a thrice-daily soak in a foot-bath containing dimethylsulfoxide (DMSO) solution for 15 weeks, reduced pain and promoted healing of chronic ulcers (n=40).[96] A larger RCT (n=181) suggested possible benefits from the use of a gel containing copper and amino acids (Iamin-2% gel) applied immediately after debridement.[97]

Hyperbaric oxygen. An RCT (n=70) involving patients with severe ulcers found that an average of 38 daily sessions in a hyperbaric (pressurised) oxygen chamber could reduce the need for major amputation (8.6% had major amputations, versus 33.3% of controls; p=0.016).[98] However, the total number of amputations was similar in both groups (31% and 30%). An RCT (n=28) in which the affected foot was put in an oxygen leg chamber found no effect.[99]

Debridement. In a Swedish study, two adhesive hydrocolloid dressings, intended to improve debridement of necrotic ulcers, produced adverse effects including

pain.[100] Ulcer healing was not reported. The results of a small study (n=41) suggested that debridement using cadexomer iodine ointment might promote healing better than standard treatment, but the difference reported was not statistically significant.[101]

Wound dressings. A variety of dressings intended to foster healing (alginate, hydrocellular dressings, etc) have been compared in small RCTs.[102–108] None yielded evidence of superiority for any particular type of dressing.

* These have been evaluated in RCTs but there is currently no UK marketing authorisation.

** These have UK marketing authorisation but are not currently licensed for treatment of diabetic foot ulcers.

C5 Recommendations for policy and research There is evidence for the effectiveness of the following interventions for prevention:

- Identification of people at high risk and referral to foot care clinics which offer education, podiatry, and footwear.
- Therapeutic shoes with custom-moulded insoles.

The following treatments may be beneficial but further trials are required:

- Total contact casting
- Growth factors
- Granulocyte-colony stimulating factor (G-CSF) for patients with severe infections.
- 2% ketanserin ointment
- Iamin gel
- Debridement with cadexomer iodine.

Research should also address the following questions:

- Is antibiotic treatment effective for improving healing, or reducing infection or pain associated with neuropathic or neuro-ischaemic ulcers?
- Is weight-bearing exercise beneficial or harmful for people with diabetic foot ulcers who wear appropriate footwear?
- What should educational interventions for people with diabetes include?

Research studies should consider long-term outcomes.

Appendix 1 – Screening for retinopathy: Review methodology

Search strategy

The following databases were searched from 1983 onwards: Cinahl, Cochrane Trials Register, Embase, Healthstar, Medline, Psychlit, Science Citation, Social Science Citation, HEED, NHS Economic Evaluation Database for Economic Evaluations and ECRI HTAIS. Trial registers were searched for ongoing and unpublished trials and conference proceedings were examined using the Index to Scientific and Technical Conference Proceedings (ISI). Access to 'grey literature' was through the HMIC database and SIGLE.

Assessment of studies

Studies covering both Type 1 and Type 2 diabetes were included if they specifically addressed screening for, and early management of, diabetic retinopathy. Assessment and grading of papers was conducted independently by two reviewers and disagreements were resolved by discussion.

No RCTs were found in the area of retinopathy screening. The best quality evidence was from cohort studies. These were assessed for quality independently by the two reviewers on the following criteria:

Prospective design; independent interpretation of test results; independent interpretation of reference standard; all patients included in the study had the reference standard examination; numbers of patients included in studies; numbers of professionals carrying out the screening method under evaluation.

Appendix 2 – Diabetic foot ulcers: Review methodology

The following bibliographic databases were searched for controlled trials in diabetic foot disease: Cochrane Trials Register, Medline, Embase, Cinahl, Healthstar, Psyclit, Science Citation, Social Science Citation, HEED and NHS Economic Evaluation Database for Economic Evaluations. Conference proceedings were examined using the Index to Scientific and Technical Conference Proceedings (ISI). 'Grey literature' was sought using the HMIC database and SIGLE. Diabetic Medicine and Diabetes Care were hand-searched.

Assessment of studies

Assessment of papers retrieved and abstraction of data was conducted independently by two reviewers and disagreements were resolved by discussion. Studies were considered if they addressed screening, management, care, prevention or education relating to the care of people with diabetic foot problems. Only RCTs were used for information on effectiveness given in the bulletin. Studies which addressed Type 1 as well as Type 2 diabetes were included.

A methodological checklist was used to check the quality of RCTs. This included the following criteria: concealment of randomisation and outcomes, intention to treat, degree of follow up, comparability of control and treatment groups at baseline and comparability of control and treatment groups on factors other than the intervention given.

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Effective Health Care

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