REPORT

T

SCREENING FOR DIABETIC RETINOPATHY

health technology assessment

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EXECUTIVE SUMMARY

Diabetic retinopathy is a microvascular complication of both insulin dependent (Type I) and non-insulin dependent (Type II) diabetes. The diagnosis is through either examination of the fundus of the eye or by fundus photography.

The study was done to determine the effectiveness, cost effectiveness and feasibility of screening for diabetic retinopathy. From the evidence obtained the following is recommended.

- A screening programme for diabetic retinopathy for all diabetic patients.

- Screening should include assessment of vision and retinal examination (ophthalmoscopy) with or without photography. Photography could be carried out using non-mydriatic fundus cameras (conventional or digital). The local cost of a conventional fundus camera is approximately RM 100, 000 per unit, while a digital camera would cost about RM 120, 000.

- Initial screening carried out by primary healthcare providers, followed by retinal photography by trained personnel (technicians, optometrists or ophthalmologists) technicians.

- Trained readers or ophthalmologists should subsequently read fundus photographs or fundal digital images.

TABLE OF CONTENTS

1. INTRODUCTION

Diabetes mellitus is one of the most prevalent chronic diseases in Malaysia - its prevalence is 8.3% among the population aged 30 years and above (National Health & Morbidity Survey, 1996). Like other non-communicable diseases related to life-styles, economic loss can be prevented and reduced by having primary and secondary preventive programmes. Among the risk factors for diabetes mellitus are uncontrolled hypertension, smoking and obesity. It is estimated that there will be a three-fold increase in the prevalence of diabetes mellitus among Asians, so that it is expected to exceed 10% in the Malaysian population by the year 2020 (Ministry of Health Malaysia, 1996). Consequently, the total costs of management of the disease will escalate. Diabetes mellitus is a complex disease with end organ complication. However, good control of the disease mellitus will prevent the onset or retard progression of the various complications including diabetic retinopathy.

The management of diabetes in Ministry of Health facilities is currently being carried out at health clinics, polyclinics, specialist clinics, and in hospital wards. While there is no comprehensive integrated diabetes control programme in Malaysia, various efforts have been made and activities are still continuing. Some of these are as follows: -

1. Improving diabetes care at all levels by drawing up and disseminating the following clinical practice guidelines (CPG) to clinics and hospitals:-
    - *CPG: Diabetic Retinopathy 1996*
    - *Practice Guidelines for Diabetes Mellitus Type 2: The Malaysian Consensus 1996*

2. Setting up a structured diabetes-screening programme in all health clinics and hospitals with the provision of glucometers and guidelines for screening.

3. Training health and hospital personnel involved in diabetes care in all states.

4. Implementing Quality Assurance programmes in primary health care facilities to assure the quality of care of diabetes.

5. Efforts are being made to integrate both screening and treatment of diabetes and cardiovascular diseases in the ambulatory wellness clinics in public health facilities and in hospitals.

6. Formulation of a national action plan to identify strategies for improvement of diabetes care in Malaysia.

With respect to eye care, in most large hospitals, diabetics with eye problems will be referred to the ophthalmologist for management. This would include patients with decreased vision or fundal changes, or, patients in whom the fundus is unable to be visualised.

1.1 Diabetic retinopathy

In recent decades, diabetic retinopathy has been the commonest cause among registration of the blind in those of the working age group in United Kingdom. In Malaysia, diabetes eye disease is the commonest cause of visual loss in adults of working age. The prevalence of retinopathy is closely linked to the duration of the diabetes. At diagnosis, less than 5 % will have retinopathy while after 10 years the prevalence rises to 40-50 %. After 20 years, almost all patients with type I diabetes and more than 60% patients with type II diabetes have some degree of retinopathy. When these changes threaten vision, early treatment can prevent sight loss in many cases. Late presentation continues to present a major challenge in terms of prevention and alleviation of blindness. A diabetic is twenty-five times more likely to develop blindness as compared to the general population.

The incidence of blindness (vision of <3/60 in the better eye) or severe visual impairment (vision between 6/18-6/60 in the better eye) is not known in Malaysia. However, the prevalence of diabetic retinopathy as measured in several population-based studies indicate a range of 3-6% of diabetics. In the Wisconsin Epidemiology Study of Diabetic Retinopathy, it was found that a larger percentage of early onset diabetics developed blindness as compared to older onset diabetics. Overall, it was found that diabetic retinopathy was the most frequent cause of new blindness among adults aged 20-70 years. In Malaysia, the National Eye Survey done in 1996, showed that the prevalence of diabetic retinopathy among non-insulin dependent diabetes mellitus (NIDDM) aged 40 years and above with a duration of more than 5 years is 14.6%. This is expected to double with increase in duration of the disease. The prevalence of diagnosed diabetes in Malaysians aged 50 years and above for 1996 is estimated to be 10.3% or about 200,000 people and 3.5% of them may have diabetic retinopathy. Hence, about 7,300 people aged 50 years and above are estimated to have diabetic retinopathy in Malaysia (National Eye Survey, 1996).

Although statistics on blindness due to diabetic retinopathy is lacking, the existing hospital based data has shown that it is becoming an increasingly important cause of blindness. This is because of rising prevalence of diabetes due to the change of lifestyles, improved medical care and the ageing population. Apart from these, many diabetics are not aware that diabetes causes blindness implying that they would not go for voluntary eye screening. In addition, most diabetics are being treated at the primary care level - general practitioner clinics, public outpatient clinics and health centres. The sheer volume of patients, compounded by the inability of health care providers to detect diabetic retinopathy by direct ophthalmoscopy, hampers effective screening. The present practice of only ophthalmologists and physicians examining the fundi of diabetics in hospitals, is unsatisfactory, since it will only reach a small percentage of diabetics.

The key measures to prevent visual loss from diabetic retinopathy are:

i. early detection of retinopathy
ii. monitoring of existing retinopathy with regular fundus examination.

iii. effective laser treatment at appropriate timings
(Retinopathy Sub-Committee of the Australian Diabetes Society for Diabetes Australia)

1.2 Screening for diabetic retinopathy

Since diabetic retinopathy is asymptomatic in its early and most easily treatable stages, it can only be detected by clinical eye examination. A screening programme must be comprehensive, that is, covering all persons with diabetes in a defined geographic area. Currently, a comprehensive register of all diabetic patients in Malaysia is not available.

Screening is currently performed in Malaysia by general practitioners, clinicians in a hospital based diabetes centres, ophthalmologists, optometrists, or (in the case of photography) a technician and a medically trained photographic interpreter. The sole screening method employed currently at the primary care level is direct ophthalmoscopy. A proportion of diabetic patients with poor vision visit optometrists directly for visual problems some of which may be due to diabetic retinopathy.

2. OBJECTIVE

To determine the effectiveness, cost- effectiveness and feasibility of screening for diabetic retinopathy.

3. METHODOLOGY

Literature search was done using the Medline database. Keywords used were *screening for diabetic retinopathy, detection, early detection, methods of screening, efficacy, effectiveness, cost-effectiveness*. These words were used either singly or in various combinations. The years searched were from 1988 to 1998. Other sources of information were health technology assessment reports from Scottish Purchasing Health Information Centre (SPHIC) and the Swedish Council of Health Technology Assessment (SBU) and clinical practice guidelines of Australia (1997) and USA (1998).

For screening methods, a total of 2,223 article titles were obtained based on the keywords. Of these, 36 titles were considered to be relevant as gauged from the abstract. Exclusion criteria were unavailability of abstracts and inability to obtain an English translation of a foreign language article. Data from these 36 articles, abstracts and reports were studied. In the final analysis, only data from 18 articles and 3 reports were included as these met the criteria. Each article was graded on the level of evidence according to the modified CAHTA scale (Appendix A).

4. TECHNICAL FEATURES

4.1 Diabetic retinopathy

Diabetic retinopathy is a microvascular complication of both insulin dependent (type I) and non-insulin dependent (type II) diabetes. The clinical manifestations of retinopathy are due to two basic pathophysiologic mechanisms:

i. increased capillary permeability, and,
ii. closure of retinal capillaries.

One of the earliest signs of diabetic retinopathy is dilatation of the veins in the retina. The small capillaries present may also undergo early changes, leading to occlusion. This result in small bulges in the vascular walls, referred to as microaneurysms. At this early stage, referred to as minimal *non-proliferative diabetic retinopathy* (NPDR), sight may not be affected.

Subsequently, the blood flow progressively deteriorates, causing damage to increasingly larger portions of the retina. Small haemorrhages and more vascular changes in the fundus of the eye appear, next to the injured areas. There is also evidence of vascular occlusion and leakage. Thus, the retinopathy progresses from minimal to mild when there is retinal haemorrhage, hard exudate (well-defined yellow deposits consisting of lipoproteins) and nerve layer infarct. In the case of moderate NPDR in addition to the above, there is venous beading and intra-retinal microvascular abnormalities (enlarged hypercellular capillaries that function as shunt vessels). Classification of NPDR is based on standard photographs as well as the extent of damage - thus, in severe NPDR there should be more haemorrhages of microanuerysms, intra-retinal microvascular abnormalities and venous beading than in moderate NPDR.

The next stage *proliferate diabetic retinopathy* (PDR) is where there is neovascularisation of the retina, where the new vessels attach themselves to the posterior surface of the body of the vitreous and may also grow into it, surrounded by strands of connective tissue. These strands of vessels and connective tissue pull on the retina and may cause it to detach thus resulting in blindness. This is the stage of *advanced PDR* (Wisconsin Epidemiological Study of Diabetic Retinopathy), while the intermediate stage is referred to as *high risk PDR*. (Clinical Practice guidelines, Australia, 1998)

The main causes of visual loss from diabetic retinopathy are disturbances to the macula, affecting central vision (macular oedema and clinically significant macular oedema) and profound retinal ischaemia leading to proliferative retinopathy.

The diagnosis of diabetic retinopathy is through either examination of the fundus of the eye or fundus photography.

4.2 Screening Modalities

The screening modalities used in screening programmes have been one or a combination of the following:

i. Ophthalmoscopy
   a) Direct
   b) Indirect

ii. Slit lamp biomicroscopic retinal examination - indirect ophthalmoscopy using special lenses in dilated pupils.

iii. Fundus photography
   a) Mydriatic
   b) Non-mydriatic

   Type of picture analysed:-
   - Polaroid
   - Colour slide
   - Photographs
   - Transparencies
   - Digital storage and transmission of images
   - Artificial Neural Network (ANN)

iv. Scanning laser ophthalmoscopy (SLO)
   a) recorded on U-Matic videotape

4.3 Screening programme

A number of studies have shown the need for a diabetic retinopathy screening programme. Bachmann (1998) concludes that screening and early treatment can prevent substantial disability. Ronald (1997) points out that severe visual loss due to clinically significant macular oedema or proliferative retinopathy can be prevented and hence the need for a screening programme. Kimberly (1998) advocates screening of type I diabetes within 5 years of diagnosis, and type II at the time of diagnosis. Ryder (1995) suggests that blindness due to retinopathy is preventable and the cost of litigation may dwarf into insignificance the cost of providing a screening programme. As diabetic retinopathy can lead to blindness, a screening programme can prevent this complication.

Screening for diabetic retinopathy fulfils the pre-requisites of an effective screening programme:-

i. *The disorder for which screening is to be conducted should be well defined*. In diabetic retinopathy, proliferative diabetic retinopathy and macular edema are easily identifiable.

ii. *Estimates of the prevalence and rate of progression of the disorder should be known*. The Malaysian figures show an estimate of about 3.5% prevalence in those above 50 years of age, but this may be an underestimate.

iii. *The disorder should be asymptomatic at least in its early stages but if left untreated, leads to significant morbidity*. There is evidence that if diabetic retinopathy is left untreated, it can lead to severe visual loss (Diabetic Retinopathy Vitrectomy Study Research Group, 1985; Early treatment Diabetic Retinopathy Study Research Group 1985; The second report of Diabetic Retinopathy Study Findings, 1983)

iv. *An effective treatment for the condition should be available*. The treatment for diabetic retinopathy which is early vitrectomy and laser photocoagulation is safe, effective and universally agreed upon (Diabetic Retinopathy Vitrectomy Study Research Group, 1985; Early treatment Diabetic Retinopathy Study Research Group 1985; The second report of Diabetic Retinopathy Study Findings, 1983)

v. *The screening procedure of choice is acceptable to both the public and made available by the health care professionals* - in this case, acceptable screening tests are available

vi. *Screening method should be simple and safe* - again screening tests are both simple and safe.

vii. *Screening should be able to discriminate between affected and unaffected individuals.*
There is sufficient evidence for this. (Diabetic Retinopathy Vitrectomy Study Research Group, 1985; Early treatment Diabetic Retinopathy Study Research Group 1985; The second report of Diabetic Retinopathy study findings, 1983; Bachmann, 1998; Kristinsson, 1997; Barbar; Kimberley, 1998; Ryder, 1995; Harper, 1995).

viii. *Screening should be cost- effective* - the major studies (Javitt, 1991; Dasbaeh, 1991) did in the United States have shown diabetic retinopathy screening to be cost- effective as reviewed by Sandra J. Ackerman.

The American Academy of Ophthalmology's Diabetes 2000 Programme is working towards informing all physicians about screening for retinopathy and to assure adequate treatment for those patients needing it. Protocols for screening and treatment for diabetic retinopathy in Europe were approved by 57 specialists, representing 30 diabetic and ophthalmic societies from 21 European countries. This protocol was drawn up to meet

the target as defined by the joint World Health Organisation/International Diabetes Federation Saint Vincent Declaration Working Group, which is to reduce diabetes - blindness by one third or more, in 5 years. The clinical practice guidelines in Australia also recommend that it is cost effective to screen for diabetic retinopathy.

5. RESULTS AND DISCUSSION

5.1 Sensitivity and Specificity of Screening Methods

5.1.1 Fundus Camera

The fundus camera is an effective tool to screen for diabetic retinopathy (Taylor, 1990; Sculpher, 1992; Pugh,1993; Kristinsson, 1995; O'Hare, 1996; Taylor, 1996; Joannou, 1996; Villalpando, 1997; Owens, 1998; SHPIC report, 1996; SBU report 1990; American Diabetes Association, 1998; Prasad, 1997; Lan, 1995; Penman, 1998; NHMRC 1997; Taylor R, 1998). The proportion of poor films varied from 10% (Taylor, 1990) to 22% (Penman, 1998). The number of poor films were reduced if the pupils were dilated before photography (Taylor, 1990).

5.1.2 Dilatation of pupils

There is limited information comparing the sensitivity and specificity of retinopathy screening through either dilated or undilated pupils, examined by the same screener and using the same method. Compared to 7-field photography, the sensitivities of detecting mild NPDR, moderate NPDR and PDR were significantly lower using non-mydriatic 45° photographs taken through undilated pupils (sensitivities 58%, 76% and 43% fell to 42%, 49% and 14%, respectively), with two thirds of PDR missed (Pugh, 1993). This difference may be due in part to the smaller pupils of some people with diabetic autonomic neuropathy or cortical cataract present in many diabetic patients. (Pugh, 1993; Penman, 1998).

These studies indicate that pupil dilatation is essential in ophthalmoscopic screening for diabetic retinopathy (Taylor, 1996). However, it may not be required for acceptable photographs of many patients using the newer non-mydriatic cameras (NHMRC 1997)

5.1.3 'Gold' standard

The 'gold' standard applied to screening for diabetic retinopathy is - 'dilated seven - standard field 30° stereoscopic fundus photography' with photographs interpreted by experienced readers, or fluorescein angiography, or indirect biomicroscopy by a senior ophthalmologist. None of these is practical as a screening tool (Prasad, 1997). Different screening methods and combinations are often compared to the above methods as a reference standard to determine their sensitivity and specificity as a screening modality.

5.1.4 Photographic fields

The sensitivities and specificity for detecting any retinopathy with a single 45° non-mydriatic retinal photograph compared to the standard, varied from 40% (Sculpher, 1992) to 65.5% (Taylor, 1996) and 5% (Pugh, 1993) to 93% (Sculpher, 1992) respectively. In the WESDR (Wisconsin Epidemiological Study of Diabetic Retinopathy

- American Diabetes Association, 1998) a population based study, the 7-photographic field was used as the reference and compared to ophthalmoscopy through dilated pupils. The sensitivities reported were 56% to 61% for any retinopathy, 30% to 79% in PDR and 40% in macular oedema. When less photographic fields were used as compared to the 7-field photography in detecting diabetic retinopathy, sensitivities of 87%, 92% and 95% were obtained using 2, 3 or 4 photographic fields respectively. In cases with PDR, the sensitivity was 74%, 86% and 90% respectively.

5.1.5 Film storage

Varying methods of film storage were used such as colour slides, transparencies, polaroid films and digital image storage. Colour slide films were reported to be better than polaroid films due to the higher resolution (Pugh, 1993) and easy magnification for close inspection (Joannou, 1996).

5.1.6 Assessment of photographs

Photographing the fundus, with assessment of the photographs later by ophthalmologists or trained readers (e.g. optometrists, physicians and general practitioners), is also effective (O'Hare, 1996; SHPIC report, 1996; Owens, 1998; Ryder, 1998). A wholly automated approach involving fundus image analysis by computer could improve the efficiency of the assessment of the image by providing an immediate classification of the fundus of the patient at the time of acquisition of the image - artificial neural network (ANN) analysis (Gardener, 1996). However, currently, there is insufficient evidence to advocate this as the method of choice for screening.

The purpose of screening for diabetic retinopathy is to detect treatable sight threatening retinopathy and sight threatening maculopathy. The sensitivity of the screening methods should be compared with the detection of these two conditions.

Whichever method is used, it should have sufficient sensitivity (>80%) and specificity (>80%) for a single modality screening process (Prasad, 1997 -Proposed UK standard). The proposed Australian standard requires a sensitivity of at least 60% (NHMRC, 1997). Combining two modalities of screening (e.g. ophthalmoscopy and retinal photography) provides excellent sensitivity but increases the cost and often is only possible in a hospital based setting.

Where feasible, general practitioners, optometrists and physicians should actively screen their patients for diabetic retinopathy using a dilated fundus examination, combined with visual acuity assessment. Their ability to detect retinopathy need to be improved by regular and appropriate education, as well as by frequent practice. A sensitivity target of at least 60% for dilated fundus examination is achievable through education.

Mydriatic retinal photography or retinal photography with newer non-mydriatic retinal cameras incorporated in the screening programme helps enhance the sensitivity of screening. However, it should be recognised that the use of retinal photography as a screening tool does not substitute for a detailed eye examination and for detection of

other eye diseases that occur with increased frequency in people with diabetes, such as glaucoma or cataract.

5.2 Manpower

5.2.1 Physicians

Physicians, registrars, clinical assistants, senior house-officers screening for diabetic retinopathy by direct ophthalmoscopy provided a wide range in sensitivity of between 22% and 77% (Taylor, 1990).

5.2.2 General Practitioners

The sensitivity in detecting retinopathy by general practitioners varied from 41-67%. Appropriate education will improve GP'S accuracy in detecting sight threatening retinopathy particularly PDR and maculopathy.

5.2.3 Optometrists and Opticians

Using ophthalmologist examination as the standard, ophthalmoscopy by UK opticians had sensitivities for detecting any retinopathy of between 48-87%.

5.2.4 Use of non-ophthalmologists in retinal photography

The use of non-ophthalmologists to take retinal photographs for assessment by well-trained graders, may be a cost-effective method of screening for diabetic retinopathy. Training a non-ophthalmologist to use a retinal camera effectively may be easier than training them to use an ophthalmoscope effectively to recognise signs of diabetic retinopathy

5.3 Cost Effectiveness of Screening

Screening for diabetic retinopathy saves vision at a relatively low cost - modelling in the US indicated predicted savings of more than $472.1 million and 94,304 person-years of sight saved (Joannou, 1996); another model suggested savings of $3,190 per quality adjusted life year saved (American Diabetes Association, 1998); yet another US model indicated savings of $167 million and 79,236 person years sight saved (Javitt 1991; NHMRC, 1997) with 100% screening. The financial benefits of a screening programme would exceed costs for Type I but not Type II (Crijns, 1995; SBU 1990). A Health Technology Assessment report by SHPIC indicated savings of £1,403 per sight saved (SHPIC, 1996), while in another study at least ATS 3 900 000 could be saved through prevention (Matz Hospital, 1996). In the United Kingdom, it has been estimated that this is many times less than the disability payments provided to people going blind in the absence of a screening programme - in 1983 the annual cost of treating a diabetic at risk of blindness was estimated to be £387 while the welfare benefits paid annually was £3,575 (Prasad, 1997). To reduce blindness due to diabetes by one -third over 5 years, the 'number of people that need to be screened is £30,000/million total population per year (Khoner, 1991). The clinical practice guidelines in Australia predict a saving of

S14.5 million per year if compliance in screening is increased from 30 to 80% (NHMRC,1997).

The local cost of a conventional fundus camera is approximately RA4 100, 000 per unit, while a digital camera would cost about RA4 120, 000.

5.4 Ethical Issues

Some ethical issues may arise in implementing this screening programme especially in relation to the target population of the said programme. The policy on whom to treat as patients does not discriminate on any ethical, social and legal grounds (since risk targeting i.e of only diabetics above the age of 12 years will increase effectiveness of the programme as well as optimise scarce resources). However, ethical issues arise because a screening programme for diagnosing diabetics is not yet in place and hence targeting only known diabetics will jeopardise the well-being of other not-yet diagnosed diabetics. Furthermore, a diabetic registry has not yet been implemented, although small pockets of the diabetic population are registered, mainly at hospital settings.

5.5 Social Issues

There does not seem to be much literature pertinent to this issue. However, a few studies do indicate the need for screening to be community-based and for the point of delivery of the screening services to be within easy reach of the population (Lau, 1995; Diabetic Retinopathy Study Research Group, 1985). Such considerations emphasise the need for accessibility to and availability of such screening services regardless of socio-economic, demographic and geographic variations.

5.6 Legal Issues

A search of available literature failed to come up with relevant articles pertaining to legal issues and screening for diabetic retinopathy. So, expert opinion was sought using a precedent case occurring in the United Kingdom, where a lawsuit was filed against the National Health Service for negligence in applying the screening programme to a patient who ultimately became blind as a result of diabetic retinopathy.

From the discussions, it appears that the Ministry of Health, as the initiator and purveyor of the proposed screening programme, will be required to run disclaimers or clauses to the effect that MOH will be absolved from any medico-legal obligation for the individual practices of its doctors amounting to negligence in implementing the recommended screening schedule.

5.7 Local Situation on Facilities for Screening

Of the l14 Ministry of Health hospitals, 24 have ophthalmology departments, while ophthalmologist visits others on a regular basis. With respect to fundus cameras, there are 14 units in all the large Ministry of Health hospitals in Malaysia. At present, there are

772 Health Clinics (polyclinics and health clinics) run by doctors and medical assistants. Most of the clinics have Snellen charts and ophthalmoscopes.

6. CONCLUSIONS

6.1 Screening

There is sufficient evidence in the literature to recommend a screening programme for diabetic retinopathy. Such a programme will prevent severe visual loss and blindness. The programme has also been found to be cost- effective and has been recommended in America, Europe and Australia.

6.2 Screening Methods

- Currently, many screening modalities are being used. There is wide variation in the sensitivities and specificity of different screening methods performed by different screeners for detecting the various retinal lesions of diabetic retinopathy. The best screening method is still unclear, but the evidence strongly favours a combined modality to maximise sensitivity.

- Examination through dilated pupils and using a dark room increases the sensitivity of retinopathy screening.

- Determination of visual acuity as part of the screening programme must be emphasised. (A fall in visual acuity is the most important indicator of macular oedema, and, although no provision was incorporated for assessing serial change in visual acuity into most studies, it must be considered an essential part of establishing a screening service).

6.3 Category of Personnel

- People with diabetes present to a variety of potential examiners, including general practitioners, physicians, registrars, clinical assistants, nurses, endocrinologists, optometrists, opticians and ophthalmologists.

- A sensitivity and specificity target of at least 80% for all screeners should be achievable with appropriate training.

7. RECOMMENDATIONS

i. It is recommended that there be a screening programme for all diabetic patients.

ii. Screening should include assessment of vision and retinal examination (ophthalmoscopy) with or without photography. Photography could be carried out using non-mydriatic fundus cameras (conventional or digital).

iii. The screening programme should be 'ophthalmologist-led' rather than 'ophthalmology based' i.e. initial screening be carried out by primary healthcare providers, followed by retinal photography by trained personnel (technicians, optometrists or ophthalmologists) technicians. Trained readers or ophthalmologists should subsequently read fundus photographs or fundal digital images.

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38. Ronald; Klien, Barbara EK. *Diabetic eye disease*. The Lancet. 1997 July; 350(9072): 197-204

39. Sandra J. Ackerman. *Benefits of Preventive Programs in Eye Care are Visible on the Bottom Line*. [A new nationwide effect to improve eye care for people with diabetes gets backing from a study on the cost - effectiveness of screening for diabetic retinopathy]. Diabetes Care. 1992 April; 15(4):

40. Sculpher MH, Buxton MH, Ferguson BA et al. *Screening for DR: A relative cost-effectiveness analysis of alternative modalities and strategies*. Health Economics 1991; 39-5l

41. *Preventing Blindness in Diabetes - Executive Summary* Scottish Purchasing Health Information Centre Report. 1995-1996

42. Study Research Group. *Early Vitrectomy for severe Haemorrhage in Diabetic Retinopathy by The Diabetic Retinopathy Vitrectomy*. Archives of Opthalmology. 1985; 103

43. Taylor R. *Practical community screening for DR using the mobile retinal camera: Report of a 12 centre study*. (British Diabetic Association Mobile Screening Group). Diabetic Medicine. 1996 November; 13(11): 946-952

44. Taylor R et al. *Comparison of non-mydratic retinal photography with ophtalmoscopy in 2159 patients: mobile retina camera study*. British Medical Journal. 1990 December; 301(1): 1243-1247

45. Taylor R, Broadbent DM, Greenwood R et al. *Mobile retinal screening in Britain*. Diabetic Medicine. 1998;15: 344-347

46. Villalpando CG. et al. *A diabetic retinopathy screening program as a strategy for blindness prevention*. Archives of Medical Research. 1997;28(1) 129-135

47. Wykes WN, Pyott AAE, Ferguson VGM. *Detection of DR by scanning laser ophthalmoscopy*. Eye. 1994; 8: 437-439

9. EVIDENCE TABLES

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
METHOD OF SCREENING				
1.	Taylor R et al. Comparison of non-mydratic retinal photography with ophtalmoscopy in 2159 patients: mobile retina camera study British Medical Journal 1990 December; 301(1): 1243-1247	Randomised-Prospective Multicentre (U.K.) 2159 DM patients (Clinic screening) 4312 eyes 2 years	10% films poor (2.2% due to cataract, 4.5% due to small pupils.) (No. Of poor films have if pupil dilated before photo). NM photo as good as ophthalmoscopy (M) under routine diabetic clinic conditions for detecting NV but better for detecting m'pathy Sensitivity/specificity NV M'pathy Photos 65.5/60.3 74.2/55.3 Ophtalmoscopy 77.5/39.7 57.4/67 Experienced photographer - w/special interest in retinal screening essential	Good
2	Sculpher MH, Buxton MH, Ferguson BA et al. Screening for DR: A relative cost- effectiveness analysis of alternative modalities and strategies.	Retrospective - Multicentre Community based 3423 DM patients. Data – direct evidence (UK)	Single modality screening have low sensitivities. Combination of single screening modalities of different technologies improve detection rates.	Good to fair

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	Health Economics 1991; 39-51			
3	*Pugh JA, Jacobson JM et al.* *Screening for DR - The wide-angle retinal camera.* 1993	Prospective Multicentre (primary care setting) Case-control (USA) 352 patients.	45° Photo (M) perform as well or better than ophthalmologist in detecting DR. Trained readers required. Cost-effective. Colour slide film better than polaroid - better resolution	Poor
4	*Wykes WN, Pyott AAE, Ferguson VGM.* Detection of DR by scanning laser ophtalmoscopy. Eye 1994; 8: 437-439	Prospective Case-control studies 108 eye patients from diabetic eye clinic Follow up = 1 year	It is not as simple to use or as mobile as the fundus camera. Initial capital outlay expensive but running cost is low. Preproliferative changes not seen clearly. Advantage is that it does not depend on the optics of the eye to produce of focused image.	Poor No mention of sensitivity and specificity
5	*Kristinsson JK, Gudmundsson ES et al.*	Prospective – Study was to identify the intervals	Eye exam by ophthalmologist reported screening protocol.	Poor

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	Screening for DR. Initiation and frequency. Acta Ophthalmologica Scandinavica 1995; 73:525-528	required for screening of the different stages of DR. Iceland 206 DM patients. Follow-up = 2 years	VA BIO –fundus (M) Fundus photo	
6	*O'Hare JP et al.* Adding retinal photography to screening for diabetic retinopathy: a prospective study in primary care. British Medical Journal 1996 March 16; 312(7032): 679–682	Prospective Nonrandomised Multicentre Controlled (UK) 1010 DM patients from primary care Mobile retinal screening unit	Combining modalities of screening improves Assessment of DR Sensitivity further improved if photos reviewed by specialist. Combining screening modalities (ophthalmoscopy + photos) improves sensitivity which is further improved by specialist review of photo. Trained & experienced primary care screeners should be able to achieve an effective, acceptable, and economical community based screening programme.	Good to fair
7.	*Taylor R (British Diabetic Association*	Non-controlled Multicentre (primary care + hospital based)	***Mobile Retinal camera + camera operator/ driver Mobile retinal camera effective, efficient & robust in DR screening***	Poor

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	Mobile Screening Group). Practical community screening for DR using the mobile retinal camera: Report of a 12 centre study Diabetic Medicine 1996 November; 13 (11): 946–952	(UK) 64 905 patients (42 803 with full data).		
8.	Gardner GG Automatic detection of DR using an artificial neural network: a screening tool British Journal Ophthalmology 1996; 80: 940–944	Randomised Prospective control 301	ANN good accuracy for detecting DR – comparable with other screening systems. Success rate dependant on preprocessing and training of ANN	Good to Fair
9.	Davies R et al.	Retrospective Cohort	Simulation approach used to evaluate the development of DR and response to treatment in	Good

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	Simulation of diabetic eye disease to compare screening policies. British Ophthalmology 1996; 80: 945–950	Meta-analysis Simulation approach (UK)	IDDM population in UK Compare: (among other things) Different personnel screening (ophthalmologist, DM physician, GP. Optometrist) Sensitivity / Specificity DM physician (ophthalmoscopy) 67% / 96% GP or Optometrist (ophthalmoscopy) 52 / 91	
10.	Hammond CJ. Comparison between an ophthalmic optician and an ophthalmologist in screening for diabetic retinopathy. Eye 1996; 10(1): 107-112	Non-randomised controlled prospective with historical control 474 DM eyes single group practice	Compare S/L biomicroscopy + D/O(M) Ophthalmologist vs Optometrist Ophthalmologist & Optometrist - 77% total agreement re.+/- DR. Sensitivity of Optometrist in comparison to Ophthalmologist = 0.92 for moderate or severe myopathy (comparable with other screening methods) personnel required: Optician Suitable training, motivation, and maintenance of skills required	Fair
11.	Joannou J *Screening for DR. in South Africa with 60° retinal colour photography* Journal International Medicine 1996	Non-randomised controlled prospective trial with historical control 663 DM patients	Photography detected 28% more DR. than clinicians; Compared to 60° photo, 1x45° field missed 31%DR.; 2x45° missed 11% DR. 60° photo (M) compares well with ophthalmologist screening & is better than diabetes clinic dr. & 1or 2 x45° field photo	Fair

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	January; 239(1): 43-37		assessment. Use of colour slide allows easy magnification and close inspection	
12.	Villalpando CG et al. A diabetic retinopathy screening program as a strategy for blindness prevention Archives of Medical Research 1997; 28(1): 129-135	Prospective 231 DM patients (Mexico)	DR detected through screening programme in an efficient and standardised manner	Poor Study does not compare effectiveness of different screening programmes
13.	Owens DR. *Screening for DR. by general practitioners: ophthalmoscopy or retinal photography as 35 mm. colour transparencies?* Diabetic Medicine 1998 February; 15(2): 170-175	Multi-centre-practice-based Non-randomised prospective with historical control 897DM patients.(597 valid comparisons obtained)	Screening of photos by trained GP's in primary care settings achieves acceptable detection rate for STDR (>87%) contrasting with opthalmoscopy alone (66%). Proposed UK standard = 80%	Fair

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
14.	**Preventing Blindness in Diabetes** Executive Summary - Scottish Purchasing Health Information Centre Report 1995-1996	(Scotland)	1. Retinal Camera in mobile vans driven by a retinal photographer 2. Screening by opticians - Camera can be used to screen patients. At health centres etc - Most people >50, likely to attend optician for glasses anyway (patients with DM entitled to free annual eye check at optometrist) BEST OPTION = Combination of both	Good
15.	*DR -The value of early detection.* The Swedish Council on Technology Assessment in Health Care Summary and Conclusions 1994	Sweden Summary of study done in 1990	Fundus examination by 1. Ophthalmoscopy/biomicroscopy(M) or 2. Photo(M) at least 2 fields including stereo of macula Simplicity, high sensitivity & specificity. With photography makes I the most suitable method for screening	Poor
16.	DR – Position Statement American Diabetes Association. Diabetes Care 1998l; Supplement, 21(1)	Clinical Practice Recommendations 1998 based on evidence reviewed in the publication : DR. (Technical review) Diabetes Care 1998; 21:143-156	***Std. 7x30^0 stereo (M) photo is more sensitive in detecting DR. than clinical examination.*** Personnel required: Skilled photographer Skilled photographer Skilled reader	Poor

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
			If above personnel do not meet standards, they cannot be substituted with ophthalmoscopy (M) by eye care provider.	
17.	Prasad S. Screening for diabetic retinopathy: An overview 08/06/97 http:/www.priory.com	Overview UK	Method of screening depends on local availability of facilities. 1. Ophthalmologist 2. Trained health care workers 3. Equipment & resources ***Single modality should have sufficient sensitivity (>80%) and specificity (>80%)*** Combining two modalities of screening provides excellent sensitivity, but increases the cost per case screened and is often possible in a hospital based setting. 1.Photos (stereo pairs) 2.Indirect ophthalmoscope on a Slit lamp Direct ophthalmopy limited use because of two dimensional view and small field – not recommended Whatever method use to examine the retina, visualization is improved by dilating the pupil and using the dark room.	Poor
18.	Lau HC; Voo YO; Yeo KT; Ling SL; Jap A *Mass screening for diabetic*	Prospective Multicentre Government polyclinic in Singapore 13 296 patient	NMRP by trained staff (read by ophthalmologist). Patient that required referral sent to specialists' clinics.	Fair Study does not compare

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
	retinopathy – a report on diabetic retinal screening in primary care clinics in Singapore. Singapore Medical Journal 1995 October; 36(5): 510-513		Personnel required: - Ophthalmologist - Staff to take photos Training: Train existing staff NMRP is accessible and effective in screening DR and recommended for mass screening.	methods. It states their method of screening
19.	Penman AD et al. Screening for DR: the utility of non- mydriatic retinal photography in Egypt adults. Diabetic Medicine 1998 September; 15(9): 783-787	Retrospective 427 DM patients Similar results for either eye. (only results from right eye presented) Egypt patients	Compare screening data: Photos alone – (M) vs. BIO (M) 22% ungradable photos – 63% due to media opacities. 12.6% of photos graded greater DR than ophthalmoscopy (Level of agreement 0.75 represents excellent agreement & ¸0.40, poor agreement) Poor agreement between BIO & photos (0.33) because high number of ungradable photos. Photo (M) useful method to screen DR but limited use in corneal disease & older patient with cataract. Indicates role for BIO in certain cases.	Poor

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
20.	*Clinical Practice Guidelines.* Management of DR National Health and Medical Research Council 1997.June	Australia	WESDR (Wisconsin Epidemiology study of DR) & Japanese-American Community Diabetes Study were population based – 7-field photo used as reference standard compared to ophthalmoscopy. In other clinic-based studies - 7-field photo compared to other screening methods or screeners. In WESDR 2,3 or 4 photographic fields sensitivity for detection of DR was 87%, 92% and 95% respectively. Compared to 7-field photos the sensitivities for detecting mild NPDRT, moderate-severe NPDR and PDR was lower for NM 45^0 photos (58, 76 and 43% fell to 42,49 and 14%). Examiners: - Sensitivity target of at least 60% with good specificity for all screeners should be achievable with appropriate training. - Significant variability to detect end stage DR between ophthalmologist and non-ophthalmologist. - GPs ophthalmoscopy sensitivity for detecting DR, ranges from 52% - 65%. GP's accuracy improved by training. Ophthalmoscopy vs. 7-field photo error rate varied from 0% for retinal specialists to 49% for	

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments, Grade of Evidence
			physicians, endocrinologist and medical residents.	
21.	Taylor R, Broadbent DM, Greenwood R et al. ***Mobile retinal screening in Britain*** Diabetic Medicine 1998; 15: 344-347	Conference report	Two main approaches: 1. Photos (some form) 2. Optometrist examine No generally agreed performance standard	Poor
COSTING				
1.	*Study Research Group.* Early Vitrectomy for severe Haemorrhage in Diabetic Retinopathy by The Diabetic Retinopathy Vitrectomy. Archives of Opthalmology 1985; 103	Multicentre, randomised clinical trial. 616 eyes with recent severe diabetic vitreous haemorrhage reducing visual activity to 5/200 or loss for at least one month were randomly assigned to either early vitrectomy or deferral of vitrectomy for one year.	25% of early vitrectomy group had visual acuity of 10/20 or better compared with 15% in deferral group (p=0.01) Type 1 diabetes who were on average younger and had more severe proliferative retinopathy, these was a clear cut advantage for early vitrectomy, as reflected in the percentage of eyes recovering visual acuity of 10/20 or better (36% vs 12% in deferral group p = 0.0001). No such advantage was found in Type 2 diabetes group (16 % in early group vs. 18% in deferral group) but evidence that this advantage deferred by diabetes type was of borderline significance.	Good

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
2.	*Study research Group.* Photocoagulation for diabetic macular edema – by The Early Treatment Diabetic retinopathy Archives of Opthalmology 1985 December; 103.	Multicentre, randomised, clinical trial. 754 eyes with macular edema and mild to moderate diabetic retinopathy were randomly assigned to focal argon photocoagulation 1490 eyes were randomly assigned to deferral of photocoagulation.	Eyes assigned to immediate focal photocoagulation were about half as likely to lose 15 or more letters on ETDRS eye chart compared with eyes deferred. 5% vs 8% at one year. 7% vs 16% at two years. 12% vs 24% at 3 years. (Z values of 2.58 or more from first year to third year of follow up) (loss of 15 letters is equivalent to a three line visual acuity decrease on this chart or a doubling of the initial visual angle)	Good
3.	*Photocoagulation treatment of proliferative diabetic retinopathy : The second report of diabetic retinopathy study findings.* Opthalmology 1978; 83(1): 82–106	Randomised, controlled clinical trial designed to determine whether photocoagulation is of benefit in preserving vision in patients with proliferative diabetic retinopathy. 867 – argon treatment group. 875 - xenon group	Visual acuity less than 5/200 at 2 or more consecutively completed follow up visits. • After two years:- Event rate was 15.9% in all untreated eyes and 6.4 % in all treated eyes (Z = 7.2) • After three years :- Event rates were 26.4% in untreated and 10.5% in treated eyes (z = 6.3)	Good

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
4.	***Bachmann MO, Nelson SJ.*** **Impact of Diabetic Retinopathy screening on a British District population :- Case detection and blindness prevention in an evidence – based model.** Journal Epidemiology Community Health 1998 January; 52(1): 45–52	Review article. Diabetic population of a typical district health authority on health board.	1. Treatment could prevent 77 % of expected cases of blindness. 2. Screening and early treatment of Diabetic. Retinopathy can prevent substantial disability. 3. With early treatment, 6 % prevented from going blind in 1 year. 10 years – 34%	Fair
5.	***Kristinsson JK*** **Diabetic retinopathy. Screening and prevention of blindness. A doctoral thesis.** ***Acta Opthalmology Supplement 1997; (223): 1-76***	Thesis Retinopathy study. Cohort Study Regular eye screening from 1980. Review done in 1990 205 Type 1 diabetics 245 Type 2 diabetics Annual eye examination and fundus photography.	Prevalence of retinopathy and visual impairment in Type 1 diabetic patients low compared with other countries. Prevalence of visual impairment in those Type 2 diabetic patients participating in screening programmes at time of study was low compared with population – based studies from other countries.	Fair
6.	Ronald, Klien, Barbara EK. **Diabetic eye disease** The Lancet 1997 July; 350(9072): 197–204	Review article	• Severe visual loss due to clinically significant macular edema or proliferative retinopathy can be prevented – therefore need for screening. • DRS study – 6 year cummulative event rate for untreated and 16 % for treated eyes.	Seminar Report Reference to RCT Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			• DRS & ETDRS showed that panretinal treatment as soon as high risk proliferative retinopathy developed could result in 90% decrease in risk of severe loss of vision.	
7.	Kimberly A, Neely, David A, Quillen, Andrew P. Schahat, Thomas W. Gardner, George W. Blankenship. **Diabetic retinopathy** Medical Clinics of North America 1998	Consensus recommendations of American Diabetes Association and American Academy of Opthalmology	• Effective treatment exists for macular edema – laser surgery and proliferative retinopathy – panretinal photocoagulation. • DRS – demonstrated efficacy of panretinal photocoagulation. • ETDRS – efficacy of focal or grid photocoagulation for diabetic macula edema	Poor
8.	Bob Ryder **Screening for diabetic retinopathy** British Medical Journal 1995; 311: 207	***Editorial***	• Important cause of blindness • Blindness due to diabetes is preventable; If sight threatening retinopathy is detected in time, then laser treatment can greatly reduce progression to blindness. • Cost of litigation may dwarf into insignificance cost of providing screening programme.	Poor
9.	Harper CA, O'Day J, Taylor HR. *Early detection of diabetic retinopathy* Medical Journal Australia 1995; 162(10): 536–538	***Review***	• Diabetic retinopathy remains leading cause of blindness in Australia. • Can be prevented by timely laser photocoagulation and this requires early detection of asymptomatic retinopathy. • Australian Diabetes Society recommends regular retinal examination through	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			dilated pupils, either at diagnosis of diabetes (onset over 30 years), of five years after diagnosis (onset under 30 years) Examination repeated every two years or in presence of visual symptoms, pregnancy and other risk factors.	
10.	*How effective are treatments for* **Diabetic Retinopathy?**	Commentary	After PDR was diagnosed, risk of severe visual loss VA < 5/200 for untreated DRS eyes at 3 years – approached 30 % only 4 % of treated eyes with PDR in ETDRS reached severe visual loss by 5 years & only 1 % had severe visual loss in both eyes. 60% reducer in blindness ensures everyone and PDR gets adequate treatment.	Poor
11.	Javitt JC, Aiello LP, Ching Yang, Ferris FL 3rd. Canner JK, Greenfield S. *Preventive eye care in people with diabetes is cost – saving to the federal government. (US)* *Implications for health care reform.* Diabetes Care 1994; 17(8): 909–917	Computer modeling using data from population based epidemiological studies and multicentre clinic trials**.**	Type 2 DM • Annual savings of 247.9 million US $ to federal budget. • 53,986 person – years of sight saved with sub optimal 60% level of care. With recommended care: • Predicted savings > 472.1 million US $ • 94,304 person – years of sight savings. Not only reduces needles vision loss but also provides a financial return on investment of	***Fair***

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			public funds.	
12.	Crijns H; Casparie AF; Hendrikse F. *Future need of eye care for patients with diabetes mellitus, costs and effectiveness.* Ned. Tijdschr. Geneeska 1995; 139(26): 1336–1341	Computer simulation study. Cohort Study Objective: To determine how much vision loss caused buy diabetic retinopathy can be prevented in Netherlands until 2020, & what resources will be needed to do so.	Full compliance with official screening guidelines would reduce prevalence of blindness in 2020 by 45 % among Type 1, and by 20 % in Type 2 DM. Financial benefits would exceed costs for Type 1 but not Type 2. Conclusion:- Sharp increase in number of diabetic patients plus proven effectiveness of photocoagulation will inevitably cause a major rise in need for opthalmic care.	Fair
13.	**Preventing blindness in diabetes** SHIPIC report 1995/96. (Scottish Health Purchasing Information Centre)	Executive summary report.	• Diabetes can cause blindness but is preventable by laser treatment and is effective before retinopathy becomes severe. Hence annual screening recommended. • Cost of blindness falls upon patients, families and social security (for disability pension), not on the NHS. Preventing it will cost the NHS more, but lead to	Consensus Report Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			considerable saving for society as a whole. Cost was pounds 1403 per sight –saved. Prevention of successful litigation by people who go blind – (who may sue NHS) Damages worth pound 250,000 per case. • Area diabetes registers necessary for organising fail safe screening, audit & evaluation. Recommended combinations of screening method (opthalmology & retinal camera) in patients who attend specialist clinic. Screening in community by opticians or mobile cameras according to local circumstances	
14.	*Screening for diabetic retinopathy; An overview.* (MS FRCS) Somdutt Prasad Fellow in Diabetic Eye Disease. Arrowe Park Hospital UK. Somprased @ enterprise. Net.	***Review***	• Diabetic retinopathy is the commonest cause of blindness in the working age population in many countries. • DRS – panretinal photo coagulation could improve prognosis of proliferative retinopathy. • ETDRS – have shown benefits of focal laser photocoagulation in eyes with macular edema. • Saves vision at a relatively low cost. Treating diabetics at risk of blindness was pounds 387 but welfare benefits paid to a	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			blind person 3575 per annum.	
15.	Lindholm LH *Diabetic Retinopathy - The Value of Early Detection* The Swedish Council on Technology Assessment in Health Care. Summary and Conclusions 1994	Expert Report	• Early detection and systematic follow-up of patients with diabetic retinopathy can prevent severe sight loss. • Type 1 diabetes – socioeconomic savings and benefits by preventing blindness • Type 2 diabetes on insulin – socioeconomic costs and benefits counterbalance each other. Cases of prevented blindness substantially lower than with Type 1. • If oral and diet Type 2 – costs is more	Poor
16.	Javitt JC, Aiello LP. *Cost– effectiveness of detecting and treating diabetic retinopathy.* Annals. of International Medicine 1996 January; 1(124): 164–169	Cost – utility analysis using computerised model of progression of diabetic eye disease and data from previously published epidemiological studies and multicentre clinical trials. Cohort Study	• Screening and treatment of eye disease in patients with Diabetes mellitus costs $:3190 per quality adjusted life year saved. • Prevention programmes aimed at improving eye care for diabetics not only result in substantial federal budgetary savings but are highly cost – effective health investments for society. • Opthalmologic screening for diabetic persons is more cost- effective than many routinely provided health interventions. • Because diabetic eye disease is the leading cause of new cases of blindness	Fair

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			among working – age Americans, these results support the widespread use of screening and treatment of diabetic eye disease.	
17.	Matz H; Falk M; G'otinger W; Kieselbach G. *Cost– benefit analysis of diabetic eye disease.* Opthalmologica 1996; 210(6): 348-53	Comparative Study Cohort Study	At 100% diagnosibility and 100% treatability, with laser photocoagulation, vision can be retained in at least one eye in 73 %of patients with proliferative retinopathy and in 67% of patients with diabetic maculopathy. ***Comparison of costs between benefits granted to a blind diabetic and those incurred though screening examination and treatment.*** ***Cost for blindness ATS 19,000,000. ATS 14,600,000 could be avoided through optimal screening, examination and treatment. Maximum cost for examination and therapy ATS 10,700,000.*** ***Minimum saving of ATS 3,900,000 in favour of preventive medicine.***	Fair
18.	Advair – Paruaby – Price. *Screening for diabetic retinopathy – adequate programme would save money.* British Medical Journal 1995; 311: 1229	***Letter***	• Certain savings that result from a comprehensive screening service • Saving $ 472.1 (3147m pound) and 94,304 person years of sight saved if all NIDDM were screened. Therefore savings of $;975 (650 pound) per person enrolled with screening programme in US	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			The need for vigorous screening speaks for itself.	
19.	Jonathan C. Javitt, Joseph K. Canner, Alfred Sommer. *Cost – effectiveness of current Approaches to the Control of Retinopathy in Type 1 Diabetics.* Opthalmology 1989; 96: 255-264	Computer Simulations Model Cohort study	Over 60 years. 72 of Type 1 diabetes will develop proliferative diabetic retinopathy. 42% - macular edema. $ 966 per person year of vision saved from proliferative retinopathy. $ 1118 per person years of central acuity saved from macular edema. [This is one seventh of $ 6900 average cost of 1 year Social Security Disability for those disabled by vision loss]	Fair
20.	Javitt JC; Aiello LP; Bassi LJ; Chiang YP; Canner JK. *American Academy of Opthalmology :Detecting and treating retinopathy in patients with Type 1 diabetes Mellitus. Saving's associated with improved implementation of current guidelines* Opthalmology 1991 October; 98(10): 565-573	Cohort Study. Representing all Americans within a specified age group who develop Type 1 Diabetes Mellitus within a given year.	Annual savings of $101.0 million and 47,374 person years sight at currently estimated 60% screening and treatment implementation level. With 100% screening and treatment predicted savings exceed 167 million and 79,236 person years sight saved. 2/3rd. of savings from treatment of proliferative diabetic retinopathy and 1/3rd. from treatment of macular edema. Additional savings of $ 9571 realised with each recruitment of newly diagnosed Diabetes	Fair

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			Mellitus. Initiating screening upon diagnosis would be cost-effective if 1 additional individual in 56 were recruited. Model suggests that improved delivery of opthalmic care to patients and Diabetes Mellitus would field substantial financial and visual savings.	
21.	Khoner EM; Porta M Eku Diabetic retinopathy Unit, Hammermitte Hospital, London U.K. *Protocols for screening and treatment of diabetic retinopathy in Europe.* J. Opthalmology 1991 January–March; 1(1); 45–54.	European Protocol approved by 51 specialist representing 30 diabetic and opthalmic societies from 21 European countries.	To reduced diabetes – related blindness by one - third in next 5 years. No. of person to be screened is 30,000 /million total population/ year. Available data indicate this is feasible and initial investments are justified by reduction of preventable blindness.	Fair
22.	Sandra J. Ackerman *Benefits of Preventive Programs in Eye Care are Visible on the Bottom Line.* [A new nationwide effect to improve eye care for people with diabetes gets backing from a study on the cost–effectiveness of screening for diabetic. Retinopathy]	Review article.	Studies agree on effectiveness in economic and clinical terms early and regular opthalmologic screening for most diabetic patients.	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
	Diabetes Care 1992; 15(4)			
23.	Dasbaeh EJ, Fryback DG; Newcomb PA; Klien R; Klien BE *Cost- effectiveness of strategies for detecting diabetic retinopathy.* Medical Care 1991 January; 29(1): 20-39	Computer model used to evaluate biannual and annual screening programmes using opthalmoscopy fundus photography with "non – mydriatic camera and photography with a mydriatic camera. 3 sub population studied:- 1. Younger onset DM < 30 years of DM 5 years or >. 2. Older onset DM (age at diagnosis greater or equal to 30 years)taking insulin. 3. Older onset DM not taking insulin. Population characteristic from well – described southern Wisconsin population but may be specialized to other populations.	Cost of screening programme appear to be recovered by avoided costs of blindness in population subgroups taking insulin. Cost of screening programmes not recovered in older onset population subgroup not taking insulin. Supplying annual examination with mydriatic fundus photography as a screening programme to a cohort of 1,000 diabetics from younger onset population diag. At least 5 years and who are currently not receiving care sight might save 319 sight years over lifetime of cohort. Will save 62 sight years in an older onset cohort taking insulin and 21 sight years in older patients not taking insulin.	Fair
24.	*Management of diabetic retinopathy clinical practice guidelines.* Australia 1997 National Health and Medical Research Council.	Clinical Practice Guideline	High compliance from 30 to 80% would result in 14.5 million $ per year from disability costs. Higher compliance from 30 to 80% with annual screening would result in 13.8 million $ per year saved.	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow Up	Characteristic & Outcome	Comments Grade of Evidence
			If higher rate of screening is applied, savings range from $11.5 million to $million per year respectively.	
SOCIAL ISSUES				
1.	Lau HC; Voo YO; Yeo KT; Ling SL;Jap A *Mass screening for diabetic retinopathy – a report on diabetic retinal screening in primary care clinics in Singapore* Singapore Medical Journal 1995 October; 36(5): 510-513	Mass screening at 6 government clinics using non-mydriatic fundal photography. A total of 13,296 patients screened.	With regards to the ethical issues, this study has important social connotations, namely accessibility of screening services. By providing screening at primary care centres, coverage of the diabetic population is ensured. Equity issues did not arise in this study, since they conducted mass-screening of the population seen at primary care clinics.	Poor
2	Prasad S. *Screening for diabetic retinopathy: An Overview* http://www.priory.com/med/eye.htm	Review Article	Recommendations made on basis of review of major studies.	Poor

No	Title, Author, Journal, Year	Type of Study, Sample Size, Follow-up	Characteristics & Outcome	Comments, Grades of Evidence
LEGAL ISSUES				
1	Bob Ryder. *Screening for diabetic retinopathy.* British Medical Journal 1995; 311: 207	Editorial	Blindness due to diabetes is preventable. If sight threatening retinopathy is detected in time, then laser treatment can greatly reduce progression to blindness. Cost of litigation for not detecting retinopathy may dwarf into significance the cost of providing a screening programme.	Poor
2	Ms Karen (from Khem Thadani & Co. Advocates and Solicitors) Legal advisor with medico-legal experience.	Personal Consultation	.Based on case precedent in UK: ***Plaintiff versus NHS***	Poor
BURDEN OF ILLNESS				
1	Preliminary Report The National Eye Survey 1996 Ministry of Health Malaysia	Population based , cross-sectional study 18,000 respondents from all states in Malaysia.	• The prevalence of DM was 10.3% for age group 50 year and over with an estimated of 200,000 cases (to the total population) • Of this an estimated of 7,300 cases (3.5%) aged 50 years and above had Diabetic Retinopathy . The distribution of DR was as follows: 1. 50% Malays, 38% Chinese and 12% Indians 2. 25% male and 75% female Note: HMIS does not capture any data on DR .	Fair

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments Grades of evidence
2	Report of the second National Health and Morbidity Survey. 1996 Ministry of Health Malaysia	Population based, cross-sectional study. Sample size : 59,903	• The prevalence of DM in Malaysia was 8.3% for aged 30 years and above and with an estimated of 600,000 cases • The prevalence of DM was increased by age.	Fair
3	S. Moss et al *Winconsin Epidemiologic Study of Diabetic Retinopathy* Personnel Communication 1996	Population based , Cohort study for 10 years. Included both type 1 and type 2 DM Sample size: 1298	• The incidence rate was 2.3% for aged 45-64 years old • After 7 years of type 1 DM (IDDM), approximately 50% of patients had some degree of DR • After 17-25 years of getting the disease, this figure rose to around 90%.	Fair
4	Centre of Disease Control US *Morbidity & Mortality Weekly Report.* 45(43): 937-941	Register of the Massachusetts Commission for the Blind (MCB) 1987- 1994	• During 1987-1994, blindness caused by DM was reported for 2990 persons , 90% were aged >45 years and above. • The mean prevalence of DR was 1.85% person with DM • During 1987-1994, the prevalence decreased by 17% among person aged 20-44 years but increased substantially (40%) among persons aged >65 years. • The reported decline in the incidence of DR was due to early detection and treatment as well as improved glycemic control. • Early detection of DR and timely intervention with laser could reduce the incidence of	***Fair***

No	Title, Author, Journal, Year	Type of Study, Sample size, Follow-up	Characteristics and Outcome	Comments Grades of evidence
			severe vision loss by 50-60% in patients with macular edema and by 90% in patients with PDR.	
5	Bertram B. *Prevalence of patients with DM without and with DR in an ophthalmology practice*. Ophthalmologe 1997; 94(6): 401-404	Prospective study of 10,000 patients in a German ophthalmology practice	• DR was present in 130 (26.6%) of 488 diabetic patients. • The prevalence of DR was 1.3% • The prevalence was significantly correlated with the duration of diabetes.	Good to Fair
6	*Mass screening for DR – a report on diabetic retinal screening in primary care clinics in Singapore.* Family Health Services, Minister of Health, Singapore	Mass screening at 6 government polyclinics using non -mydratic fundal photography. A total of 13,296 patients were screened.	• 2,9111 patients or 21.8% of total screened were found to have DR. • About half of these (10.8% - 1,436 patients) had sight threatening retinopathy. The most common sight threatening retinopathy was maculopathy (8.0% - 1,064 cases).	Fair

Appendix A

LEVELS OF EVIDENCE SCALE

Level	Strength of Evidence	Study Design
1	Good	Meta-analysis of RCT, Systematic reviews.
2	Good	Large sample of RCT
3	Good to fair	Small sample of RCT
4		Non-randomised controlled prospective trial
5	Fair	Non-randomised controlled prospective trial with historical control
6	Fair	Cohort studies
7	Poor	Case-control studies
8	Poor	Non-controlled clinical series, descriptive studies multi-centre
9	Poor	Expert committees, consensus, case reports, anecdotes

SOURCE: ADAPTED FROM CATALONIAN AGENCY FOR HEALTH TECHNOLOGY ASSESSMENT (CAHTA), SPAIN

THE FOLLOWING HTA REPORTS ARE AVAILABLE ON REQUEST:

REPORT	***YEAR***
1. LOW TEMPERATURE STERILISATION	1998
2. DRY CHEMISTRY	1998
3. DRY LASER IMAGE PROCESSING	1998
4. ROUTINE SKULL RADIOGRAPHS IN HEAD INJURY PATIENTS	2002
5. STROKE REHABILITATION	2002
6. MEDICAL MANAGEMENT OF SYMPTOMATIC BENIGN PROSTATIC HYPERPLASIA	2002
7. CHILDHOOD IMMUNISATION	2002
8. ROUTINE NEONATAL VITAMIN K ADMINISTRATION AT BIRTH	2002
9. MANAGEMENT OF NEONATAL HYPERBILIRUBINEMIA	2002
10. SCREENING OF DIABETIC RETINOPATHY	2002