

**Health Technology Assessment  
of  
Organisation of Services for Diabetic Retinopathy Screening**

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(see Appendix 1)**

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**CONTENTS**

<b>1</b>	<b>EXECUTIVE SUMMARY.....</b>	<b>8</b>
<b>2</b>	<b>INTRODUCTION .....</b>	<b>13</b>
<b>3</b>	<b>BACKGROUND.....</b>	<b>14</b>
<b>3.1</b>	<b>Introduction.....</b>	<b>14</b>
3.1.1	Rationale for this Health Technology Assessment .....	14
<b>3.2</b>	<b>Description of health problem in Scotland .....</b>	<b>15</b>
3.2.1	Epidemiology of Diabetes .....	15
3.2.2	Multi-specialty nature of diabetes care .....	15
3.2.3	Organisation of diabetes care in Scotland .....	16
<b>3.3</b>	<b>Diabetic Eye Disease.....</b>	<b>16</b>
3.3.1	Blindness due to diabetic retinopathy in Scotland .....	17
<b>3.4</b>	<b>Perspectives.....</b>	<b>18</b>
3.4.1	Introduction of Systematic Screening .....	18
<b>3.5</b>	<b>Description of the technology .....</b>	<b>18</b>
3.5.1	Retinal Imaging .....	18
<b>3.6</b>	<b>Current Service Provision of Diabetic Retinopathy Screening in NHSScotland .....</b>	<b>19</b>
3.6.1	Optometry services.....	21
<b>4</b>	<b>SOURCES OF EVIDENCE .....</b>	<b>22</b>
<b>5</b>	<b>CLINICAL EFFECTIVENESS .....</b>	<b>23</b>
<b>5.1</b>	<b>Search strategy .....</b>	<b>23</b>
<b>5.2</b>	<b>Methods for the Evaluation of Clinical effectiveness.....</b>	<b>23</b>
5.2.1	Outcome measurements .....	23
5.2.2	Methods for estimating sensitivity and specificity.....	24
5.2.3	Benefits and disbenefits .....	25
<b>5.3</b>	<b>Clinical Effectiveness Results .....</b>	<b>25</b>
5.3.1	Quantity and Quality of research available .....	25
5.3.2	Description of studies excluded by HTBS .....	26
5.3.3	Description of studies included .....	26
5.3.4	Failure rates of screening methods .....	26
5.3.4.1	Failure of non-mydriatic photography .....	27
5.3.4.2	Failure of mydriatic photography.....	27
5.3.4.3	Direct comparison of mydriatic and non-mydriatic photography .....	28
5.3.4.4	Are failures of photography associated with disease? .....	28
5.3.4.5	Failure of laser scanning ophthalmoscope .....	29
5.3.4.6	Failure of conventional ophthalmoscopy .....	29
5.3.4.7	Conclusion with respect to failure rates of retinal imaging .....	29
5.3.5	Accuracy of retinal imaging methods .....	30
5.3.5.1	The Gold Standard method .....	30
5.3.5.2	Methods of screening .....	30
5.3.5.3	Issues in analysis of screening studies .....	31
5.3.5.4	Statistical model combining all studies with ‘gold standard’ comparators .....	32
5.3.5.5	Conclusions concerning screening accuracy.....	35
5.3.6	Disbenefits.....	36
5.3.6.1	Adverse effects .....	36

## Assessment Report 3: Draft for Consultation

<b>6</b>	<b>ORGANISATIONAL ISSUES .....</b>	<b>38</b>
<b>6.1</b>	<b>Organisation of Systems .....</b>	<b>38</b>
<b>6.2</b>	<b>Learning from other Screening Programmes.....</b>	<b>39</b>
<b>6.3</b>	<b>Screening issues.....</b>	<b>39</b>
<b>6.4</b>	<b>Modes of delivering screening .....</b>	<b>40</b>
<b>6.5</b>	<b>Population to be invited for screening .....</b>	<b>41</b>
<b>6.6</b>	<b>Screening interval.....</b>	<b>41</b>
<b>6.7</b>	<b>Clinical IM&amp;T .....</b>	<b>41</b>
6.7.1	IM&T developments related to diabetes in NHSScotland .....	41
6.7.2	Clinical IM&T required for diabetic retinopathy screening.....	42
6.7.3	Identification, invitation and recall .....	42
6.7.4	Attendance for screening and results .....	43
6.7.5	Incorporation of results into electronic medical record .....	43
6.7.6	Monitoring the screening process .....	44
6.7.7	Implementation plan.....	44
<b>6.8</b>	<b>Data protection.....</b>	<b>44</b>
<b>6.9</b>	<b>Grading .....</b>	<b>44</b>
6.9.1	Automated Grading .....	50
<b>6.10</b>	<b>Retinal cameras and software necessary for manipulation of digital images..</b>	<b>50</b>
6.10.1	Recommendations on cameras and image manipulation .....	52
<b>6.11</b>	<b>Quality Assurance .....</b>	<b>52</b>
<b>6.12</b>	<b>Examples of large diabetic retinopathy screening service programmes in the UK.....</b>	<b>54</b>
6.12.1	The Bro Taf Diabetic Retinopathy Screening Service.....	54
6.12.2	Optometry schemes.....	55
<b>6.13</b>	<b>Staffing and professional involvement .....</b>	<b>55</b>
6.13.1	Managed clinical networks.....	55
6.13.2	Organisation of staffing.....	56
6.13.3	Training .....	56
6.13.4	Training for retinal screeners .....	57
6.13.5	Optometrists involvement and training .....	57
6.13.6	GP involvement in retinal screening invitations .....	58
<b>6.14</b>	<b>Audit</b>	<b>59</b>
<b>6.15</b>	<b>Conclusions concerning organisational issues .....</b>	<b>60</b>
<b>7</b>	<b>PATIENT ISSUES .....</b>	<b>61</b>
<b>7.1</b>	<b>Background.....</b>	<b>61</b>
<b>7.2</b>	<b>Methods for Evaluation of Patient Issues .....</b>	<b>61</b>
<b>7.3</b>	<b>Results .....</b>	<b>62</b>
7.3.1	Patient Education and Empowerment for People with Diabetes.....	62
7.3.2	Communicating the Risks of Diabetic Retinopathy and the Benefits of Screening.....	62
7.3.3	Patient Information Leaflets .....	64
7.3.4	Other Methods to Improve Screening Attendance .....	65
7.3.5	Professional Educational Initiatives.....	67
7.3.6	Patient Views.....	68
7.3.6.1	NSC Patient Expert Group .....	68
7.3.6.2	Breast Screening Survey .....	69
7.3.6.3	Mydriasis .....	70
7.3.6.4	Research.....	70
<b>7.4</b>	<b>Conclusions .....</b>	<b>70</b>

## Assessment Report 3: Draft for Consultation

<b>8</b>	<b>ECONOMIC EVALUATION</b> .....	<b>72</b>
<b>8.1</b>	<b>Search strategy</b> .....	<b>72</b>
<b>8.2</b>	<b>Data Extraction</b> .....	<b>73</b>
<b>8.3</b>	<b>Methodology</b> .....	<b>73</b>
8.3.1	Objectives .....	73
8.3.2	Basis for Economic evaluation.....	73
8.3.3	Cost measurement .....	75
8.3.4	Estimation of Net Benefits and Budgetary Impact.....	77
8.3.5	Discounting .....	77
8.3.6	Sensitivity Analysis.....	77
8.3.7	Assumptions .....	78
<b>8.4</b>	<b>Economic Evaluation Results</b> .....	<b>78</b>
8.4.1	Costs of Screening Modalities.....	78
8.4.1.1	Mydriatic Photography Cost Calculation.....	78
8.4.1.2	Mydriatic Photography Costing Results and Sensitivity Analysis .....	80
8.4.1.3	Non-Mydriatic Photography Cost Calculation.....	83
8.4.1.4	Non-Mydriatic Photography Costing Results .....	83
8.4.2	Exploratory Cost Effectiveness Analyses .....	84
8.4.2.1	Anticipated Cost Effectiveness of Moving to Systematic Screening...	85
8.4.2.2	Cost Effectiveness Analytical Assumptions .....	88
8.4.3	Budgetary Considerations .....	89
<b>8.5</b>	<b>Assumptions</b> .....	<b>90</b>
<b>8.6</b>	<b>Conclusions</b> .....	<b>91</b>
<b>9</b>	<b>TOPICS FOR FURTHER EVALUATION</b> .....	<b>92</b>
<b>10</b>	<b>RECOMMENDATIONS FOR THE NATIONAL SCREENING PROGRAMME FOR DIABETIC RETINOPATHY</b> .....	<b>93</b>
<b>10.1</b>	<b>Technical components of the screening service</b> .....	<b>93</b>
<b>10.2</b>	<b>Structural components of the screening service</b> .....	<b>94</b>
<b>11</b>	<b>ACKNOWLEDGEMENTS</b> .....	<b>95</b>
<b>12</b>	<b>REFERENCES</b> .....	<b>96</b>
<b>12.1</b>	<b>References (referred to in the text)</b> .....	<b>96</b>
<b>12.2</b>	<b>Bibliography (Other submitted references, not directly cited)</b> .....	<b>103</b>

**LIST OF TABLES**

<b>Table 5-1</b>	<b>Estimated sensitivities (95% CI) vs. specificities for sight threatening, referable or proliferative retinopathy .....</b>	<b>33</b>
<b>Table 5-2</b>	<b>Estimated sensitivities (95% CI) vs specificities for sight threatening, referable or proliferative retinopathy Mydriatic: 1 vs 2 field .....</b>	<b>35</b>
<b>Table 6-1</b>	<b>Key aspects of a screening programme .....</b>	<b>40</b>
<b>Table 6-2</b>	<b>Comparison of CRAG and NSC grading systems .....</b>	<b>47</b>
<b>Table 6-3</b>	<b>Recommended grading protocol based on adaptation of CRAG system</b>	<b>49</b>
<b>Table 6-4</b>	<b>Quality standards for diabetic retinopathy screening (UKNSC, 2000) .</b>	<b>59</b>
<b>Table 7-1</b>	<b>Recruitment strategies used for diabetic retinopathy screening (Lee et al., 2000) .....</b>	<b>67</b>
<b>Table 8-1</b>	<b>Annualised cost per screen by screening modality .....</b>	<b>80</b>
<b>Table 8-2</b>	<b>Annualised cost per screening modality .....</b>	<b>81</b>
<b>Table 8-3</b>	<b>Annualised cost per screen by screening modality for base case.....</b>	<b>83</b>
<b>Table 8-4</b>	<b>Cost per QALY of systematic screening relative to opportunistic screening: Mydriatic .....</b>	<b>85</b>
<b>Table 8-5</b>	<b>Cost per QALY of systematic screening relative to opportunistic screening: Non-mydriatic .....</b>	<b>87</b>

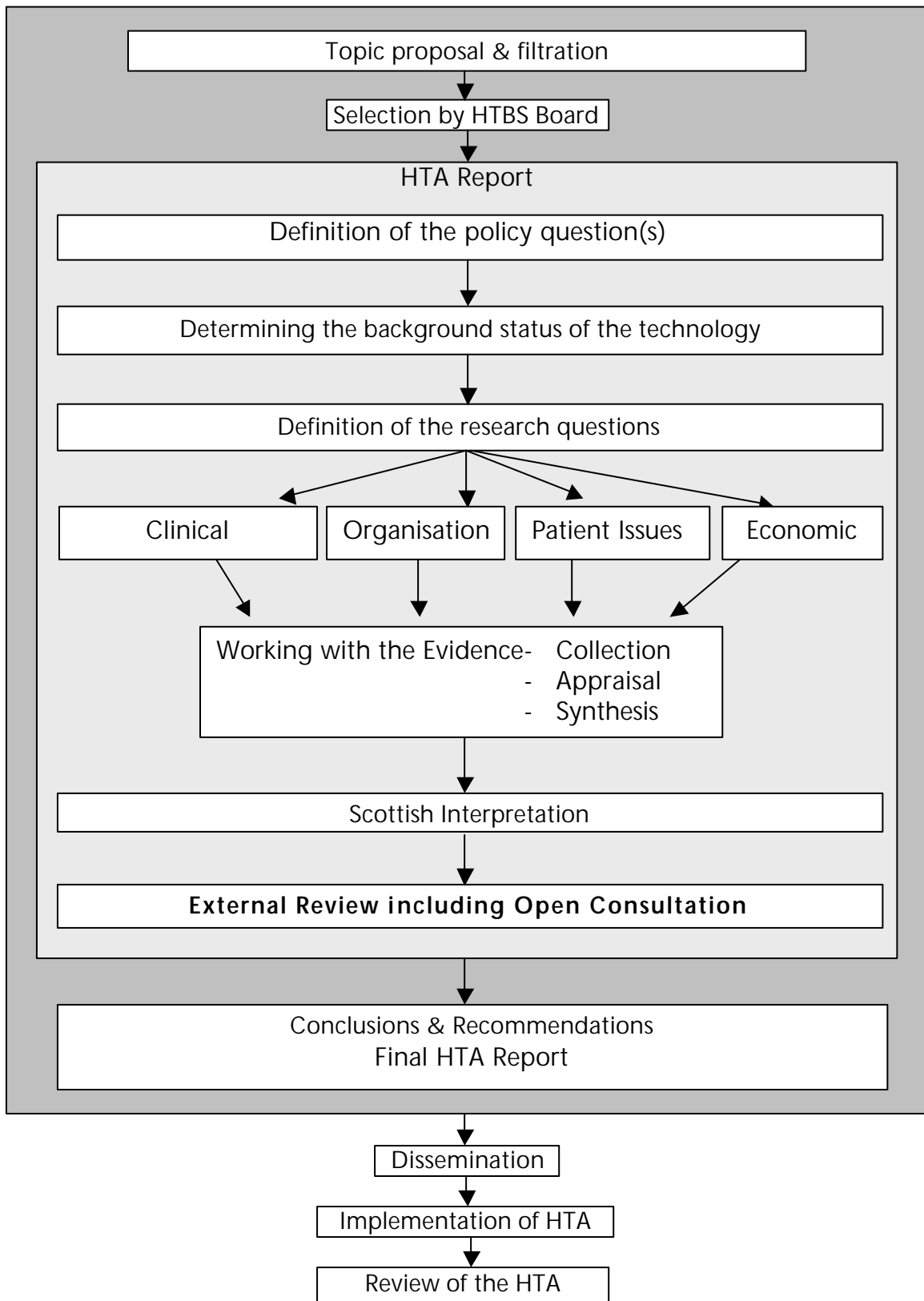
## Assessment Report 3: Draft for Consultation

### APPENDICES

Appendix 1:	Expert Advisers.....	2
Appendix 2a:	Scottish Executive Health Survey.....	4
Appendix 2b:	Health Board Questionnaire to Facilitate HTBS Assessment of Services for Diabetic Retinopathy Screening.....	5
Appendix 3:	HTBS Survey of Retinopathy Screening in Scotland – May/June 2001.....	15
Appendix 4:	Summary of HTBS Baseline Survey.....	19
Appendix 5:	Clinical and Cost Effectiveness Literature Searches.....	23
Appendix 6:	SIGN Revised Grading System for Recommendations in Evidence Based Guidelines.....	28
Appendix 7:	Clinical Effectiveness Analysis: Model and Data Listing.....	29
Appendix 8:	Use of Mydriatic Agents.....	46
Appendix 9:	CRAG Clinical Care Dataset for Diabetes: Eye Care Data.....	55
Appendix 10:	Accuracy and Feedback of Referrals.....	57
Appendix 11:	Bro Taf Diabetic Retinopathy Screening Service – Organisational Structure.....	60
Appendix 12:	Cardiff and Vale NHS Trust – Job Descriptions.....	61
Appendix 13:	Sample Job Description – Retinal Screener.....	67
Appendix 14:	Draft Training Schedule for Newly Appointed Retinal Screener.....	69
Appendix 15:	Optometrists Training and Accreditation with Indirect Ophthalmoscopy....	70
Appendix 16:	Sample Patient Information Leaflets Re Diabetic Retinopathy Screening...	72
Appendix 17:	Tabulations of Cost Effectiveness Study Summaries.....	94
Appendix 18:	Base Case Assumption Used for Economic Analysis.....	102
Appendix 19:	Cost Basis and Estimates.....	103
Appendix 20:	Indicative Additional Costs Required to Establish the National Screening Programme.....	120
Appendix 21:	Mobile Drive Time and Patient Turnaround Time.....	124
Appendix 22:	Balance Between Single Staffed Mobile and Optometrist Provision.....	127
Appendix 23:	Model Structure.....	130
Appendix 24:	Downstream Referral and Treatment Costs.....	137

### Assessment Report 3: Draft for Consultation

Figure 1: Health Technology Assessment process



## 1 EXECUTIVE SUMMARY

### Background to Diabetic Retinopathy Screening and this Assessment

1. There are estimated to be approximately 156,000 people with diabetes in Scotland.
2. Diabetic retinopathy is the biggest single cause of blindness in Scotland amongst people of working age. The rising prevalence of diabetes means that it will remain a major health and economic problem in Scotland. At any time up to 10% of people with diabetes will have retinopathy requiring ophthalmological follow up or treatment.
3. The personal and social costs of blindness in terms of higher possibilities of dependence, potential loss of earning capacity, and increased likelihood of greater social support needs, are significant for individuals, for the caring services and for society.
4. In its early stages, diabetic retinopathy is symptom free and progression of disease can be prevented by laser treatment, so early detection by regular screening is beneficial.
5. A comprehensive HTBS survey has shown that no NHS Boards have all the components in place to undertake quality assured population screening for diabetic retinopathy. Initiatives are underway to establish the screening service, but these are generally at early stages of development.
6. *Our National Health* (Scottish Executive Health Department, 2000) recognised that NHSScotland should create a national screening strategy for diabetic retinopathy. **The Scottish Diabetes Framework recognises eye care as one of the first stage priority issues and sets the milestone that all people with diabetes will have their eye status (retinopathy) recorded on the local diabetes register by September 2003.**
7. **This HTBS Health Technology Assessment aims to determine the most effective and efficient approach to achieving, implementing and sustaining a quality assured, national screening programme for diabetic retinopathy that takes account of patient requirements.**

### Clinical Effectiveness

1. There are two main approaches to screening for diabetic retinopathy: ophthalmoscopy, or retinal photography with subsequent grading.
2. Direct ophthalmoscopy does not achieve sufficient sensitivity to act as a screening test for sight-threatening disease and therefore should not be the basis of any national programme.
3. Indirect ophthalmoscopy (biomicroscopy) using a slit lamp has been shown to be sensitive and specific enough to be viable as a model for a national screening programme when used by appropriately trained individuals. However, it carries the disadvantage that there is no hard record of the test for quality assurance or monitoring progressive changes.

### **Assessment Report 3: Draft for Consultation**

4. Retinal photography, with one or two fields (photographs), has been shown to achieve high sensitivity and specificity for sight-threatening disease. Advantages of digital photography are ease of image acquisition and storage. The image may also be transmitted electronically, facilitating external quality assurance. Consequently, digital retinal photography is the screening medium of choice.
5. Some eye pupils are small and need to be dilated with eye drops (mydriasis) before screening is performed. Furthermore if more than one image per eye is required mydriasis is essential because of constriction of the pupil after the first flash photograph.
6. This HTBS Assessment has found no clear evidence that mydriasis or the use of more than one image significantly alters the sensitivity or specificity of screening.
7. Studies using older (not digital) retinal cameras indicate that the proportion of unusable images is probably slightly lower when mydriasis is used. Currently, there is no evidence that this applies to digital retinal cameras. This needs to be investigated.
8. Studies canvassing patient opinion have suggested that mydriasis may reduce attendance for retinopathy screening because of its temporary effects on vision.
9. If mydriasis is used, tropicamide is the recommended agent. It must be administered by a professional complying with the Patient Group Directions and the possible effects of the mydriatic agent should be clearly communicated to patients.

### **Organisational Issues**

1. The main features of the proposed national screening programme in Scotland are:
  - a. Systematic call and recall of all eligible patients
  - b. Trained professionals
  - c. Recorded outcomes and robust quality assurance
  - d. Integration with the process of care for those with diabetes
  - e. Evaluation and research as an integral part of the programme.
2. The national screening programme must be organized within current health service structures within Scotland, under the auspices of the National Services Division, who have responsibility for national screening programmes in Scotland.
3. Quality assurance is key to any national screening programme. These will be developed on the basis of the recommendations in this report by the National Services Division and the Clinical Standards Board for Scotland (who have national responsibility for Quality Assurance).
4. A network of regional screening offices should be established to work with GPs and NHS Boards to establish accurate diabetes registers of those eligible for screening. These regional offices will arrange screening sessions, issue invitations and oversee grading and result reporting. These offices will work to the methodological, IT and quality assurance standards as defined in this report and coordinated by the National Services Division.

### Assessment Report 3: Draft for Consultation

5. To be effective, the national screening programme must be integrated with routine diabetes care. Tight glycaemic control and careful blood pressure control both reduce the development and progression of diabetic retinopathy in type 1 and type 2 diabetes. Clinicians responsible for ongoing diabetic care must be fully informed of results, not only for sight-threatening retinopathy requiring referral to the ophthalmologist but also for any retinopathy.
6. All patients diagnosed with either type 1 or type 2 diabetes mellitus and aged over 12 years, or post puberty should have annual examinations of the retina (back of the eye). For those with type 1 diabetes onset post puberty, 3 years past diagnosis is an appropriate time to start screening.
7. No upper age limit is suggested, but those who are already receiving treatment from an ophthalmologist, who are medically unfit to receive laser treatment or are completely blind will not benefit from screening.
8. For call-recall, simple regional systems are recommended at the outset, with medium term development of a fully integrated call-recall system as part of the national IM&T system.
9. Screening using higher resolution digital cameras (1365x1000 pixels) is recommended, with images graded at capture resolution (i.e. not compressed). Image transfer should use a direct digital route to avoid degradation of quality. The image should be graded on a PC with a CRT monitor.
10. Specially trained and accredited non-medical graders should read the digital images, supported by second opinions, if necessary, from ophthalmologists and/or diabetologists. The same staff may be used for both grading and screening given suitable training for both roles.
11. A standard grading nomenclature for diabetic retinopathy is essential for consistent grading. In Scotland, the CRAG grading system is currently used. This assumes that two images are used, so this report proposes a modification to the current system to enable use with a single image.
12. Those patients who have sight-threatening retinopathy should be referred to special assessment clinics at the most convenient ophthalmology departments and treated according to Royal College of Ophthalmologists guidelines.
13. The clinical IM&T functions of the retinopathy screening programme should be consistent with the national IT system for diabetes care that is being established in Scotland. Furthermore, the screening result and image should be incorporated into the computerised medical record.

#### Patient Issues

1. The individuals involved in this screening programme are unlike those involved in most other screening programmes because they are not otherwise healthy. Patients are

### Assessment Report 3: Draft for Consultation

of both sexes, come from a wide age range and there is a higher prevalence in some ethnic minorities.

2. People with diabetes may have a number of other complications of their disease to consider and diabetic retinopathy screening will be just one component of their annual screening programme. Consequently this screening visit should be integrated with other health care visits.
3. A variety of methods should be used to inform patients about the screening programme and to encourage attendance. Research is required to determine the most efficient methods to obtain screening compliance.
4. When patients are reluctant to attend screening, contact with healthcare professionals to discuss issues can be highly beneficial.
5. GPs and patients should be informed of results in a timely fashion.

#### Economic Evaluation

1. All economic analyses were performed assuming that digital retinal cameras will be used and those patients not amenable to digital photography (who experience technical failure) can be identified in advance and will receive slit lamp examination. These analyses will be adjusted during consultation to take account of the final programme model to be proposed and any other new costing information.
2. Costings are based on information obtained from several large area diabetic retinopathy screening programmes within the UK. This allows comparison of a variety of screening modalities: these include provision in a mobile unit vs. hospital centre, mydriasis vs. no mydriasis, number of staff required to perform screening.
3. The following table presents the combined imaging and grading cost per patient for the different screening modalities:

**Imaging and grading cost/patient (£)**

	Mobile 1 Staff GP Premises	Mobile 1 Staff Car Park	Mobile 2 Staff GP Premises	Hospital 1 Staff	Hospital 2 Staff
<b>Mydriatic</b>	18.62	18.83	20.30	15.76	17.52
<b>Non Mydriatic</b>	-	10.02	-	10.25	-

4. The components that have most influence on these costs are the drive time of the mobile unit and the number of staff used. The figures presented above assume the base case scenario with an average drive time in the mobile unit of 2 hours and patient turnaround time of 20 minutes for 1 staff and 15 minutes for 2 staff. In the report, these assumptions have been varied to allow individual regions to calculate the likely cost in their area given different drive times and patient turnaround times. These calculations will also allow comparison with community optometrist provision.
5. For efficiency, no more than 10 regional screening offices are required in Scotland.

### Assessment Report 3: Draft for Consultation

6. Exploratory cost effectiveness analyses demonstrate cost savings when a national non-mydriatic screening programme is compared to the current situation in Scotland of opportunistic screening.

#### HTBS Proposed programme model

1. A quality assured diabetic retinopathy screening programme is proposed that is sufficiently flexible to accommodate the needs of patients living in all communities (urban, rural and island) in Scotland.
2. In 2000, the UK National Screening Committee recommended that mydriasis should be used with all patients receiving diabetic retinopathy screening, in order to obtain two images in each eye. This HTBS Health Technology Assessment has included new data not considered by the NSC and put these into the context of the HTA framework considering the clinical effectiveness, organisational issues, patient issues and economics.

HTBS proposes the following model for a national systematic screening programme for diabetic retinopathy:

- 1. Single field digital retinal photography without mydriasis should be offered to all patients annually**
- 2. Single field digital retinal photography with mydriasis should be offered to those people in whom there is a technical failure without mydriasis:**
- 3. Biomicroscopy with a slit lamp should be offered to those people in whom there is technical failure with or without mydriasis.**

This sequential and pragmatic model optimizes cost-effectiveness and patient preference. Patients known to require mydriasis, should start at step 2.

3. Several important research questions have been identified in the HTA. These should be addressed at an early stage of the rollout of the programme, so that modifications can be made to improve the efficiency of the programme.

#### Consultation period

- 1. This report has been issued for open consultation. Comments should be returned to Mr James Morgan at HTBS by 7 January 2002.**
2. The Assessment report will be finalised and published with an accompanying plain English summary and patient information in early summer 2002.

### 2 INTRODUCTION

HTBS uses the internationally recognised definition of Health Technology Assessment (HTA) (INAHTA, 2000), which describes HTA as a multidisciplinary field of policy analysis that studies the medical, social, ethical and economic implications of the development, diffusion and use of health technology.

This form of Health Technology Assessment takes account of the four components identified in Figure 1 (page 7): clinical effectiveness, organisational considerations, patient issues and economic aspects. National and international evidence is critically appraised, taking account of Scottish circumstances, so that clear practicable recommendations can be made to NHSScotland. The aim is to influence decision-making based on critically appraised evidence and shared best practice.

This Health Technology Assessment follows the process published by HTBS in January 2001 (HTBS, 2001) involving submission of evidence from a wide variety of sources, expert staff to undertake the analyses, a multidisciplinary expert Topic Specific Group to collect and critique evidence and analyses, quality assurance by the HTBS Governance Board and wide-ranging open consultation.

**The key objective of this Health Technology Assessment (HTA) is to determine the most effective and efficient approach to achieving, implementing and sustaining a quality assured, comprehensive national screening programme for diabetic retinopathy that takes account of patient requirements.**

This detailed, scientific assessment report will be updated after the open consultation period, to become an Open Final Assessment Report. At this final stage, an overview of the report and Advice (including patient specific advice) will also be published.

This Assessment is currently at the stage of open consultation. **Comments on this consultation Assessment Report should be submitted by 7 January 2002** to Mr James Morgan, Assessment Coordinator, Health Technology Board for Scotland, Delta House, 50 West Nile Street, G1 2NP.

### 3 BACKGROUND

#### 3.1 Introduction

##### 3.1.1 Rationale for this Health Technology Assessment

In 1989, a meeting of international diabetes experts and patient group representatives resulted in the St Vincent Declaration (WHO, 1989). It specified research and organisational goals to improve diabetes care and set five-year targets for reduction of complications arising from diabetes. In 1995, a multidisciplinary group in the UK issued key targets in the St Vincent Joint Task Force for Diabetes to reduce new blindness due to diabetes by at least one third (St Vincent Joint Task Force for Diabetes, The Report 1995). This goal was set for the year 2000, but has not yet been achieved in Scotland.

When deciding upon its first topics for Health Technology Assessment, the Health Technology Board for Scotland (HTBS) identified the Government's commitment in *Our National Health: A Plan for Action, A Plan for Change* (Scottish Executive Health Department, 2000), to establish a national screening strategy for diabetic retinopathy. 'In 2001, we will launch a Scottish Diabetes Framework to draw together existing guidance and best practice in order to raise the standard of diabetes care. The Framework will include plans to establish a national screening strategy for diabetic retinopathy. Although there are SIGN guidelines already in place and much work being done in diabetes, we need to consolidate and build on this in order further to raise the standard of care.'

The Scottish Diabetes Framework (Scottish Diabetes Framework Working Group, 2001) will shape the delivery of diabetes care in Scotland over the next 5-10 years. **The Scottish Diabetes Framework recognises eye screening as one of the first stage priority issues and sets the milestone that all people with diabetes will have their eye status (retinopathy) recorded on the local diabetes register by September 2003.**

Important work has been performed recently in the field of diabetic retinopathy screening. The SIGN guideline (Scottish Intercollegiate Guidelines Network, 2001) evaluates the clinical effectiveness of methods for prevention of visual impairment in people with diabetes. A clinical guideline is in preparation by the National Institute of Clinical Excellence (NICE, 2000) and the UK National Screening Committee (UK NSC, 2000) has considered many aspects of the establishment of a screening service. These documents give insights into the key requisites for a screening programme, but they do not fully address issues related to the organisation of such a programme, including patient issues, in Scotland or an economic evaluation of various diabetic retinopathy screening service options.

The aim of this Health Technology Assessment is to advise on a comprehensive screening strategy for diabetic retinopathy that is state of the art, feasible and sustainable. The goal is to produce a quality assured, effective and efficient, systematic national screening programme integrated with clinical services for diabetes in primary, secondary and community care, which takes account of patient requirements to obtain a service in which they have confidence, hope, empowerment, clarity and knowledge.

### 3.2 Description of health problem in Scotland

#### 3.2.1 *Epidemiology of Diabetes*

Type 2 (non insulin dependent) diabetes is the most common form of diabetes (approximately 80% of people with diabetes are Type 1). Type 1 diabetes usually appears in people aged over 40 and has a high prevalence in people of South Asian and African-Caribbean origin. The remainder of the diabetic population have Type 1 (insulin dependent) diabetes, which usually occurs before the age of 40, often in childhood.

The Diabetes UK Campaign 2001 – ‘Too many, too late’ - stated that there are approximately 120,000 people who have been diagnosed with diabetes in Scotland and there could be as many as 90,000, as yet undiagnosed. These prevalence data were extrapolated from the Tayside DARTS project (Evans et al., 2000) and those undiagnosed were extrapolated from Forrest et al. (1986), Harris et al. (1987) and Simmons et al. (1991).

The baseline survey carried out by HTBS (section 3.6) suggests that the recorded prevalence of diabetes is approximately 2.5%. However, as the establishment of diabetes registers is now mandated across Scotland, recorded prevalence is likely to increase with improved case ascertainment as has been seen elsewhere (Grimshaw et al., 1999). Example of this are seen in Lanarkshire, where the recorded prevalence of diabetes has risen from 2.0% to 2.8% in 4 years and in Tayside where prevalence has increased from 2.2% to 2.5% from 1991 to 2001.

The Audit Commission (2000) estimated that diabetes currently affects approximately 3 per cent of the population in the UK and that this figure may double by 2010 as a result of obesity and an ageing population. Applying these figures to the Scottish population of 5,200,000 people implies that **an estimated 156,000 people in Scotland have diabetes.**

#### 3.2.2 *Multi-specialty nature of diabetes care*

Diabetes is a common, lifelong disease that results in an impaired ability to control the amount of sugar in the blood. Diabetes can lead to premature death and long-term complications. However, with regular assessment and good management the serious complications associated with diabetes can be minimised.

People with diabetes require comprehensive care, to maximise quality of life by detecting and treating the disease and its complications at an early stage, to minimise premature morbidity and mortality in those people with diabetes, and to provide equal access to high quality diabetes care for all patients. This requires close collaboration between many health care professionals to ensure:

- continuing education
- yearly checks of eyes and vision, kidney function, feet and general well-being
- assessment of risk factors for macrovascular and microvascular disease such as glycated haemoglobin (HbA1c), blood pressure, cholesterol, anaemia and smoking habits
- assistance with self monitoring and injection techniques
- eating and lifestyle advice.
- regular review of progress and treatment.

## Assessment Report 3: Draft for Consultation

Screening for diabetic retinopathy is just one vital component of diabetes care which must be integrated into the total care package of people with diabetes.

### 3.2.3 *Organisation of diabetes care in Scotland*

In view of the multi-specialty nature of diabetes care, Diabetes UK advocates the model of local diabetes services advisory groups (LDSAGS) that provide a forum for monitoring, reviewing and appraising local services [ref]. The Scottish Diabetes Framework has endorsed the creation of LDSAGS at Board level, perhaps overseeing the development of managed clinical networks (MCNs) for diabetes care at local level. The Framework consultation has recommended that:

- Managed Clinical Networks for Diabetes Care should be established at Board level.
- Boards will be responsible for the clarity of network arrangements – this will be co-ordinated through the successful model of Local Diabetes Services Advisory Groups (LDSAGs).
- Each Board will publish a publicly available annual written report as well as submitting information to the Scottish Diabetes Survey.
- The local report will contain a clear statement of specific service and clinical improvements, and objectives for service improvement.
- LDSAGs will be truly multi-disciplinary/multi-professional with representation from patients playing a central role.
- LDSAGs will develop a clear policy of patient involvement and dissemination of information to patients.
- The LDSAG will oversee a quality assurance programme consistent with the standards established by the Clinical Standards Board for Scotland.
- The LDSAG will establish clear educational, training and continuing professional development programme as integral parts of the Network.

Effective care involves partnerships between patients and all health care professionals who contribute to diabetes care in a locality. This philosophy and culture of behaviour applies fully to systematic screening for diabetic retinopathy as much as to all other aspects of effective care provision.

## 3.3 **Diabetic Eye Disease**

### *Background Retinopathy*

Diabetic retinopathy is a complication of diabetes that affects the small blood vessels of the retina in the back of the eye. Diabetes can cause these small blood vessels to block off resulting in the retina being starved of food and oxygen. If enough small blood vessels block then the eye tries to grow new blood vessels (proliferative retinopathy).

### *Proliferative Retinopathy*

The new vessels created by proliferative retinopathy are useless because they grow into the middle of the eye. They can cause blindness by bleeding and or by pulling the retina off the back of the eye.

### *Sight-threatening Retinopathy and Referable Retinopathy*

Sight-threatening retinopathy and referable retinopathy are often used interchangeably leading to confusion. Sight-threatening retinopathy refers to the presence of new vessels and or

### Assessment Report 3: Draft for Consultation

clinically significant macular oedema. Referable retinopathy refers to retinopathy that should be screened more frequently, often in a more detailed way, as it is anticipated that there is a high chance that sight-threatening retinopathy will occur soon. (Ideally ophthalmologists would only wish to see patients with sight-threatening retinopathy, because it is these patients who require assessment for laser treatment.)

#### *Maculopathy*

If small blood vessels block off in the centre of the retina then sight can be affected before new blood vessels are formed. This can be a result of the damaged vessels leaking fluid and blood or simply because so many small vessels are damaged that that part of the retina 'dies'. Laser treatment is effective at treating small areas of leakage but cannot treat areas of 'dead' retina. Early detection of retinopathy and stringent control of risk factors is the most important aspect of treatment.

#### *Screening and Laser Treatment*

In its early stages retinopathy causes no symptoms, so if it is to be detected and treated before it becomes sight threatening, regular retinal examination is necessary. Timely laser photocoagulation is effective at treating the new vessels in the retina to prevent the extensive neovascularisation, haemorrhage, and traction and detachment of the retina that leads to visual impairment.

Visual problems caused by diabetic retinopathy are one of the most common specific complications of diabetes (NHS CRD, 1999). The percentage of patients newly diagnosed with Type 2 diabetes who have some retinopathy is not clear but thought to range between approximately 20% and 40% (NHS CRD, 1999) and approximately 5-10% of all people with diabetes have sight-threatening retinopathy (NHS CRD, 1999). Blindness is one of the most feared complications of diabetes with an incidence of 50-65 per 100,000 diabetic population per year in Europe (SIGN, 2001). Furthermore, diabetes is the most common cause of blindness in people of working age in industrialised countries (Williams, 1994).

The UK National Screening Committee (NSC) report (UK NSC, 2000) presents the following results from peer reviewed articles. Untreated, between 6-9% of people with proliferative retinopathy or severe non-proliferative disease would become blind each year. However, laser treatment for proliferative retinopathy with high-risk characteristics achieved a relative risk reduction in severe visual loss of 51.5%. This protection has been shown to endure for over 10 years in 2/3 of laser-treated patients and epidemiological data indicate that each successful treatment will give at least 5 years of preserved sight. With appropriate medical and ophthalmological care blindness may be prevented in at least one eye in over 90% of patients with proliferative retinopathy.

#### **3.3.1 *Blindness due to diabetic retinopathy in Scotland***

Cormack et al. (2001) have studied social work department blindness registration records in Fife from the period 1990-1999 to identify those patients whose main diagnosis was diabetes. Out of 2,529 people with diabetes, the mean number of blind registrations per year due to diabetes was 4.3 (95% CI 3.3 to 5.3).

At the end of December 1999, the prevalence of blindness due to diabetes was 210 per 100,000 diabetic population and the incidence of blindness due to diabetes was 64 per 100,000 diabetic population per year (95% confidence interval – 49 to 79 per 100,000 diabetic

## Assessment Report 3: Draft for Consultation

population per year). However, these are probably underestimates of the level of disease because the only record of legally recorded blindness in the UK comes from social work records. Also, patients may have mixed aetiology and diabetes may not be specifically identified. Furthermore, existing routine health service record systems do not reliably identify patients with diabetic eye disease or events associated with health care of diabetic eye disease. Consequently, special surveys or clinical audits are needed at present to identify the real burden of diabetic retinopathy and to link cases identified to previous screening histories.

### 3.4 Perspectives

#### 3.4.1 Introduction of Systematic Screening

Experience from the Breast and Cervical Cytology Screening programmes in Scotland (Scottish Cervical Screening Programme, 2000) and other in other countries such as New Zealand and Iceland has shown clearly that the establishment and maintenance of population based systematic screening programmes is complex. (Forrest et al. 1987; Lancet editorial, 17 August 1985; Independent Inquiry into Cervical Screening call/recall in Fife, Forth Valley and Tayside NHS Boards, 1999). The introduction of the 'technology' of systematic screening for diabetic retinopathy in Scotland will require detailed attention to organisational and training issues as well as to the choice of the screening tests or procedures. There must be explicit responsibilities at NHS Board level to determine optimal approaches for the local population, but local approaches must link in to a national unified system, which has comprehensive audit and quality assurance in place.

### 3.5 Description of the technology

#### 3.5.1 Retinal Imaging

Screening for diabetic retinopathy and maculopathy is accomplished by imaging the retina of the eye through the pupil. Various instruments exist for this purpose. Ophthalmoscopes are instruments containing an arrangement of lenses and a source of illumination that allows direct visual inspection of the interior of the eye. The hand-held direct ophthalmoscope forms part of the armamentarium of most general practitioners but studies have reported low screening accuracy for this instrument (section 5.3.5.4) and hence the indirect ophthalmoscope or biomicroscope illuminated by a slit-lamp, is preferred by many optometrists and ophthalmologists. The biomicroscope has an added advantage in that it gives a stereoscopic view to give an appreciation of depth.

Retinal cameras are a newer technology that allows photographs of the retina to be taken. They consist of an optical system designed to focus on the retina upon which is mounted an image capture device such as a 35mm or a digital camera. The current established gold standard photographic method for diagnosis of retinopathy uses 7 overlapping stereoscopic fields with an angle of view of 30 degrees. However this method would be too time consuming for a mass screening programme. The cameras for screening generally have an angle of view between 45 and 50 degrees. This allows the whole of the posterior pole of the eye to be captured in a single image but it may still be necessary to view the more peripheral retinal areas and hence two or more overlapping images can be taken. The early retinal cameras used conventional photographic film but modern cameras produce digital images that can be stored on a computer for subsequent review (section 6.10). However, most of the clinical studies have used conventional film cameras.

### **Assessment Report 3: Draft for Consultation**

The most recent development in imaging is the scanning laser ophthalmoscope (Optos, 2001) which produces digital images similar to a retinal camera but with a much wider angle of view (120°) allowing the entire retina to be viewed on a single image.

All these imaging methods are non-invasive and require no contrast enhancement agents. However, it is usually easier to image the retina when the pupil is dilated and so mydriatic eye drops are often used in conjunction with these instruments. Many retinal cameras use light of a wavelength to which the eye does not respond for focusing and this allows an image to be taken without mydriasis. However, the pupil contracts in response to the camera flash and so only single images can be taken in a short time span. Such cameras are referred to as non-mydriatic. Scanning laser ophthalmoscopy is also a non-mydriatic technique.

The protocol that specifies how to classify the pathological features observed during retinal imaging and the subsequent grading of the patients is an important part of the screening system. It should be sensitive and specific to the conditions to be detected, clearly specified and capable of producing reproducible results from different observers.

This Health Technology Assessment investigates a screening programme for diabetic retinopathy. However, there are two distinct forms of retinal change that commonly threaten the sight of people with diabetes, retinopathy and maculopathy (section 3.3). Retinopathy can be detected by 2 dimensional retinal images alone but the thickening of the macula associated with maculopathy cannot be directly detected and must be inferred from other abnormalities. This makes the impact of screening on maculopathy less clear.

The National Screening Committee distinguish three types of maculopathy: exudative, diffuse, and ischaemic. The NSC has suggested that the accuracy of maculopathy detection can be enhanced by combining the imaging results with the visual acuity test. They also state that ‘Ophthalmoscopic screening, which must utilise stereoscopic biomicroscopy, allows for the detection of diffuse macular oedema; digital camera based systems not using stereo imaging may not detect this feature. The lack of stereoscopic assessment in these cases generally means that the accurate assessment of the macula for the definition of clinically significant macular oedema as defined by the Early Treatment Diabetic Eye Study (ETDRS – Early Treatment of Diabetic Retinopathy Study Group, 1985) is not possible. However the ophthalmologist uses this definition in the decision to treat and so it is important to appreciate that grades of screen positive maculopathy are surrogates for the features that indicate to the ophthalmologist that treatment is required’ (UK NSC, 2000).

Exudative or focal maculopathy responds well to laser treatment and can be detected from non-stereoscopic images such as from digital cameras. Diffuse maculopathy may not always respond very well to laser treatment. In such patients laser may be best reserved for when vision first starts to decline, as recently suggested by ETDRS. Decline in vision may be reported by the patient or detected on testing visual acuity, as recommended by the NSC. Laser treatment should not be given for ischaemic maculopathy.

### **3.6 Current Service Provision of Diabetic Retinopathy Screening in NHSScotland**

The Scottish Executive undertook a survey in 2000 (Appendix 2a) to identify the extent of services for diabetic retinopathy screening across Scotland. The responses demonstrated large variance in service provision for diabetic retinopathy screening across Scotland; and there

### Assessment Report 3: Draft for Consultation

appears to be potential for sharing of good practice in areas where systems are currently under development. For example, some areas do not yet have registers fully in place, are unsure of the number of people with diabetes in their area and have no systematic screening in place, but one area (the Western Isles) screens 93% of all known diabetic patients over the age of 12 annually (using the Tayside mobile screening unit).

The survey indicates that a variety of methods exist for delivery of screening, including mobile vans, static cameras located in healthcare facilities and local optometrists. As there was no consistency in screening methodology across the country, HTBS undertook a more detailed baseline survey in June 2001 about diabetic retinopathy screening service provision in each NHS Board. The HTBS questionnaire is presented in Appendix 2b. As all 15 NHS Boards in Scotland responded to this detailed questionnaire, this survey provides invaluable information about current service provision from the whole of Scotland. The full listing of responses is presented in Appendix 3, with a detailed overview in Appendix 4. In summary:

- No NHS Board has all the components of a comprehensive population based systematic screening programme for diabetic retinopathy in place at the present time. Most areas, however, report initiatives to establish such services, the majority being at the early stages of development.
- Diabetes Registers are stated as ‘established’ in seven Board areas, ‘being developed’ or ‘being populated’ in 6 further areas and ‘being planned’ in the remaining two Board areas. However, updating of the established registers varies from daily to annually with a similar variation in the frequency and depth of quality assurance checking. Linkage of the Diabetes register to NHS Board Community Health Indexes also varies considerably.
- While use of standardised data collection sheets is stated to be in place in ten NHS Board areas, systematic collection and compilation of the results in order to enable organised call/recall is completely in place in only four areas. However, other areas are actively planning to do this.
- Accreditation of ‘screeners’ is organised locally, usually by ophthalmologists. These have focused upon community optometrists with some hospital clinicians and a ‘few GPs’ in some areas. Formal refresher training after accreditation is also in place in at least five Board areas. No scheme appears to have a national context.
- Formal quality assurance of registers, screening test and/or overall screening process is highly variable with most areas being at very early stages of development. The baseline survey identified only four NHS Board areas where audit of cases of diabetic retinopathy took place and only two areas where audit of the previous screening history of new cases took place.
- Most Boards have established steering groups using the LDSAG model.
- Four NHS Board areas state that there is organised screening using digital camera technology. The other areas use a mixed model of accredited optometrists (and some GPs) with some digital camera use mainly in hospital clinic settings. Two NHS Boards are at the earliest stage of setting up programmes.

### **Assessment Report 3: Draft for Consultation**

- Most areas reported use in the past of Board or Trust ‘development monies’, audit budgets or other funds to employ facilitators or to purchase equipment. While three areas reported substantial recent investment, others stated that existing or historical funding was either now insufficient or uncertain for future full systematic screening to be sustained or achieved.

#### ***3.6.1 Optometry services***

Slit lamps are widely available in all areas in Scotland, in both hospital and community settings. They are used by a variety of professionals, but it is important to note the important contribution of optometrists with this modality, with over 300 optometrists involved in the current systematic and opportunistic screening programmes in Scotland. This fact is confirmed by another survey performed by the Common Services Agency of NHSScotland, which indicated that during 1999/2000, optometrists in seven NHS Boards performed 8494 diabetic screening tests.

#### 4 SOURCES OF EVIDENCE

The Health Technology Assessments undertaken by HTBS use international evidence from a variety of sources: published literature, grey literature (e.g. academic and government reports, website publications, conference abstracts) and information submitted from a variety of interested parties.

The following interested parties were invited to submit evidence for this Assessment (those marked \* did submit evidence):

##### Manufacturers

All ABHI members: one submission received from Optos plc\*

(Further evidence taken from websites of the following manufacturers – Zeiss, Haag-Streit, Canon, Topcon).

##### Professional/Specialist Groups

College of Optometrists\*  
Scottish General Practitioners Committee\*  
Royal College of Ophthalmologists\*  
Association of British Clinical Diabetologists\*  
Royal College of Nursing (Scottish HQ)  
Breast and Cervical Screening Co-ordinators Group\*  
Royal College of Physicians (Edinburgh)\*  
Royal College of Physicians and Surgeons of Glasgow\*  
Royal College of General Practitioners (Scotland)  
Scottish Association of Health Councils  
Social Work Services Group

##### Patient Groups

Diabetes UK\*  
Royal National Institute for the Blind

##### Advisers

The Topic Specific Group of experts (Appendix 1) who assisted HTBS staff with this assessment submitted a variety of forms of evidence including patient leaflets, NHS Board Joint Investment Fund plans, position papers, job descriptions, etc. Also, special advisers from across the UK submitted valuable information about existing local screening programmes.

For clinical effectiveness, the SIGN Guideline on Management of Diabetes, section on prevention of visual impairment (2001), the draft NICE Guideline (2000) and the 2<sup>nd</sup> report of the UK National Screening Committee (2000), were used as the main bases for evidence.

For the economic evaluation information was obtained from existing UK diabetic retinopathy screening programmes and a comprehensive systematic literature review was performed.

For organisational and patient issues, focus was placed on the submitted evidence, selected literature references and grey literature from a variety of sources.

## 5 CLINICAL EFFECTIVENESS

### Conclusions

- The primary method of screening should be digital retinal cameras
- A single retinal image using non-mydratric photography will provide good screening accuracy in many patients.
- Direct ophthalmoscopy is not recommended for a national screening programme.
- Studies have produced inconsistent technical failure rates for screening methods but all methods will result in some failures.
- Mydratric retinal photography and slit-lamp biomicroscopy should be available as second-line screening methods.
- If mydriasis is used, tropicamide is the recommended agent. It must be administered by an appropriately qualified professional under Patient Group Directions.

### 5.1 Search strategy

A large body of evidence is available on the clinical effectiveness of screening for diabetic retinopathy. This includes a number of recent, high quality, systematic reviews by UK research groups (SIGN, 2001; UK NSC, 2000; NICE, 2000). In order to avoid duplication, the HTBS clinical effectiveness analyses use these reviews as a basis for further detailed analysis, augmenting them with additional references identified by the HTBS expert group and publications issued in 2001.

Details of the sources searched by SIGN, the NSC and NICE are presented in Appendix 5.

### 5.2 Methods for the Evaluation of Clinical effectiveness

The effectiveness of screening for diabetic retinopathy may be reduced by two separate types of failure. Firstly the chosen method may fail to produce a clear image for evaluation. The frequency with which this occurs is called the technical failure rate. Secondly, after successful imaging, the screening result may differ from the true state of the patient (called a false positive or false negative result). The impact of these two modes of failure on screening effectiveness can be considered separately.

#### 5.2.1 Outcome measurements

The measure of technical failure rate is the probability that a screening episode will fail to produce an interpretable image. It is estimated by the proportion of such uninterpretable images in a study.

The purpose of retinopathy screening is to detect diabetic eye disease for which a clinical intervention is required. Referable retinopathy (section 3.3) requires referral to an

### Assessment Report 3: Draft for Consultation

ophthalmologist as soon as possible. Detection of less severe disease is also important for more general disease management and can influence decisions to try to improve glycaemic or blood pressure control. For cost effectiveness, referable retinopathy has the greatest implications and is most important to detect. Hence it is also the focus of this clinical effectiveness section.

After technical failures have been excluded, the measures used in clinical effectiveness studies of screening technologies are usually expressed as sensitivity and specificity. Sensitivity and specificity may be calculated by considering the decision matrix, which arises from a diagnostic test that yields a dichotomous (positive/negative) result. Four combinations of test result and disease state are possible (The European Agency for the Evaluation of Medicinal Products, Committee for Proprietary Medicinal Products, 2000):

#### Diagnostic decision matrix

		True disease state	
		Present	Absent
Test result	Positive	TP True Positive	FP False Positive
	Negative	FN False Negative	TN True Negative

Sensitivity is the probability that a test result is positive given the subject has the disease. In a suitable experiment the sensitivity can be estimated by:  $TP/(TP+FN)$ . Specificity is the probability that a test result is negative given a subject does not have the disease. In a suitable experiment the specificity can be estimated by:  $TN/(TN+FP)$ .

In designing a screening programme the technical failure rate of the screening method is also an important outcome. The failure rate is the proportion of patients in whom the screening method fails to return a useful assessment of the extent of diabetic eye disease. This may occur because of other eye conditions which obscure the retina or because infirmity or other circumstances interfere with the screening process.

The term 'accuracy' is used to refer to the probability that a screening test will reveal the true disease state for a randomly selected patient. It will vary with the prevalence of the condition to be detected and is thus not often estimated in clinical studies. Furthermore it does not distinguish false negative and false positive test results. However, it can be a useful concept in discussion of alternative screening methods for the same population.

#### 5.2.2 *Methods for estimating sensitivity and specificity*

Interpretations of test screening methods performed on groups of diabetic patients were compared with methods expected to give accurate results (Gold Standard).

The screening method can be considered as a combination of the mechanical imaging process, which will be performed according to a clinical protocol, and a set of rules which specify how the images are to be interpreted and what combination of observations should lead to referral to an ophthalmologist. Variation in this set of rules will result in changes in the sensitivity of the method. However, a reduction in sensitivity will usually be offset by an increase in specificity and vice versa. Different studies may use different sets of rules and, since primary

## Assessment Report 3: Draft for Consultation

interest is in the inherent ability of the screening devices, it is usual to combine the sensitivity and specificity using a mathematical model of the dependence between the two. This allows a single index of screening performance to be analysed, which, under certain assumptions, is independent of the set of rules for interpretation of the image.

The approach to modelling used in this report is set out in Appendix 7. It allows the performance of a screening test to be described in terms of a curve relating sensitivity to specificity – for historical reasons called a receiver-operator characteristic (ROC) – and hence calculation of the likely sensitivity at various specificities (achieved by alterations in the rules of interpretation).

The performance of each screening method is characterised by a measure of its ability to discriminate people with retinopathy from those without. These measures are combined across studies using a random effects meta-analysis model.

### **5.2.3 Benefits and disbenefits**

For the purpose of the effectiveness assessment the primary outcome of screening is considered to be the accurate detection of referable disease. This is a clinical variable and the true benefit – detection and successful treatment of disease - will be considered within the cost-effectiveness analysis. In addition to clinical consequences it is generally the case that patients are spared unnecessary anxiety when screening accuracy is high. Incorrect referrals impact both on the patient and on the ophthalmology service to which the referral is made. Failure to produce a sufficiently clear image for grading also incurs a disbenefit as such patients will have to be subjected to additional tests. Generally speaking the imaging process does not carry important risks but the use of mydriasis can cause adverse effects, discomfort and inconvenience (see section 5.3.6.1).

## **5.3 Clinical Effectiveness Results**

### **5.3.1 Quantity and Quality of research available**

A number of high quality reviews were consulted. These included the SIGN guideline (SIGN, 2001) which uses the evidence grading system developed by SIGN (Harbour and Miller, 2001) and is reproduced in Appendix 6.

Two other key reviews were the UK National Screening Committee's recommendations on Preservation of Sight in Diabetes (UK NSC, 2000); a risk reduction programme, and the draft report on Clinical Guidelines for Type 2 Diabetes sponsored by NICE and collaboratively written by members of the Royal Colleges of General Practitioners, of Physicians, and of Nursing with Diabetes UK. For brevity, this document will be referred to as 'the NICE guideline' (NICE, 2000).

These were based on systematic literature searches and the NICE guideline gives a description of some of the difficulties inherent in the interpretation of the studies identified. Studies differ in the nature of the Gold Standard test procedure, whether a Gold Standard was included, the severity of retinopathy to be detected, the handling of cases in whom no interpretable test result could be obtained, and the type of patients enrolled. The general problem appeared to be that few studies were identified which had been specifically and appropriately designed to give information relevant to a large scale screening programme.

### Assessment Report 3: Draft for Consultation

Despite these difficulties it is possible to combine the results of selected studies with caveats as detailed in the results section of this report.

Discussion and any new analysis presented here is based on the studies used in the NICE guideline augmented by new studies and other studies identified by members of the HTBS Topic Specific Group.

#### **5.3.2 Description of studies excluded by HTBS**

Some studies have been excluded by HTBS for calculations of screening accuracy. Most of these evaluated agreement between screening methods rather than concordance of a screening method with a gold standard. Studies that evaluated methods not appropriate for a national screening programme were also excluded.

#### **5.3.3 Description of studies included**

All studies with relevant data were included for assessment of technical failure rates.

For analysis of accuracy, the included studies were:

Those in the NICE guideline, which fulfilled the following criteria:

- The use of a credible gold standard: either 7 field stereoscopic photography or slit lamp investigation (biomicroscopy or indirect ophthalmoscopy) by a qualified ophthalmologist.
- A sample of diabetic patients.
- Within patient comparisons.
- All patients accounted for in study report.
- Different methods of investigation reported – not interobserver variation for a single method.
- Adequate masking where appropriate.

(Some of these studies use older technologies and screening methods. This will be highlighted in discussions.)

Additional studies identified by HTBS:

- Burnett et al., 1998
- Leese et al., 1997
- Olson et al., (Personal Communication, 2001).

Attachment 1 of Appendix 8 presents the number of patients in the clinical effectiveness studies and associated cases of detected retinopathy.

#### **5.3.4 Failure rates of screening methods**

The frequency with which photography proves impossible is not generally well reported. This is possibly because the studies are conducted from the point of view of diagnosis – i.e. when an adequate photograph is available is it informative? – rather than the point of view of

### Assessment Report 3: Draft for Consultation

a screener who must decide how to get a view of the eye that allows a referral decision to be made.

The SIGN guideline states that ‘between 3% and 14% of retinal photographs are ungradeable although this rate may be improved by digital imaging (Taylor, 1996 and Harding, 1995). Slit lamp biomicroscopes with dilated indirect ophthalmoscopy used by properly trained individuals can achieve sensitivities similar to retinal photography, with a lower technical failure rate (Hutchinson, 2000).’

The failure rates were not reviewed in the NICE Guideline report, but a number of the studies within this review provide some evidence, which is presented in the sections relating to each screening method below.

Three concomitant questions arise:

- (1) Does mydriasis significantly reduce the proportion of failures for photography?
- (2) Does digital photography have lower technical failure rates than photography using colour slides?
- (3) If photography fails, do other methods of screening perform better?

This is a difficult question because, whilst photography produces a permanent image which can be reviewed in order to reach a consensus on gradeability, ophthalmoscopy and slit lamp does not. The decision as to whether an ophthalmoscopic inspection has provided adequate data is purely that of the operator. Thus it must be recognized that the failure rates from retinal photography and ophthalmoscopy are judged by different criteria. Data that may illustrate this issue are given in Lairson (1992). Here, although an ophthalmologist using both direct and indirect ophthalmoscopy reported no failures to visualize, 49 false negatives were recorded in 347 examinations. This was higher than from photographic methods – 29 without mydriasis, 14 with mydriasis – and may suggest that difficult visualization tended to result in a negative finding. The reference method in this study was 7-field 30-degree stereoscopic photography.

Both 7-field photography and indirect ophthalmoscopy by an ophthalmologist are used as reference standards in screening studies and this level of disagreement found by Lairson raises concerns over the validity of calculations of sensitivity and specificity based upon them.

#### *5.3.4.1 Failure of non-mydriatic photography*

One of the largest studies of single field non-mydriatic photography was Buxton (1991). In 6304 Polaroid images 5% were found to be unusable. Another 19% were graded as having ‘some detail’ and were interpreted by the graders. In Williams (1986) no detail was visible in 5.8% (7/120) eyes photographed with a 45 degree non-mydriatic camera.

#### *5.3.4.2 Failure of mydriatic photography*

Five-field non-stereoscopic photography through dilated pupils was used as a reference standard by Forrest (1987). From 508 eyes, 26 images (5.1%) were ‘unobtainable for clinical reasons’. Of the remaining 482, 12 (2.5%) were unassessable due to cataracts/ptosis and a further 32 (6.6%) were rated unassessable for other reasons. However, of these last, 11 in a subset of 16 who were rephotographed proved assessable. Hence perhaps only 10 ( $[5/16] \times 32$ ) were truly unassessable. This suggests that 9.4% might have required non-photographic

### Assessment Report 3: Draft for Consultation

imaging in a screening programme. Gibbons (1994) found a 4.2% (6/143) failure rate for two-field<sup>1</sup> photography. A further 6% of photographs had rather poor quality but were interpretable by an ophthalmologist. A further study, Gibbons (1998), used 2-field 45-degree slides as a reference standard and only 1.7% of 1245 were ungradeable. However, 22% were omitted from the study as being less than good. Harding (1995) compared 3-field 45-degree photography with slit lamp biomicroscopy. Of 326 patients, 6 (1.8%) were ungradeable by either method. A further 46 of 640 photographic images (7.2%) were considered ungradeable. Thus 9% of images overall would have required review by an alternative method. Of the 46 ungradeable photographs, 12 were due to problems with posture or tremor, the other 34 due to eye defects. Penman (1998) judged 22% (92/427) right eye, single field photographs to be ungradeable in a group of Egyptian people with diabetes. This may be somewhat high because 10 patients were judged to be unsuitable for photography on the basis of ophthalmoscopy and no attempt was made to photograph them. Media opacities were present in 35% of eyes.

The mean technical failure rate in the studies of mydriatic photography was 7%. That in studies without mydriasis was 5.5%. However, this low figure for non-mydriatic photography is strongly dependent on the large study by Buxton.

The discussion above is of failure rates using conventional photography. Olson et al. (personal communication, 2001) provided a direct comparison of technical failure rates in digital and conventional photography. Two fields per eye were imaged and the definition of failure was that any of the four images per patient be ungradeable. 26/586 (4.4%) of patients had technical failures by digital imaging whilst 70/586 (11.9%) failed with conventional slide photography. If the definition of technical failure was restricted to the macular image these rates became 3.5% and 8.1% respectively.

#### 5.3.4.3 *Direct comparison of mydriatic and non-mydriatic photography*

Klein (1985) investigated single field 45-degree photography with and without mydriasis. The reported failure rates were 6.8% (5/74) with and 12.7% (8/63) without mydriasis. Three fields from a 30-degree stereoscopic camera used as a reference failed in 3% (3/99) cases but undilated direct ophthalmoscopy failed in 17% (16/94). Lairson (1992) performed both 2 field (nasal + stereoscopic macular) 45-degree photography with mydriasis and single field 45-degree without mydriasis. Recorded failure rates were 3.7% (13/351) with mydriasis and 14% (49/351) without. The comparison in this case is confounded with the numbers of fields, which, in addition, meant that the comparison could not be masked. An additional methodological doubt in this study is raised by the decision to assess the test for each patient in the same order. It was hoped that a time interval between assessments would render the assessments independent but if this failed, the assessment would be biased in favour of the test assessed later – mydriatic 2-field. Thus it is unclear whether the lower failure rate is due to mydriasis, the presence of extra information, or preconceptions of the reader about preferred methodology.

#### 5.3.4.4 *Are failures of photography associated with disease?*

Conflicting evidence has been found on the question of whether diseased eyes are more likely to result in technical failures of imaging. In the study by Harding (1995) many of the eyes

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<sup>1</sup> Possibly single field stereoscopic – reporting unclear

### Assessment Report 3: Draft for Consultation

judged ungradeable by photography were considered abnormal on ophthalmological review by slit lamp. Five of the 8 failures on non-mydratic photography in Klein were judged to have microaneurysms or more severe NPDR. On the other hand, Pugh (1993) found that 10/50 (20%) of patient ungradeable by undilated photography and 3/13 (23%) ungradeable by dilated photography had moderate retinopathy or worse. This compares with 74/351 (21%) in the entire study, suggesting no association between gradeability and retinopathy. These inconsistent findings do not provide adequate support for a recommendation to refer technical failures directly to ophthalmological departments.

#### 5.3.4.5 *Failure of laser scanning ophthalmoscope*

In relation to failure rates for the laser scanning ophthalmoscope, a study (Baumal and Puliafito, 2000) reports that 22% (19/86) of images were not assessable. These data are of limited value because they relate to a general eye examination in healthy patients and not diabetic retinopathy screening. More specific data on the use of this device in a standard diabetic retinopathy screening setting are required.

Optos PLC has informed HTBS that such research is underway in the UK and further details of this will be provided during consultation.

#### 5.3.4.6 *Failure of conventional ophthalmoscopy*

The failure rate of ophthalmoscopy due to cataracts or a poor view is reported in Forrest (1987) as 4.3%. It is not clear what form of ophthalmoscope was used. In Penman's study (1998) 5.3% (23/427) could not be visualized by indirect ophthalmoscopy.

#### 5.3.4.7 *Conclusion with respect to failure rates of retinal imaging*

One study (Klein, 1985) suggested a reduction in technical failure rate with the use of mydriasis but the result was not statistically significant. A larger study (Lairson et al., 1992) showed a similar effect but it was not clear that this was due to mydriasis. Studies with current technology are needed. The failure rate of photography with mydriasis averaged over the studies considered here is 7% whilst that without mydriasis is 5.5%. Differing definitions of failure complicate interpretation of these figures. It is fair to say that no strong evidence has been found to suggest that mydriasis reduces failure rates but that those studies containing a direct comparison favour the hypothesis.

A different, but important, issue with respect to mydriasis was raised by Klein (1992) who asked for patient preferences and estimated that dilation was unacceptable to 6% of patients with a further 5% stating that it was acceptable only if necessary.

The study by Olson et al. (personal communication, 2001) has indicated that lower technical failure rates are achievable with digital photography than with conventional slide photography. As most of the current evidence relates to conventional photography and the screening programme is likely to use digital cameras, this is an important finding. If digital photography reduces the technical failure rates for non-mydratic photography in a similar way this is likely to be a viable screening option, but reliable estimates of technical failure rates for non-mydratic digital photography should be determined early in the screening programme.

### Assessment Report 3: Draft for Consultation

When the failure rate for ophthalmoscopic investigations has been reported it was not greatly different from photography and this may indicate that changing between the two imaging methods will not unduly increase the number of ophthalmological referrals due to inability of the screener to come to a decision. However, as discussed above, definition of technical failure for these techniques is not the same and hence such comparisons must be viewed with caution.

Only one small study presents failure rates for non-mydratic scanning laser ophthalmoscope and these do not relate to diabetic patients.

#### *5.3.5 Accuracy of retinal imaging methods*

The following section reviews the sensitivity and specificity of retinal screening by various methods using only those screening episodes which were technically successful.

##### *5.3.5.1 The Gold Standard method*

The single most important feature of any study testing diagnostic accuracy is the inclusion of a gold standard method. This is an alternative way of performing the diagnosis, which is known to be very accurate. It is debatable whether a gold standard exists in the detection of diabetic retinopathy but various methods are thought to have better properties than others. The two methods, which might possibly be considered as gold standard, are 7-field stereoscopic photography and indirect ophthalmoscopy or biomicroscopy with a slit lamp carried out by a skilled ophthalmologist through dilated pupils. However, these methods have been compared in four of the studies discussed by NICE (Kinyoun et al., 1992; Pugh et al., 1993; Moss et al., 1985; Schachat et al., 1993) and do not show perfect agreement. Hence it is clear that one or both allow fairly frequent errors in detecting retinopathy. It is not possible to decide objectively which is in error but Kinyoun did subject disagreements to an expert review, which tended to favour the 7-field photography – two errors – over the indirect ophthalmoscopy – 12 errors. Moss also examined the disagreement closely and came to the conclusion that many involved detection of microaneurysms from photographs that were not detected by ophthalmoscopy. No matter which method was correct, this might suggest that disagreements tend to happen in milder disease states.

The direct comparisons of indirect ophthalmoscopy with 7-field photography also raises questions about the standards of 80% sensitivity and 95% specificity seen as desirable by the St Vincent Joint Task Force for Diabetes. Since these standards were not invariably met in comparisons of these two ‘gold standard’ methods, they may represent an unrealistic target for other methods.

##### *5.3.5.2 Methods of screening*

Deciding which methods of screening will be appropriate for a national screening programme is not simply a matter of selecting a particular imaging method and a policy for the use of mydriasis. There is also the question of who should operate the device and, for photographic methods, interpret the results. This question is addressed in a number of studies but may, of course, occasionally be confounded by the use of different devices by different professionals. Hence it may be impossible to differentiate effects due to operators and to screening devices.

### Assessment Report 3: Draft for Consultation

Other features also varied between studies. Some studies were restricted to patients who had not had a diagnosis of retinopathy before or who were not in the current care of an ophthalmologist. The nature of the conditions detected also varied: any retinopathy, proliferative retinopathy and sight-threatening retinopathy being common choices. In addition, the camera technology has changed and improved over the years in which these studies were performed. An important change is that the current digital cameras allow immediate viewing of the image so that imaging failures can be immediately logged and re-attempted if appropriate.

The number of images of each eye obtained with a retinal camera is also a choice that may affect the accuracy of screening. The cameras used as a gold standard in many studies use 7 stereoscopic images in an overlapping pattern, each with an incident angle of 30-degrees at the camera. The cameras that have been assessed for screening use an incident angle of about 45-degrees – i.e. larger coverage – but only a single image or two images have usually been tested. A non-mydratic camera can only take a single image in a short time span since the flash causes the pupil to contract. It can, of course, take multiple images with mydriasis in the same way as a mydratic camera.

There is limited evidence concerning the number of fields that should be viewed with a retinal camera. Interestingly, on average the studies using a single field gave marginally better results than those with 2 or more fields. However, this may be due to differing failure rates and it is clear that this question is still very much a matter that requires further well-designed clinical trials. The SIGN guideline does not give a judgment on this issue but the National Screening Committee guideline (UK NSC, 2000) recommends the EURODIAB protocol of 2x45 (or 50) degree fields.

#### *5.3.5.3 Issues in analysis of screening studies*

Any set of retinal images may be interpreted with more or less stringent criteria for retinopathy. As these criteria are relaxed the number of patients considered to have retinopathy will increase – thus increasing the sensitivity but simultaneously decreasing the specificity. This dependence of sensitivity and specificity means that neither index can ever make sense if presented alone. It also means that sensitivity and specificity estimates should not be combined across studies without allowing for the dependence. This issue alone requires that a statistical model be used for rational synthesis of a number of diagnostic or screening studies. In comparing differing imaging methods an adjustment should ideally be made for the effect of different operators – e.g. GPs or optometrists. However, particular imaging methods tend to be associated with particular operators and hence such analyses can lead to unrealistic conclusions about the performance associated with certain operators with instruments they do not generally use. For this reason it is better to report results only for imaging methods with specific types of operator.

A further issue, which varied between studies, was the treatment of image failures. Most studies excluded such failures from analysis, but a few (Pugh et al., 1993; Lairson et al., 1992) treated them as positive diagnoses. For the purpose of planning a screening programme it may be best to separate the issues of technical failure and clinical diagnosis. Combining them would imply that the only strategies for dealing with image failure would be either referral to an ophthalmologist or assuming them clear of retinopathy. Thus, where sufficient data have been presented, the sensitivities and specificities used exclude failures.

### Assessment Report 3: Draft for Consultation

#### 5.3.5.4 *Statistical model combining all studies with ‘gold standard’ comparators*

The main features of this analysis are:

1. It does not consider studies that did not include a comparator that could be a gold standard – e.g. inter-observer agreement studies for photographs.
2. Converts sensitivity and specificity to a single variate using ROC curves to model the effects of varying the index of suspicion.
3. Analyses estimates of accuracy for ‘any retinopathy’ and more severe retinopathy (PR/STDR/Referable DR) separately.

It should be noted that this statistical technique does not allow for the possibility that a supposed gold standard is less than perfect. Such potential imperfections could be allowed for if credible bounds could be placed upon the accuracy of the standard but such bounds are not available.

A further analytical complication with the studies used by NICE is that several groups were often compared with a single gold standard within a study with respect to detection of a number of different conditions. Thus correlations may also exist between apparently separate comparisons. This issue would be best addressed within a meta-analysis of individual patient data that are not available to these authors, and so is ignored in the current analysis.

The details of the model and a listing of the final dataset are included as Appendix 7.

Table 5-1 presents the estimated sensitivities for selected specificities for detection of more severe diabetic retinopathy (sight-threatening, referable or proliferative) by various professions using various imaging methods. For comparison with the aspiration of the St Vincent declaration (80%) the sensitivities at 95% specificity are shown in bold. The equivalent figures for detection of any retinopathy are given in Appendix 7.

**Table 5-1 Estimated sensitivities (95% CI) vs. specificities for sight threatening, referable or proliferative retinopathy  
Various screening modalities**

<b>GP using direct ophthalmoscope through dilated pupils</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	73% (52,87)	64% (42,82)	<b>50% (29,71)</b>	40% (21,62)
<b>Optometrist using direct ophthalmoscope through dilated pupils</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	79% (56,92)	71% (47,88)	<b>57% (33,79)</b>	48% (25,72)
<b>Other professional using direct ophthalmoscope through dilated pupils</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	88% (74,95)	82% (65,92)	<b>71% (51,85)</b>	62% (42,79)
<b>Mydriatic photography graded by trained graders</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	96% (90,98)	93% (85,97)	<b>87% (76,93)</b>	81% (68,90)
<b>Non mydriatic photography graded by trained graders</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	96% (54,100)	93% (44,100)	<b>86% (31,100)</b>	80% (23,99)
<b>Optometrists with slit lamp</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	82% (63,93)	75% (54,90)	<b>62% (39,82)</b>	53% (30,75)
<b>Ophthalmologist with slit lamp/indirect ophthalmoscope</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	97% (90,99)	95% (85,99)	<b>91% (76,97)</b>	86% (68,95)

The bottom row of this table differs from the others in that ophthalmologists with slit lamps are not an available screening option. Indeed, this modality has been regarded as a gold standard in evaluating other methods. To calculate sensitivities for this row 7-field photography has, arbitrarily, been taken as the preferred gold standard. However, it should be borne in mind that it is not possible to determine whether discrepancies between these two methods arise from errors in one or the other. The reason for presenting this comparison is firstly to emphasize that the methods do occasionally disagree and hence that neither can be assumed error free and secondly to suggest that these sensitivities provide a realistic upper bound on what might be expected of any screening method. Whilst these mean figures achieve the St Vincent criteria of 80% sensitivity at 95% specificity the 95% confidence interval on the sensitivity extends from 76% to 97%. Hence these studies do not provide conclusive evidence that the St Vincent criteria are achievable for detection of sight-threatening retinopathy. The sensitivity estimate for detection of any retinopathy is 79% (95% confidence interval 60% to 91%) at a specificity of 95% and hence the St Vincent criteria were not achieved in this case (See appendix 7)

The point estimates of sensitivity for mydriatic and non-mydriatic photography interpreted by trained graders are identical. However, due to the small numbers of cases in the studies, the confidence intervals for non-mydriatic photography are wide and hence these results should be interpreted with caution. Some supplementary evidence lends weight to the conclusion of equivalence. Firstly, the discrimination of any retinopathy is very similar. At 95% specificity mydriatic photography had 73% (95%CI: 52,87) sensitivity whilst non-mydriatic had 86%

### Assessment Report 3: Draft for Consultation

(95%CI: 68,96) sensitivity. Any failure of non-mydratic photography to reveal fine detail would be expected to adversely affect this comparison since the distinction between normal pathology and mild retinopathy may be based on only one dot haemorrhage or microaneurysm. Secondly, studies of non-mydratic photography in which professions other than trained graders screened for referable retinopathy suggest a sensitivity of 72% (95%CI 52,86). It seems likely that the accuracy of this group would be inferior to that achievable with specifically trained graders.

It should be noted that there is little evidence within the studies considered by NICE regarding optometrists using slit lamps – a small study by Kleinstein (1987) in which a sensitivity of 74% and specificity of 84% were estimated for sight-threatening retinopathy - and none for ‘other professionals’. However, ophthalmologists achieve good results with them.

Most of the evidence concerning optometrists using slit lamps comes from Leese et al. (1997) and Olson et al. (personal communication, 2001), which were not part of the NICE evidence base.

Burnett et al. (1998) reported a programme of retinal screening by optometrists in North London. A sample of 28 patients referred to ophthalmology and 88 not referred were assessed by a consultant or registrar ophthalmologist with a slit lamp. All the negative screens and 22/28 positive screens were confirmed. This suggests a sensitivity of 100% (95% CI 84 to 100) and a specificity of 94% (95% CI 87 to 98). These figures are better than found in the other studies. However, the confirmation by ophthalmologist in this study was not masked. Thus the assessments were not independent. The question being answered might be worded ‘was the initial referral decision acceptable to the ophthalmologist?’ This may be rather different from the question ‘was the initial referral decision identical to that the ophthalmologist would have made in the absence of any knowledge of the optometrist’s recommendation?’ However, this study does suggest that there were no strongly held differences in clinical opinion over the non-referrals. This appears to be a reassuring finding as regards optometrist assessments using slit lamps. However, direct comparison of the sensitivity and specificity obtained with other studies is not valid and hence this study was not included in the meta-analysis. The high sensitivity and specificity estimated from this study without masking should be taken into consideration when setting targets if an unmasked audit procedure is incorporated into the quality assurance of the national screening programme.

Thus no overall difference was seen between mydratic and non-mydratic photography. However, the results were restricted to those images judged to be readable.

Table 5-1 does not differentiate mydratic photographic screening using a single image of the macula alone from screening using two or more fields per eye. Two studies (Klein, 1985; O’Hare et al., 1996) have looked at single image and two (Penman et al., 1998; Pugh et al., 1993) have looked at two images. The estimates of sensitivity are shown below.

### Assessment Report 3: Draft for Consultation

**Table 5-2 Estimated sensitivities (95% CI) vs specificities for sight threatening, referable or proliferative retinopathy  
Mydriatic: 1 vs 2 field**

<b>Mydriatic photography graded by trained graders – single field</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	97% (93,99)	95% (89,98)	<b>90% (80,95)</b>	85% (73,93)
<b>Mydriatic photography graded by trained graders – two fields</b>				
Specificity	85%	90%	<b>95%</b>	97%
Sensitivity	88% (66,98)	83% (56,96)	<b>72% (41-91)</b>	63% (33,87)

This unexpected superiority of the single field, which disagrees with expert opinion, may be a chance effect since the confidence intervals for sensitivity at 95% specificity for two-field photography extend from 41% to 91% while those for 1 image go from 80% to 95%. However, this analysis does suggest that more evidence is required concerning the two field protocol.

Some evidence is provided by Olson (personal communication, 2001) who has made a direct comparison of one image with two images, albeit using a research registrar rather than a trained grader. This study of 586 patients estimated sensitivity and specificity for referable eye disease using digital photography of 94% (95% CI 85 to 99) and 87% (95% CI 85 to 90) for a two-field protocol compared with 93% (95% CI 83 to 98) and 87% (95% CI 84 to 90) for a one-field protocol. In other words, almost identical accuracy was obtained.

Interesting research is underway (Leese, research protocol, 2001) to compare the digital retinal images obtained using undilated pupils (single field) and dilated pupils with tropicamide 1% (multiple fields), with the gold standard of slit lamp biomicroscopy by a trained ophthalmologist. In this study 400 patients will receive all methods of evaluation using a modern camera (Canon CR5). Sensitivity, specificity, failure rates and costs will be evaluated for all methods. This research is due to be finalised in early 2002 and should be considered at the outset of the national screening programme.

Two NHS R&D Health Technology Assessments addressing specific aspects of diabetic retinopathy screening are due for publication at the end of 2001 and will be considered in the final report.

#### *5.3.5.5 Conclusions concerning screening accuracy*

Direct ophthalmoscopy does not produce consistent levels of accuracy for screening. The highest estimated accuracy was for 'other professionals', who included diabetologists, and reached around 72% sensitivity at 95% specificity.

Screening by optometrists using slit lamps has lower accuracy than photographic screening but is likely to be an indispensable screening method in the short term and quality assurance measures should be in place to ensure that it reaches a high and uniform quality standard. An unmasked assessment by Burnett (1998) of trained optometrists, found a sensitivity of 100% and specificity of 94%, which supports the need for good training schemes.

## Assessment Report 3: Draft for Consultation

Retinal cameras achieved the highest levels of accuracy of any practical screening method in these studies and have the major advantage of providing permanent images for quality control and clinical review. Digital retinal cameras showed similar accuracy to conventional photography and have the additional advantages of easily transmissible and storable images, lower intensity flash, and the potential to move to automated grading systems. These should be the preferred screening modality within a national screening system.

Retinal cameras provided high levels of accuracy but a percentage of technical failures were encountered in all studies. Most data on technical failure rates relate to conventional photography and data are insufficient to estimate the level of technical failure likely in a screening programme with digital retinal cameras. However, a recent study estimated a rate of about 4.4% for a two-field protocol with mydriasis and 3.5% for one-field. These rates were significantly lower than achieved with conventional photography in the same patients.

Retinal photography with mydriasis, which allows the collection of multiple images, is the standard technique for diabetic retinopathy screening in many countries. However, there appears to be little difference between the accuracy and failure rates of modern cameras when used with or without mydriasis. Therefore it is recommended that all cameras should be non-mydriatic, as these cameras can be used with or without mydriasis (but mydriatic cameras can only be used with mydriasis). The issue of mydriasis will be addressed further in the economic evaluation.

### *Recommendation*

- **The national screening programme should use digital retinal cameras suitable for use without mydriasis.**

### *5.3.6 Disbenefits*

#### *5.3.6.1 Adverse effects*

The main source of adverse effects associated with diabetic retinopathy screening arises from the installation of eye drops used for mydriasis. Mydriacyl® (tropicamide BP) is a short-acting cholinergic agent licensed for mydriasis and the British National Formulary (BMA and RPSGB, 2001) notes its use in retinal photography. Minims phenylephrine hydrochloride is licensed for topical use in the eye as a mydriatic and may be indicated to dilate the pupil in diagnostic or therapeutic procedures. Some services in Scotland use these drops in combination for mydriasis prior to retinal examination (but there is no clear indication for this).

Appendix 8 presents key sections from the UK Summary of Product Characteristics for tropicamide and phenylephrine hydrochloride. Although a number of side effects are listed with these agents, major adverse effects are extremely rare. However, as mobile units permit the administration of drops outside a general healthcare setting, all those administering the drops should be trained about the reported side effects, contraindications and potential for interactions with tropicamide.

Mydriatic drugs will need to be administered under a Patient Group Direction and it is essential that the person doing so is a member of one of the legally defined professional groups for this purpose (see list in Appendix 8). Under these Directions, neither a medical

### Assessment Report 3: Draft for Consultation

technical officer nor a medical photographer can initiate administration of eye drops. In a van, a Grade D nurse would seem to be essential to administer the eye drops.

The protocol for administration of tropicamide and phenylephrine hydrochloride used in Moray and Grampian is presented in Appendix 8. These protocols directly contravene the contraindications relating to use in closed angle glaucoma. However, Pandit and Taylor (2000) found that the risk in these patients was negligible and recommended use in all patients irrespective of perceived glaucoma risk. Also many physicians (including those in Scotland) use the products during pregnancy, whilst patients are still wearing soft contact lenses and to the elderly. Furthermore phenylephrine hydrochloride is actually contraindicated in “long-standing insulin dependent diabetes mellitus”, hence its use cannot be recommended as standard in the national screening programme.

The most common adverse reactions to these agents occur locally, with blurred vision and sensitivity to light. Complete recovery from the effects may take up to six hours, so patients should be warned not to engage in hazardous activities unless vision is clear. The British National Formulary states that patients should be warned not to drive 1-2 hours after mydriasis. However, Jude et al. (1998) found that patients with diabetes who met the visual legal requirements to drive (Binocular visual acuity  $\leq 6/9$ ) prior to dilation may not fulfil the requirements post dilation. Post dilation, sunglasses did not improve the binocular visual acuity and so did not enhance the ability to drive post-dilation. They note that the time course of the phenomenon requires further study but recommend that patients should be warned not to drive after mydriasis for at least 2 hours. Consequently patients should receive notification prior to attending the screening visit of the need for mydriasis and the effects that they may anticipate with the eye drops.

#### *Recommendation*

- **A national treatment protocol should be developed for the use of tropicamide when mydriasis is required according to Patient Group Directions.**
- **Use in combination with phenylephrine hydrochloride should be considered in research.**

## 6 ORGANISATIONAL ISSUES

### Conclusions

- The Scottish national screening programme for diabetic retinopathy should be fully quality assured and integrated with other clinical management systems for the care of people with diabetes.
- A national coordinating centre should be established as directed by the National Services Division.
- A network of regional screening offices should be established for local organisation of screening visits, using methodologies defined nationally.
- All patients diagnosed with either type 1 or type 2 diabetes mellitus and aged over 12 years, or post puberty should have annual examinations of the retina (back of the eye). For those with type 1 diabetes onset post puberty, 3 years past diagnosis is an appropriate time to start screening.
- Higher resolution digital retinal cameras (1365x1000 pixels) are recommended, with images graded at capture resolution (i.e. not compressed). Image transfer using a direct digital route is preferred to avoid degradation of quality. The image should be graded using a modification of the CRAG grading system (to allow for one field) on a PC with a CRT monitor.
- Specially trained and accredited non-medical graders should read the digital images, supported by second opinions from ophthalmologists and/or diabetologists. The same staff may be used for both grading and screening given suitable training for both roles.
- The clinical IM&T functions of the retinopathy screening programme should be integrated with the national IT system for diabetes care being established in Scotland.

### 6.1 Organisation of Systems

There is considerable literature on soft systems methodology and key success factors needed within 'complex human activity systems' such as those for systematic population based screening (Checkland, 1999). An important component for the management of complex systems is the creation of 'information systems' and ensuring that the 'people' components of the entire 'system' are enhanced by the 'Information Technology' (IT) components and not the reverse.

Experience has demonstrated that a national screening programme requires central coordination and in Scotland this will be achieved with the help of the National Services Division (NSD) within the Common Services Agency of NHSScotland. The details of the size, location and functioning of the local screening coordination units and the mode of delivery locally is addressed in the economic evaluation. This provides a proposed outline for a national screening programme, but the details of the establishment of the national and local coordinating centres will need to be decided at the roll-out of the programme.

## Assessment Report 3: Draft for Consultation

Scottish Healthcare Supplies (SHS), also within the Common Services Agency of NHSScotland supply a procurement service to NHSScotland. They can provide comparative evaluations of equipment required by the Health Service and for the national breast screening programme they provide professional advice to NSD for the purchase and maintenance of all mobile breast units. To ensure best value for money, it is recommended that SHS are involved in the equipping of this national screening programme, wherever possible.

### 6.2 Learning from other Screening Programmes

Guidance on the Scottish Breast and Cervical Screening Programmes was updated in NHS MEL(1999)82. Guidance is provided on commissioning each programme as 'a comprehensive entity' with details provided about specific services, quality assurance processes and standards and individual roles, responsibilities and accountabilities.

These existing Scottish screening programmes provide good models for establishment of quality assurance mechanisms and national standards, but it must be remembered that a diabetic retinopathy screening programme is also quite different. It is not screening otherwise healthy individuals, but people from a wide age range (from teenagers through to the elderly) of both sexes, who are at high risk of a number of complications. Consequently, diabetic retinopathy screening must be fully integrated into comprehensive diabetes care and this will be facilitated by the work undertaken on the Scottish Diabetes Framework.

### 6.3 Screening issues

Two essential features of a systematic retinal screening programme will be integration into the overall care for individuals with diabetes and adequate quality assurance.

Systematic diabetic retinopathy screening is a fundamental component of overall care of individuals with diabetes. While the process of eye examination may not always be carried out at the same time or in the same place as other diabetes checks, it is essential that relevant clinicians, as well as the person with diabetes, have ready access to the findings of retinal examinations. The organisation of the screening visit and subsequent results must be managed as part of the totality of care. A variety of health care providers may be involved in providing patient care and all (or most) of these will wish to access and contribute to a shared care record. This is different from most screening programmes that offer a test to apparently healthy individuals. However, the ethical issues surrounding, for example, informed consent, quality assurance or minimising risks of harm from screening remain relevant.

The organisation of a systematic screening programme has three main strands: the 'patient journey' and the associated health service functions of 'service provision' and 'programme management'. These are shown in schematic outline in Table 6-1.

## Assessment Report 3: Draft for Consultation

**Table 6-1 Key aspects of a screening programme**

<b>Patient</b>	<b>Service Provision</b>	<b>Programme Management</b>
Identify person	Maintain population register* and screening 'diary'	Co-ordination of individual components and overall programme
Invite person	Invitation and recall. Education and Information	Planning and work scheduling
Screen person	Apply screening test	Quality Assurance of test process
Advise on result and future action	Interpret test and determine future action	Evaluation of screening test and quality assurance of screening process
Provide diagnostic assessment and treatment as necessary	Referral Protocols Investigation, Treatment and Follow up	Training Staff recruitment and retention Workload implications for each activity
Provide follow up as necessary	Follow up and Fail safe Education and Information	Information for Quality Assurance and Programme Monitoring
Information provision to individuals	Education Programme Monitoring and reporting	Clinical Governance and formal Performance Review

\*As a result of issues related to data protection, the term 'register' is sometimes replaced by 'clinical information system'. This report will use the term 'register' throughout.

### 6.4 Modes of delivering screening

There are three main ways in which diabetic retinopathy screening can be offered to patients:

1. In a fixed medical facility (e.g. hospital outpatient unit)
2. From a mobile unit:
  - a. With the camera and associated equipment taken into a medical facility (e.g. GP surgery)
  - b. Taken to a local site, with patients entering the van to receive the examination
3. In an optometrist's practice.

The mobile facilities are custom made and the specifications of the equipment in the van and the van itself will depend on whether option a or b is chosen.

For option a, a smaller van can be used, but robust equipment must be used to transport the camera and associated equipment into the medical facilities. The Grampian Screening Programme uses such a van. It has a hydraulic lift, special arrangements to secure the equipment in the van and a custom made trolley to carry the equipment safely.

For option b, the van must be big enough to allow patients to have the screening test in the van and also to allow patients to wait for screening. The Tayside screening programme uses a van the size of a Ford Transit and a parking facility is required close to an electricity supply, so that the van can be plugged in. The Tayside van has been modified to provide air conditioning running from the diesel: to cope with hot summer conditions and the cold

## Assessment Report 3: Draft for Consultation

conditions experienced in Scotland in winter. This van does not include disabled access and it is currently only used to take a non mydriatic image.

It is recommended that a national contract be organised for procurement and fit out of diabetic retinopathy screening vans: taking account of current experience in local UK diabetic retinopathy screening programmes and remembering the need to enable disabled access.

### 6.5 Population to be invited for screening

The SIGN guideline (2001) recommends that all people with diabetes should be offered systematic screening for diabetic eye disease. It states that people with type 2 diabetes should be screened from diagnosis (Grade A evidence). For people with type 1 diagnosis, it is recommended that screening start at age 12 or at onset of puberty, whichever is first, or if onset of type 1 diabetes is post-puberty, screening after 3 years duration is recommended (Grade D evidence). These recommendations should be used for the national programme, but only those who are capable of benefiting from receiving laser treatment should be screened (i.e. excluding those who are blind or medically unfit for treatment).

The screening programme does not need to include those under regular review by ophthalmologists in the hospital setting, but it is essential that information from specialist retinal examination is fully integrated into the medical record and call/recall systems for retinopathy screening.

In a computer based system, excluding a small proportion of patients should not pose many administrative problems, provided that all individuals known to have diabetes can be identified and that their records can be linked to the retinal screening results and clinical management recommendations of previous retinal examinations. A key issue concerns the process for invitation and, in particular, clearly definition of 'who' has 'responsibility' for this task. This is covered later in the section on quality assurance (section 6.11) and GP involvement (section 6.13.6).

### 6.6 Screening interval

SIGN (2001) evaluated a number of studies performed to evaluate the optimal frequency of diabetic retinopathy screening, including options to evaluate patients at low risk bi-annually. However, at the introduction of this programme it will be logistically easier to maintain a single screening frequency for all patients, with additional early referral possible for those patients at high risk. As general diabetic screening takes place annually and this is the screening interval recommended by the NSC, annual screening is recommended in the Scottish programme. However, further research is required to establish those who are at low risk of developing sight threatening retinopathy and so consider increasing the screening interval.

### 6.7 Clinical IM&T

#### 6.7.1 IM&T developments related to diabetes in NHSScotland

The Scottish Clinical Information (SCI) initiative is at the centre of the new Scottish Executive IM&T policy. It includes a series of projects to create national, integrated IM&T systems, which can be used to support clinicians in the care of diabetes, cancer, mental health,

### Assessment Report 3: Draft for Consultation

coronary heart disease and pharmacy systems. A clinical steering group is directing each initiative, and the SCI Diabetes Collaboration (SCI-DC) will support the care of diabetic patients across primary, secondary and community care.

The SCI Diabetes Collaboration plans two parallel streams of activity; firstly the consolidation roll-out, and support of existing systems, and secondly the development of a new national system incorporating the best of existing systems and converging with other new strategic, national developments.

SCI-DC will build on the existing systems in the Lanarkshire Diabetes System (LDS) and Diabetes Audit and Research in Tayside Scotland (DARTS) project. This work will be linked with other NHSScotland IT systems, such as GPASS and the work on national patient registers and electronic patient records undertaken by ISD.

It is therefore essential that any clinical IM&T recommendations for diabetic retinopathy screening are consistent with the SCI Diabetes Collaboration. An essential requirement of screening is that the result and image can be incorporated into the computerised medical record that is under development.

#### ***6.7.2 Clinical IM&T required for diabetic retinopathy screening***

Any system for retinopathy screening should fulfil the following functions:

- Identification, invitation and recall of eligible people with diabetes for screening
- Attendance for screening and results
- Incorporation of results into electronic medical record
- Monitoring the screening process.

It is proposed that the SCI-Diabetes Collaboration will work closely with the National Services Division who have vast experience from other programmes (breast, cervical) of merging individual local systems into comprehensive national quality assured systems. A parallel track of development is proposed

- Initial implementation of simple regionally based call-recall systems
- Medium term development of a fully integrated call-recall system as part of the SCI-DC Diabetes Collaboration.

#### ***6.7.3 Identification, invitation and recall***

The eligible population (section 6.5) can be best identified from the regional diabetes register. This is a comprehensive register of all people with diabetes who are resident in a defined NHS Board region. This will include names, addresses and dates of births, as well as the names and addresses of their general practitioners.

At NHS Board level, the HTBS survey has shown that there is considerable work to be done to ensure comprehensive ascertainment of residents with diabetes. Several Boards are only able to estimate numbers. Established registers have taken several years to compile and quality assurance checks and procedures are, in most cases, at the early stages of development. Support for general practitioner participation in the screening programme including submission of names of individuals eligible is therefore essential (section 6.13.6).

### **Assessment Report 3: Draft for Consultation**

With computerisation, a simple invitation system will be implemented with the general practitioner's participation and consent, both for initial screening and for subsequent routine repeat visits. A centralised approach to implementing this call-recall functionality will take time to develop. In the short-term the only way to deliver screening using consistent datasets across Scotland is to develop a simple application designed for that purpose. An MS-Access or similar database would suit and would provide a focus for regional screening in the immediate future. If regions are committed to this approach, an upgrade to a more tightly integrated, centralised solution, as part of SCI-DC will be simplified. In addition, the use of a standard database would lead to standardisation of call/recall mechanisms.

The HTBS survey shows that even where systematic diabetic screening programmes are in place in Scotland, call/recall capability is at the earliest stages of development. Experience from other population programmes based upon the Community Health Index (CHI: Womersley, 1996) such as for childhood immunisation, child health surveillance, breast and cervical screening, has shown the benefits of a national central index for locating and following up individuals who move. Universal use of the CHI number in NHS information systems for patient identification should facilitate the design of IT systems to minimise the risk that an individual may be overlooked.

The CRAG dataset for diabetes (Scottish Executive Health Department, 2000) (section 6.9) includes data fields defined for retinal screening. Although this does not currently include standards for a call/recall system, the intention is to ensure each region commits to using consistent methods of call/recall that can be supported by one simple screening management database.

#### ***6.7.4 Attendance for screening and results***

A simple record will be developed giving identification particulars, date of attendance, current retinal status, and essential clinical information. This record will accompany the digital images and will facilitate the clinical decision making process in terms of routine recall, repeat screen or referral for assessment. Only the current image should be viewed by the grader.

Some individuals may, for clinical or other reasons, be too unwell to participate in systematic screening or to receive laser treatments. The call/recall process will also need to accommodate such circumstances. It is proposed that lists of patients who will be invited for screening will be sent to general practitioners for approval before invitations to attend are issued (see 6.13.6).

#### ***6.7.5 Incorporation of results into electronic medical record***

The date of attendance and result will be added to the computerised diabetic record and sent to the general practitioner. If a referral for assessment is made, the record will be flagged to expect a final diagnosis and this will provide a check that an appropriate referral has taken place.

## Assessment Report 3: Draft for Consultation

### 6.7.6 *Monitoring the screening process*

Linkage to the local clinical diabetes information system is essential so that the diagnosis of diabetic retinopathy can be added to the diabetes record. Together with the records from the call-recall system the following aspects of the process can be monitored: acceptance rates, self referrals, cases of retinopathy detected by screening, proportion of people with diabetes referred for assessment, proportion receiving laser therapy, and incidence of visual impairment.

### 6.7.7 *Implementation plan*

The following implementation plan is proposed:

#### *Stage 1: Short-term implementation with call/recall at region level:*

- Definition of a retinal screening dataset
- Ascertainment of the data linkage requirements to populate regional screening databases
- Development of a simple retinal screening administration database
- Procurement of additional retinal cameras and the development of screening software
- Initial testing of the administration database in one region
- Gradual wider implementation and database seeding across Scotland.

#### *Stage 2: Medium term implementation using SCI-DC:*

- Collaboration and integration with national IM&T strategy
- Design and implementation of SCI Outpatients, LDS and DARTS interfaces
- Incorporation of the retinal screening and administration dataset into SCI-DC
- Gradual migration to SCI-DC from the MS-Access based administration database
- Development of web screening mechanisms incorporating best of breed capability such as automated retinal grading and incorporating extensive educational material
- Incorporation of automated primary care links as part of SCI-DC.

## 6.8 **Data protection**

The Data Protection Act (Great Britain, 1998) has important implications for the handling of patient data and collation of data from a variety of sources via a patient identifier with identifiable characteristics (such as CHI). The outcome of the consultation process to the paper issued by the Confidentiality and Security Advisory Group for Scotland in July 2001, will drive the requirements to observe patient confidentiality in all aspects of healthcare in Scotland and must be followed for this national screening initiative.

## 6.9 **Grading**

At the outset a 3-level grading system is envisaged with the retinal cameras, similar to that used in Bro Taf (section 6.12.1). Initial graders (MTO grade 3 or above) would identify images with any potential sign of retinopathy and send them to second level graders. These graders would then review the images and pass on those with suspected referable retinopathy for final grading by an ophthalmologist. The ophthalmologist would also perform the quality

### Assessment Report 3: Draft for Consultation

assurance of a percentage of the images. For any technical failures, patients would be referred for slit-lamp examination. This 3-level approach should reduce the number of unnecessary referrals to ophthalmologists.

A standard grading nomenclature for diabetic retinopathy is essential for consistent grading, for internal and external quality assurance purposes, for ease of exchange of data between clinical information systems, and for agreement on referral thresholds. The grading system needs to be of sufficient complexity to enable triage of patients into appropriate clinical outcomes e.g. referral to ophthalmology, routine re-screen, re-screen at reduced interval, but should not be unnecessarily complex. The important break points are the presence of *any* diabetic retinopathy and the presence of *referable* or *potentially sight threatening* diabetic retinopathy. The latter category may include the presence of lesions within the vicinity of the macula.

The CRAG Working Group on IT to Support Shared Care in Diabetes (Scottish Executive Health Department, 2000) in its diabetes dataset recommends a 10 point mutually exclusive grading nomenclature, with the presence or absence of maculopathy assessed separately. The CRAG dataset does not include definitions of each level, but refers to the Royal College of Ophthalmologists 1997 guidelines for diabetic retinopathy for the precise definition of the grades. These are based on the EURODIAB grading system, which in turn was validated using two overlapping 45° photographic fields against the gold standard of a modified Airlie House classification applied to 7-field 30° photography, as used in the definitive Early Treatment of Diabetic Retinopathy Study (ETDRS). In the CRAG dataset the term *background diabetic retinopathy (BDR)* is used in place of *non-proliferative diabetic retinopathy (NPDR)* as used in the Royal College Guidelines. Four quadrants of the retina, centred on the disc, must be available to permit complete assessment by this methodology. However recent evidence suggests that the CRAG nomenclature can be applied to grading using only the macular centred field with no loss of sensitivity or specificity for detection of referable retinopathy (defined as moderate non proliferative retinopathy or worse, proliferative retinopathy, or clinically significant macular oedema) (Olson et al., personal communication, 2001).

The National Screening Committee through its Photographic Grading and Disease Management Working Party (2000) has produced an alternative grading system to the EURODIAB system. There are minor differences in language e.g. *background retinopathy* vs. *non proliferative* retinopathy, but more fundamental differences in terms of the number of grades defined and the requirement for any lesion counting - severity being assessed in comparison with standard photographs. As in the CRAG nomenclature maculopathy is assessed separately, but there are important differences in that the main area of interest is less (circle of radius 0.5 DD vs 1.0 DD), except where circinate exudates are present in which case the area of interest is substantially larger. Haemorrhages alone in the macula are disregarded in the absence of a reduction in visual acuity. The NSC grading system is pragmatic, based on consensus expert opinion, but does not have a rigorous outcome related evidence base, and has not been widely adopted in screening programmes elsewhere in England & Wales.

Table 6-2 compares the two systems, and is set out so that in each row there is rough equivalence. The NSC system reduces the retinopathy grades to four based on the requirement to identify both any retinopathy and sight threatening retinopathy. In this model R0 and R1 do not require referral whilst R2 and R3 require referral and urgent referral respectively. In the CRAG system R2 is divided into three categories of BDR (moderate,

### Assessment Report 3: Draft for Consultation

severe and very severe), which might allow the option for a reduced screening interval for the BDR moderate group as opposed to referral. The NSC system includes advanced diabetic eye disease with proliferative retinopathy on the basis that both would necessitate urgent referral. The definition of diabetic maculopathy is quite different in the two systems, with a three step process and an effectively twice as large area of potential interest in the NSC system.

There may be advantage in recording the presence or absence of specific lesions within the reporting software. This would then allow the derivation of a summary grade through the application of a rule based algorithm.

The CRAG grading system is an objective, reproducible methodology which has an evidence base that relates grade to risk, and has been shown to be effective in the detection of referable retinopathy when applied to the macular field in isolation. The NSC system is untested, lacks a firm evidence base and relies on qualitative comparisons with standard retinal photographs, which are not currently available.

In view of the above points, a modification of the CRAG grading system (Table 6-3) is recommended for use in Scotland for all retinal grading, including single field macular photography, two field EURODIAB protocol photography and slit lamp examination. The modifications comprise; disregard of cotton wool spots in isolation, as these lesions have no greater prognostic significance than hard exudates (ETDRS, 1991); addition of a separate record for laser photocoagulation burns and other significant non diabetes related coincidental lesions; an alteration to the grading rules for single field photography to guarantee no possibility of undergrading non proliferative retinopathy at any break point.

Referable retinopathy comprises any of; BDR of grade severe or worse, PDR, or diabetic maculopathy. Patients graded BDR-Moderate in the absence of other features of referable retinopathy need not necessarily be referred to an ophthalmologist as laser therapy would not be immediately indicated. However this policy should only be followed provided that arrangements can be made to re-screen this group at six monthly intervals.

### Assessment Report 3: Draft for Consultation

**Table 6-2 Comparison of CRAG and NSC grading systems**

CRAG		NSC	
1	No diabetic retinopathy anywhere	R0	No diabetic retinopathy
2	Background diabetic retinopathy (BDR) - mild At least one dot haemorrhage or microaneurysm with or without hard exudates	R1	Background diabetic retinopathy At least one dot haemorrhage or microaneurysm or blot haemorrhage of extent less severe than NSC standard photo 1, with or without exudates
3	BDR - moderate Any one of the following Four or more blot haemorrhages per quadrant in one to three quadrants Venous beading in one quadrant only Cotton wool spots in one or more quadrants	R2	Preproliferative diabetic retinopathy Any of the following Multiple blot haemorrhages of density in any area more severe than NSC standard photo 1 Venous beading Venous loop or reduplication IRMA Cotton wool spots are not diagnostic of R2, but should promote a careful search for other lesions.
4	BDR - severe Any one of the following Four or more blot haemorrhages per quadrant in four quadrants Venous beading in two or more quadrants IRMA in one quadrant		
5	BDR - very severe The presence of any two categories for BDR – severe		
6	Proliferative diabetic retinopathy (PDR) New vessels outwith a radius of one disc diameter of the centre of the optic disc	R3	Proliferative diabetic retinopathy Any of the following features New vessels on optic disc (NVD) New vessels elsewhere NVE) Pre-retinal or vitreous haemorrhage Pre-retinal fibrosis ± tractional retinal detachment
7	PDR - High risk New vessels within a radius of one disc diameter of the centre of the optic disc		
8	Advanced diabetic eye disease Any of the following Vitreous haemorrhage Rubeosis Iridis Retinal detachment		
9	Enucleated eye		
10	Not adequately visualised Retina not visible sufficient for assessment	U	Ungradeable Images ungradeable due to any of Poor quality Photographs not obtainable

### Assessment Report 3: Draft for Consultation

CRAG		NSC	
Macula	Diabetic maculopathy present Hard exudates and/or microaneurysms or haemorrhages within a radius of one disc diameter of the centre of the fovea	M	Exudate within a radius of half a disc diameter of the centre on the fovea  Circinate or groups of exudates within a circle centred on the fovea with a radius equal to the distance between the centre of the fovea and the temporal margin of the disc.  Any microaneurysm or haemorrhage within a radius of half a disc diameter of the centre of the fovea only if associated with a VA of $\leq 6/12$
		P	Photocoagulation Presence of photocoagulation scars
		OL	Other lesions Central/branch retinal occlusion Age related macular degeneration / drusen Glaucomatous disc cupping Cholesterol emboli Asteroid hyalosis Pigmented lesion Myelinated nerve fibres

### Assessment Report 3: Draft for Consultation

**Table 6-3 Recommended grading protocol based on adaptation of CRAG system**

Grade	EURODIAB two field or slit lamp	Single macular field photography
1	<i>No diabetic retinopathy anywhere</i>	<i>No diabetic retinopathy anywhere</i>
2	<i>Background diabetic retinopathy (BDR) – mild</i> <ul style="list-style-type: none"> <li>• At least one dot haemorrhage or microaneurysm with or without hard exudates</li> </ul>	<i>Background diabetic retinopathy (BDR) – mild</i> <ul style="list-style-type: none"> <li>• At least one dot haemorrhage or microaneurysm with or without hard exudates</li> </ul>
3	<i>BDR – moderate</i> Any one of the following <ul style="list-style-type: none"> <li>• Four or more blot haemorrhages per quadrant in one to three quadrants</li> <li>• Venous beading in one quadrant only</li> </ul> (Quadrants defined by two perpendicular lines intersecting at the centre of the optic disc, with one line also passing through the centre of the fovea)	<i>BDR – moderate</i> <ul style="list-style-type: none"> <li>• Four or more blot haemorrhages in one hemi-field only</li> </ul> (Inferior and superior hemi-fields delineated by a line passing through the centre of the fovea and optic disc)
4	<i>BDR – severe</i> Any one of the following <ul style="list-style-type: none"> <li>• Four or more blot haemorrhages per quadrant in four quadrants</li> <li>• Venous beading in two or more quadrants</li> <li>• IRMA present (one or more quadrants)</li> </ul>	<i>BDR – severe</i> Any of the following <ul style="list-style-type: none"> <li>• Four or more blot haemorrhages in both inferior and superior hem-fields</li> <li>• Venous beading present</li> <li>• IRMA present</li> </ul>
5	<i>BDR - very severe</i> <ul style="list-style-type: none"> <li>• The presence of any two categories for BDR – severe</li> </ul>	<i>BDR - very severe</i> <ul style="list-style-type: none"> <li>• The presence of any two categories for BDR - severe</li> </ul>
6	<i>Proliferative diabetic retinopathy (PDR)</i> <ul style="list-style-type: none"> <li>• New vessels outwith a radius of one disc diameter of the centre of the optic disc</li> </ul>	<i>Proliferative diabetic retinopathy (PDR)</i> <ul style="list-style-type: none"> <li>• New vessels outwith a radius of one disc diameter of the centre of the optic disc</li> </ul>
7	<i>PDR - High risk</i> <ul style="list-style-type: none"> <li>• New vessels within a radius of one disc diameter of the centre of the optic disc</li> </ul>	<i>PDR - High risk</i> <ul style="list-style-type: none"> <li>• New vessels within a radius of one disc diameter of the centre of the optic disc</li> </ul>
8	<i>Advanced diabetic eye disease</i> Any of the following <ul style="list-style-type: none"> <li>• Vitreous haemorrhage</li> <li>• Rubeosis Iridis</li> <li>• Retinal detachment</li> </ul>	<i>Advanced diabetic eye disease</i> Any of the following <ul style="list-style-type: none"> <li>• Vitreous haemorrhage</li> <li>• Rubeosis Iridis</li> <li>• Retinal detachment</li> </ul>
9	<i>Enucleated eye</i>	<i>Enucleated eye</i>
10	<i>Not adequately visualised</i> <ul style="list-style-type: none"> <li>• Retina not visible sufficient for assessment</li> </ul>	<i>Not adequately visualised</i> <ul style="list-style-type: none"> <li>• Retina not visible sufficient for assessment</li> </ul>
Macula	<i>Diabetic maculopathy present</i> <ul style="list-style-type: none"> <li>• Hard exudates and/or microaneurysms or haemorrhages within a radius of one disc diameter of the centre of the fovea</li> </ul>	<i>Diabetic maculopathy present</i> <ul style="list-style-type: none"> <li>• Hard exudates and/or microaneurysms or haemorrhages within a radius of one disc diameter of the centre of the fovea</li> </ul>
Photocoagulation	<i>Laser photocoagulation scars present</i>	<i>Laser photocoagulation scars present</i>
Other	<i>Other non diabetic lesion present</i> <ul style="list-style-type: none"> <li>• Pigmented lesion</li> <li>• Age related macular degeneration/ drusen</li> <li>• Myelinated nerve fibres</li> <li>• Asteroid hyalosis</li> <li>• Retinal vein thrombosis</li> </ul>	<i>Other non diabetic lesion present</i> <ul style="list-style-type: none"> <li>• Pigmented lesion</li> <li>• Age related macular degeneration/ drusen</li> <li>• Myelinated nerve fibres</li> <li>• Asteroid hyalosis</li> <li>• Retinal vein thrombosis</li> </ul>

### 6.9.1 Automated Grading

Automated detection of diabetic retinopathy has progressed rapidly in the last decade, and commercial programmes are now becoming available (Hipwell J et al., 2000; Ege B et al., 2000; Lee S et al., 2001). Research work is also being undertaken in this field by the TIDES project (Gray et al., 1998) at the Tennent Institute in Glasgow.

Automated techniques have the advantage of repeatability and the algorithms can also be set for any particular sensitivity or specificity. Individual human graders tend to have their own varying internal reference standards which are difficult to make conform even with training leading to intra- and inter-observer variability.

Grading of photographs or digital images is a repetitive task and where two thirds are expected to be normal this leads to fatigue and boredom (Hipwell JH et al., 2000). Computers do not face these problems but they are heavily reliant on images being of a sufficient quality to enable analysis. Images will therefore have to be graded for image quality before being processed. This is, however, a far simpler and quicker task than actually grading the image.

In a screening context, assuming a prevalence of retinopathy of 30%, it has been estimated that automated grading, acting as a first level grader, could correctly classify 51% of a diabetic population as having no retinopathy.

However, to date, automated grading has not been used in a large screening programme. The largest study recruited 586 patients (Olson et al., personal communication, 2001) but this is small in comparison to the total number of people with diabetes to be screened in Scotland. These have not been fully validated for use in a national programme, but they could provide significant advantages in terms of efficiency. Therefore they should be systematically studied early in the screening programme.

### 6.10 Retinal cameras and software necessary for manipulation of digital images

From an IT perspective, of prime concern in the procurement of new cameras and software is ensuring that images and the results of any screening can be easily extracted. Initiatives such as TOSCA (Zahlman, 2001) are attempting to provide value added services such as automated initial grading that Scotland may wish to implement in the longer term. To make the most of these opportunities, flexibility is vital. The most flexible camera solutions provide a TWAIN interface to the cameras. This allows the design of screening software to meet specific needs without relying on the development timescales of a camera manufacturer or forcing procurement of cameras from any one manufacturer. In addition, the cost of screening software from camera manufacturers is often high. If many new cameras are required, there may be a good economic argument for developing screening software for NHSScotland.

A simple MS-Access retinal screening database that incorporates digital image capture and image manipulation is already available for use in NHSScotland (in Tayside). Here the Topcon TWAIN driver is used to physically capture the image. The Access database coordinates the capture of this image via the provided driver. It displays and stores the image, and provides image manipulation facilities. Images are then compressed and uploaded to the website. In this system, screening can be done at the Access database (original image) or on

### Assessment Report 3: Draft for Consultation

the website (compressed image). The Tayside system appears to be effective and could provide a useful starting point for development of a national system.

The image captured by the camera is initially stored as a fine grid of coloured dots (pixels). In digital systems, where the image is captured direct to a computer terminal two methodologies are currently used. The most common method relies on an analogue output from a video camera (most commonly operating at a 625 line TV standard), which is digitised in the capture PC by a frame grabber capture card installed in the PC. When the TV standard is in use as is the case in the widely used Sony 3 chip DXC 950P camera, a digital image of medium resolution (785 x 576 pixels) is obtained. More modern higher resolution cameras using charged couple devices can offer a true digital output via a SSCI connection, or can offer a high resolution analogue output following digital to analogue conversion, requiring subsequent re-digitisation within the capture PC. The National Screening Committee (UK NSC, 2000) states that the current generation of medium resolution TV video cameras using analogue to digital conversion are inadequate for the purpose of diabetic retinal screening. They recommend the use of a true digital camera with a resolution of at least 1365x1000 pixels, such as the JVC KY-F70U. This statement is based on the theoretical pixelation required to resolve a lesion with the diameter of a small microaneurysm. There is however little evidence on the performance of the two resolutions in the detection of lesions in actual practice or on the effect on the sensitivity for detection of referable retinopathy.

The use of a higher resolution camera does have some disbenefits. Image file size is approximately 4Mb compared to 1.3Mb for medium resolution which has significant implications for storage and transmission over networks of limited bandwidth. Some high resolution cameras have been found to suffer from significant internal noise which degrades the image. This can be dealt with by noise reduction filters within the camera, although these intrinsically reduce resolution by smoothing the captured image. For storage the grid of pixels can be recoded into a more efficient form. However, some forms of image compression can reduce the quality of the picture and its use is an area of current debate.

A small study of 49 diabetic fundi (Newsom et al., 2001) photographed using 35mm transparencies were digitised to tagged information file format (TIFF) using a scanner with a resolution of 3000 dots per inch. The images were then converted to JPEG files at 0%, 70%, 80% and 90% compression, randomised and graded on a laptop computer with a SVGA (super extended graphics array), thin film transistor flat (TFTF) screen (1024x768 pixels, 0.28mm dot pitch). The images were presented in random order to two masked graders. The gold standard comparator was the original 35mm image projected to a diameter of 1.4  $\mu\text{m}$  (x4300). At 90%, 80%, 70%, 0% compression, the sensitivities (specificities) were 0.38 (1.0), 0.5 (1.0), 0.65 (0.83), 0.72 (0.84) respectively. These results demonstrate a large reduction in sensitivity with increased image compression. However, it is interesting to note that even with no compression, the sensitivity is less than 80%. The authors indicate that this was as a result of using the TFTF screen.

It is unclear how the scanning of 35 mm transparencies in this study relates to current digital systems where the image is captured directly to the PC, so the value of these results is questionable. However, the conclusions regarding the use of the TFTF screen on the laptop are important and should be considered in equipment purchase.

Monitor resolution is an important consideration because a 3 million pixel image cannot be viewed pixel for pixel on most systems. A 19 or 21 inch monitor running at a screen

### Assessment Report 3: Draft for Consultation

resolution of 1600x1200 will only display two-thirds of a 3MB pixel image. To make an image fit the screen pixels will be merged and some information lost. Consequently, some professionals believe that a CRT monitor should be used and that grading should not be performed on a laptop screen.

Another small study of 68 diabetic fundi (Basu et al., 2001) compared photographs with the SONY DXC-950P (1.3MB) and the JVC KY – F70U (4MB), and investigated the effect of four levels of JPEG compression (20-50KB). Microaneurysms and drusens were more easily detected against SONY's better contrasting background, but the JVC detected more lesions in the peripheral, less illuminated, portions of the SONY image. However, adjusting brightness and contrast allowed compensation for the differences between cameras. With regards to compression, there was no loss of lesion detection between the bitmap and jpeg formats for all four compression levels. In 11/68 of the fundi, tiny microaneurysms were detected by ophthalmoscopy, which had been missed by both cameras.

This study is more relevant to the options being considered in this screening programme. It suggests that image compression is not a major problem with the older or newer cameras. However, the quality of the study is questionable. An appropriate gold standard has been used, but it is unclear how many graders were used and whether there was any masking or randomisation of images.

Some algorithms claim to achieve compression with no loss of information (lossless compression). These algorithms are new and require further investigation.

#### **6.10.1 Recommendations on cameras and image manipulation**

- Images should be graded at capture resolution until further evidence on the acceptability of compression becomes available.
- Images should be graded on a high resolution large format (19 or 21 inch) cathode ray tube monitor.
- Software used for image grading should be capable of full image manipulation.
- Legacy cameras in current use based on the video (785 x 576 pixels) resolution can continue to be used, but consideration should be given to upgrading to a higher resolution.
- New purchases of image capture devices should meet the 1365 x 1000 pixel standard, and should support image transfer to the PC by a direct digital route to avoid degradation of image quality in a digital to analogue and analogue to digital conversion.
- The reliability of thin film transistor flat (TFTF) screens (as used in laptop computers) for grading should be investigated.

#### **6.11 Quality Assurance**

The HTBS Baseline Survey has clearly identified the absence of systematic and comprehensive quality assurance processes throughout Scotland at the present time. A whole systems approach within an organised learning culture (Checkland, 1999) is needed to move from the rather haphazard position at present towards a model that has coherence with the present reality of NHSScotland (Scottish Executive Health Department, 2001).

### Assessment Report 3: Draft for Consultation

The quality assurance process must be capable of enabling activities at an individual level (patient or practitioner) as well as at population levels (practice, hospital, LHCC, Trust, Board or national). Standards need to be clearly defined, published and monitored. If this is inadequate or slow in development, it can provide the basis for successful litigation. Entry to such a programme requires informed consent and failure to obtain this could be considered as negligent. However, it is also essential to be able to demonstrate that each eligible individual had been given the opportunity to make an informed decision. Key to all of this is clear presentation and dissemination of agreed policies, procedures and responsibilities. The roles and responsibilities, for example, of a general medical practitioner to his/her patient, need to be considered alongside their complementary roles and responsibilities within a national systematic population based screening programme. The policy for areas of potential ambiguity or confusion should be clearly stated within the national guidance and operational procedures designed to 'fail safe' to protect and respect each eligible individual being considered for invitation for screening.

The Scottish Diabetes Framework (Scottish Diabetes Framework Working Group, 2001) commends the adoption of LDSAGs (section 3.2.3) at NHS Board level and the development of Managed Clinical Networks (section 6.13.1) for diabetes (MEL(1999)10). It will also be important to identify 'lead clinicians', 'key contacts' and programme co-ordinators. These are likely to be individuals who also have other responsibilities and they should not be confused with programme managers who are likely to have well defined key functions and responsibilities specific to screening or other aspect of the service. In addition, controls on patient identifiable data (section 6.8) will require explicit arrangements for Caldicott Guardian and CNORIS requirements. All of these individuals should have 'named person' authority with clear remits, authorisation, support and accountability arrangements explicitly in place.

Quality Assurance standards and processes for different components of the programme should be set nationally as in other screening programmes (MEL (1999)82). These would be areas to be examined in the future by the Clinical Standards Board for Scotland. The specific areas include:

- Quality Assurance of population register
- Quality Assurance of screening register such as agreed data items and standard data sheet
- Quality Assurance of image capture equipment
- Accreditation of screener(s)
- Quality Assurance of 'negatives' (MEL (1995)64)
- Quality Assurance of register of 'positives'
- Quality Assurance of screening history of 'positives'
- Quality Assurance of programme co-ordination, governance and scrutiny
- Quality Assurance of treatment.

The College of Optometrists has produced a clear clinical audit framework for optometric practice that is designed to help the optometrist improve patient care (College of Optometrists, 2001). It notes that audit should involve the whole practice team and explains the role and benefits of audit including sections on non attendance, recall, complaints and accuracy and feedback of referrals. Clear checklists are also provided to facilitate widespread use of the framework. Appendix 10 presents the checklist provided to evaluate accuracy and feedback of referrals. The only weak part of the proposed system is that for a national

## Assessment Report 3: Draft for Consultation

screening programme, the accuracy of the screening for patients who are not referred would also have to be systematically checked.

### 6.12 Examples of large diabetic retinopathy screening service programmes in the UK

#### 6.12.1 *The Bro Taf Diabetic Retinopathy Screening Service*

The Bro Taf Health Authority in Wales has established a diabetic retinopathy screening scheme which provides a good example of many of the key elements that are essential to a systematic screening programme with digital cameras.

In 2000, Bro Taf had a population of approximately 742,373 people and an estimated prevalence of diabetes of approximately 2.34% (17,372 patients). The objectives of the Service are:

- To provide annual fundal photography for people with diabetes resident in the Bro Taf locality with the exclusion of those registered blind, under the age of 12 years, currently under the care of an Ophthalmologist, or regarded as medically unfit.
- To provide equitable access to patients by provision of mobile screening units to both community and hospital locations.
- To provide grading and reporting service to both primary and secondary care physicians within 10 working days of patient's screening, i.e. grading images within approximately 10 days of screening, followed by distribution of retinopathy report.
- To ensure all components of the Screening Service have appropriate quality assurance standards applied.
- To assist in the onward referral of patients to Ophthalmologists (only patients with sight threatening diabetic retinopathy).
- To provide a call and recall system for patients.
- To review non-attendance rates and take appropriate action to maximize patient attendance.
- To efficiently archive all digitised images for future analysis and retrieval.

The Service uses 3 mobile screening units using digital cameras (Canon and Topcon) with mydriasis. The organisational infrastructure of the Service is presented in the diagram in Appendix 11. The Service is based at one hospital, with one central service manager. Each van is staffed by a photographer and health care assistant. The vans travel to hospitals or community locations and the screening takes place in that site. The unit spends 2 to 4 days at each site.

Patients are referred by their GP, Practice Nurse or Hospital Consultant via a screening request form. Retinopathy Screening Coordinators located at 4 hospitals schedule screening sessions and contact patients directly about their appointments. (Registers are not in place, but these data regarding diabetic patients who require screening are held on a dedicated

## Assessment Report 3: Draft for Consultation

computer system to aid call-recall.) Sessions are scheduled 3 months in advance and patients are sent appointments approximately 4 weeks in advance. Timings may vary between localities.

Laptop computers are used for image acquisition and on return to base images are uploaded through the network onto the service database.

All images are graded by trained non-medical retinal primary graders using specially developed software with image manipulation facilities (Orion Imaging DRSS software). Those graded as having sight threatening retinopathy or with difficult or questionable images are reassessed by the screening service clinicians. A percentage of all images graded as normal are also checked. At fortnightly intervals, difficult cases and the appropriateness of referrals are reviewed with Consultant Ophthalmologists. Internal and external quality control systems are in place.

The Retinopathy Screening Coordinators distribute the screening results to diabetologists within 5 working days for sight-threatening cases and to GPs or diabetologists in 20-25 working days for the remainder of patients.

### **6.12.2 Optometry schemes**

The Staffordshire diabetic screening service started in 1995 and covers approximately 90% of the known diabetic population in the area. It involves 143 accredited optometrists (out of a total of 146) and all GP practices. A slit lamp with Volk lens is used with mydriasis. The importance of a team approach to patient care including ophthalmologists, optometrists, GPs, diabetologists, diabetes nurse specialists, dieticians and chiropodists was stressed. A local training scheme that was agreed against a national framework was implemented, with accredited practitioners and agreed referral protocols. The total number of examinations made annually is 13098 or 18400 single visits in an 18-month period. The service costs £12.50 per patient and is estimated to have saved 2912 hospital appointments over 18 months. A clinical audit scheme was established from the outset. However, the Director of Public Health suspended the clinical audit of hospital referrals after the scheme had been running for 2 years because no false positives were identified.

In Argyll and Clyde an optometrists retinopathy screening scheme was established in 1994 using mydriasis and direct ophthalmoscopy. In spring 2000 this was altered to utilise slit lamps, with direct referral to ophthalmologist if necessary. The focus of the scheme is on the need for joint working with other members of the primary care team, recognising that the GP has the overall responsibility for the care of the patient. Since 1996, a protocol has been agreed with the Area NHS Board. The scheme involves initial and ongoing training to receive accreditation. For audit purposes, 10% of all negatives are recalled and examined by ophthalmologists.

## **6.13 Staffing and professional involvement**

### **6.13.1 Managed clinical networks**

Effective care involves partnerships between patients and all health care professionals who contribute to diabetes care in a locality.

### **Assessment Report 3: Draft for Consultation**

The Acute Services Review (Scottish Executive, 1997) saw the development of managed clinical networks as the most important strategic issue for the acute services in NHSScotland. The core principles that underpin network activity as outlined in MEL (1999) 10 are particularly relevant today.

The Scottish Diabetes Framework (Scottish Diabetes Framework Working Group, 2001) will facilitate service redesign strategies that allow MCN development at local and regional level. Many Boards already have the origins of effective clinical network activity with the creation of multi-professional diabetes advisory groups with representation from both primary and secondary care. The Framework aims to accelerate the development of collaborative diabetes care agreements at Board level.

#### ***6.13.2 Organisation of staffing***

The report on the Quality Improvement Review of Cervical Screening Call-Recall Arrangements in Scotland by the Scottish Cervical Screening Programme review (March 2000) highlighted that the key components of that programme were highly dependent on a small number of individuals, who are often in low salary grades. Major review exercises have detrimental effects upon public perceptions but they also are harrowing for individuals working within or with these programmes. This can lead to long-term effects upon recruitment and retention of individuals with key skills and expertise.

The setting up of a screening programme for diabetic retinopathy will therefore require careful planning and substantial managerial effort. Recruitment and retention of staff and the identification of support and training needs are key issues for all the professional groups who contribute to the screening programme.

The economic evaluation makes clear recommendations about the typical staffing requirements for the whole program for a variety of screening models (section ?). However, the types of staff involved to provide the care is flexible and requires a motivated, educated, supported multidisciplinary team, with input from a variety of disciplines.

For the retinal photography, one staff member is found to be more cost effective than two staff members. However, care must be taken to give practical and moral support to any member of staff working alone. This individual must be eligible to administer mydriatic eye drops under a Patient Group Direction (Appendix 8).

Examples of the staffing structure for the Bro Taf Service are presented in Appendix 11, with accompanying job descriptions for the Screening Service Manager and the Retinopathy Screening Coordinator presented in Appendix 12. Another sample job description for a retinal screener, as proposed by the British Diabetic Association (1997 b) is presented in Appendix 13.

#### ***6.13.3 Training***

Education and training of practice and community teams and secondary care teams should include diabetes clinical training, care pathways and procedural training, motivational interviewing and counselling skills, clinical information systems.

Separate issues arise for various professionals including:

### **Assessment Report 3: Draft for Consultation**

- Screeners – ideally a national template should be applied by accredited trainers locally
- Graders
- Those administering eye drops and dealing with patients (see disbenefits section)
- Call/recall, administration – learn from existing population programmes such as immunisation, Child Health Surveillance and cervical screening
- Monitoring and evaluation – need to consider who does this, how resourced and lines for reporting and accountability, location such as NHS Board level, regional managed clinical networks, role of CSBS.

#### ***6.13.4 Training for retinal screeners***

Initial and continuing training for the retinal screener is of paramount importance. A suggested programme for initial training is described in Appendix 14. Plans for a systemic training programme of retinal screeners should include a nation-wide (Scotland) programme for personnel undertaking:

- retinal photography
- retinal graders who will reliably identify sight threatening diabetic retinopathy.

Learning outcomes will include clinical and technical skills, patient management and confidentiality, communication skills, quality assurance and audit and IT technology. A training programme has been suggested for Scotland (Ellingford, personal communication) that includes an intensive residential course, followed by workshops and lectures. Continued learning and support would be achieved through distance learning packages, facilitated through a web site. Competencies would be assessed through a final written examination which should be taken within the first year of training. Furthermore, accreditation will be sought through the Royal College of Ophthalmologists.

In order for such a training programme to succeed, it should preferably operate from an academic base and be supported on a nation-wide basis. It is anticipated that this support will be achieved through the setting up of a national training 'steering group', which will look at the training needs of each region and incorporate them accordingly.

The recently formed British Association of Retinal Screeners (BARS) group will be expected to strongly support any successful training programmes and will provide further workshops and lectures and may even facilitate the final examination.

#### ***6.13.5 Optometrists involvement and training***

Issues of training, accreditation, continuing appraisal, external links, quality assurance and establishment of standing operational procedures are essential for a national screening programme. These are all included in optometrist undergraduate training, which is subsequently reinforced by a comprehensive Continuing Education and Training scheme and system of modular higher qualifications, which can include diabetes.

The College of Optometrists emphasizes that training of screeners is an important element in the establishment of an efficient and effective optometry screening programme for diabetic retinopathy. The form of the training programme will vary between localities and depend upon the experience of those practitioners taking part in the scheme, but the College is preparing clear guidance on training issues and the elements required for accreditation.

### Assessment Report 3: Draft for Consultation

The second draft of this guidance, as available at July 2001, is presented in Appendix 15. It aims to provide education about epidemiology, natural history and signs of diabetic eye disease, and to indicate clearly those patients who should be referred. This programme is thorough and should create consistency across practices, but it will be important to clearly specify the minimum number of patients that an optometrist must screen to maintain competence.

The following features can also be stated about optometrist practices:

- conveniently located in most local communities, even in rural areas
- open at times to suit patients and offer individual appointment times at times to suit patients
- nearly all have slit lamps
- increasing numbers are investing in digital cameras
- most operate comprehensive computer based recall systems
- optometrists can advise patients of the outcome of screening at once and can recognise and rectify screening failures at once if using digital cameras
- most people with diabetes have to attend an optometrist for refraction, so using an optometrist avoids duplication of visits by patients
- optometrist fees include all overheads.

#### ***6.13.6 GP involvement in retinal screening invitations***

Unlike other screening programmes, individuals for diabetic retinopathy screening will not be all those of a certain sex and over a certain age. Cooperation of GPs, within the national quality assurance programme, will be essential to populate a diabetes register and screening database.

Various models for GP involvement in breast and cervical screening programmes are available within Scotland. Models could be built on the following basis:

- Initial visit to the practice by screening coordinator, explaining the services and the options for GP practice participation.
- Individual practices prepare an individualised pro-forma letter (based on a national template), advising a patient that they will shortly be called for screening and encouraging them to attend.
- A list is sent to the practice giving the names of the patients which the screening service thinks need to be called for screening. The practice 'cleans' this list, indicating patients who should not be called (e.g. due to death, terminal illness, loss of sight etc) and this may be cross checked by another party.
- The screening service merges the cleaned list with the pre-prepared letter pro-forma and produces the individualised letters of encouragement for the practice's population. These letters are sent to the practices, signed by the GP, and posted by the practice.
- Shortly afterwards the screening service sends out to patients their appointments for screening, using the information from the cleaned list.

As noted in the patient issues section, timely notification of screening results (section 7.3.6) to the GP and then to the patient is essential to avoid unnecessary anxiety.

### Assessment Report 3: Draft for Consultation

#### 6.14 Audit

The NSC report (UK NSC, 2000) presents proposed quality standards for a diabetic retinopathy screening programme, as shown in Table 6-4.

**Table 6-4 Quality standards for diabetic retinopathy screening (UKNSC, 2000)**

	Objective	Criteria	Minimal standard	Achievable standard
1	To reduce new blindness due to diabetic retinopathy	Annual blind registration, compared to 1990/1 rate of 9.5 per million per yr.	10% reduction within 5 yr.	40% reduction within 5 yr.
2	To identify and invite all eligible persons with known diabetes to attend for the DR screening test	Completeness of database 1. Proportion of GPs participating 2. % of population in register	90% 1.5%	95% 1.8%
3	To ensure database is accurate	Accuracy of database of persons age 12 or more, as determined by Post Office returns	95%	98%
4	To maximise the number of invited persons accepting the test	Percentage of eligible persons accepting the test 1. Prevalent screen 2. Incident screen	70% 80%	90% 95%
5	To ensure photographs are of adequate quality	Percentage ungradeable (Level U)	5%	3%
6	To ensure grading is accurate	Intra-grader agreement Inter-grader agreement Uncertain grading (Level Q)	90% 90% 10%	95% 95% 5%
7	To ensure timely consultation for all screen-positive patients	Time before notification of positive test to consultation: Level 2 Maculopathy Level 3 Mod NPDR Level 4 PDR	70% < 26wks 70% < 13wks 70% < 2wks	95% < 26wks 95% < 13wks 95% < 2wks
8	To ensure timely treatment of those listed by ophthalmologist	Time between listing and laser 1. Proliferative DR 2. Maculopathy	70% < 2wks 70% < 13wks	95% < 2wks 95% < 13wks
9	To ensure GP is informed of negative tests	Time before notification	70% < 3wks	95% < 3wks
10	To monitor adverse effects of the programme	Adverse incident reporting (sight or life threatening)	<0.1%	<0.1%
11	To monitor adverse effects of treatment	Adverse incidents from FFA/laser (sight or life threatening)	<0.1%	<0.1%
12	To follow up screen-positive patients	DNA rate for ophthalmologist For PDR within 1 month For maculopathy within 9 months	10% 10%	5% 5%
13	To minimise the anxiety associated with screening	Monitor false positive rate of DR test	5%	3%
14	To ensure timely rescreening	Time to rescreening compared to suggested screening interval	70% within 6 weeks of 1 year interval	95% within 6 weeks of 1 year interval
15	To ensure the public and health care professionals are informed at regular intervals	Production of annual report		

### Assessment Report 3: Draft for Consultation

Coordination of data collection to monitor performance and obtain audit data to enhance and improve the screening will be essential. These objectives and criteria appear to be a sound basis on which to build an audit system for the Scottish programme and a number of items will be easily fulfilled within newly defined diabetes reporting structures. However, it is recognised that some modifications will be required for the Scottish programme.

Other schemes of similar detail are in place in Scotland (e.g. in Grampian) and areas that may need enhancement in the NSC scheme have been identified, such as quality assurance of capture image equipment (cameras, reporting software and monitors should be properly maintained and tested to demonstrate their ability to resolve an image of a test object).

An important issue raised by patients in section 7.3.6.1 is that they should be quickly informed in writing of the screening outcome, whether it is positive or negative. Consequently a quality assurance objective should be set for the Scottish programme to monitor performance on this issue.

#### 6.15 Conclusions concerning organisational issues

- Non mydriatic digital cameras should be used.
- New purchases of image capture devices should meet the 1365x1000 pixel standard, and should support image transfer to the PC by a direct digital route.
- If mobile units are to be used, special consideration should be given to the fit out of the vans, taking account of existing learning from the use of eye screening vans within the UK.
- For the Scottish screening programme in diabetic retinopathy SHS should be involved in the equipping of this national screening programme, wherever possible.
- All people with type 2 diabetes, who are capable of receiving laser treatment, should be screened from diagnosis. For people with type 1 diagnosis, it is recommended that screening start at age 12 or at onset of puberty, or 3 years after diagnosis if diagnosis is after puberty.
- Annual screening should be used, unless more frequent screening is clinically indicated.
- The CRAG dataset should be used for grading with modifications for one image.
- Digital photography is the screening method of choice, initially without mydriasis, if the image is insufficient, mydriasis may then be used.
- Images should be graded at capture resolution.
- Screening failures will be referred for slit lamp examination.
- Call-recall will be based at Board level initially with links to the regional diabetes clinical information system. Software development will be in keeping with the Scottish Diabetes Computing System Strategy (SCI-DC).
- Development of IT systems will facilitate centralised call-recall in the longer term.
- Wide ranging professional involvement in the national screening programme will be essential, along with appropriate professional training and support, as necessary.
- A national quality assurance scheme should be used (this will be developed during open consultation).

## 7 PATIENT ISSUES

### Conclusions

- In common with all aspects of diabetes, patients must be empowered to help manage their disease; this requires support and collaboration from clinical and patient organisations.
- Diabetic retinopathy screening must be coordinated with other diabetes screening visits.
- Patients must be informed of the need for diabetic retinopathy screening and the process involved.
- Patients should be informed of the possible need for mydriasis (pupil dilation) and its effects before attending the screening visit. It should be clearly explained that there will be an increased sensitivity to light and that driving is not recommended for at least 2 hours after mydriasis.
- Studies show that use of more than two written reminders has little impact on attendance rates.
- Use of a variety of educational approaches (written, video, posters, television, World Wide Web, personal contact) is worthwhile and must be targeted to suit specific audiences.
- Patient preferences should be elicited regarding the provision of screening.
- Results of screening should be communicated to patients and GPs in a timely manner.

### 7.1 Background

The consideration of patient issues is key to any Health Technology Assessment and fits with Scottish aims to create a patient-centred National Health Service.

For any screening programme, success depends upon continued consistently high levels of uptake, thus patient satisfaction with the scheme, their preferences and willingness to return for screening are of vital importance. Key issues to be considered include delivery of the service, patient information and education.

Other screening programmes involve a clearly defined group of otherwise healthy people, e.g. of a certain sex and age range. For diabetic retinopathy, the screening population is much broader, covering patients from their teens through to old age, of either sex and with the possibility of other related health problems. People with diabetes are expected to follow dietary constraints and may be on medication to help control the diabetes or its associated complications. They will also be expected to attend for a variety of annual screening visits and so coordination with healthcare initiatives is particularly important.

### 7.2 Methods for Evaluation of Patient Issues

The qualitative questions relating to patient issues have not been reviewed systematically, but have been investigated using a variety of grey literature and published sources, including the

## Assessment Report 3: Draft for Consultation

patient group summary from the NSC report (UK NSC, 2000), educational materials from Diabetes UK, surveys of patient attitudes to NHSScotland breast screening programme (SHPIC, 1997), an HTA about diabetes education (Corabian and Horstall, 2001) and various published papers about recruitment strategies for diabetic retinopathy screening from other countries.

A Cochrane review of interventions for improving coverage of screening schemes for diabetic retinopathy (Grimshaw G et al., 2001) is underway and will provide important information for consideration at the end of 2001.

Before the national screening programme is finalised, further research on patient preferences will be undertaken by HTBS using patient focus groups, during the consultation period.

### 7.3 Results

#### 7.3.1 *Patient Education and Empowerment for People with Diabetes*

The Expert Patient Report (Department of Health, 2001) recognises that people who live with chronic medical conditions are often in the best position to know what they need to manage their own condition. However, support is needed and the collaboration of patient and clinical organisations is crucial to develop effective self-management initiatives.

Education about diabetes, its complications and control is essential. Education and information should be provided in a manner that is relevant and appropriate to the needs of patients (e.g. considering age, language and culture). Education is not sufficient to create change. Methods should be used which consider psychological and motivational aspects to create behavioural change. Patient empowerment is essential and people with diabetes need to be supported and encouraged to take an active involvement in their own health care.

A recent Health Technology Assessment on Patient Diabetes Education in the Management of Adult Type 2 Diabetes (Corabian and Harstall, 2001) found that in the last decade there has been a move for formal patient diabetes education to focus on patient-centred perspectives, self-efficacy, self-management and empowerment issues. However, quantitative research on the value of formal patient diabetes education is limited and studies are generally of poor quality, with no evidence about long-term diabetes control outcomes. Further investigations are needed to determine what methods are most effective and which category of patients would benefit most from these educational interventions.

In Scotland, liaison should take place with the Health Education Board for Scotland to facilitate educational activities and encourage attendance at screening visits.

#### 7.3.2 *Communicating the Risks of Diabetic Retinopathy and the Benefits of Screening*

The complications of diabetes must be explained sensitively to patients taking account of the patient's situation. Patients should not be overloaded with information at their first diagnosis and the fear of patients should be recognised.

The patient group report of the UK NSC report (2000) states that:

‘Although some people with diabetes are paragons of self discipline, most of us are human and have failings, like forgetting appointments. Others may be unable to face

### Assessment Report 3: Draft for Consultation

up to the gravity of possible complications and stick their heads in the sand. Some will be frightened of blindness, frightened of doctors, frightened of treatment and doubtful about its efficacy. Irrational fear and false beliefs about health are difficult to tackle but should present a meaty challenge to any health professional! The point we are making is that the continuing application of support and encouragement is essential.'

Diabetes UK produces a wide variety of educational material about diabetes. General educational material includes information about the diabetic retinopathy and the importance of annual screening. They also produce a specific booklet entitled *Diabetes and your eyes* (British Diabetic Association, 1997). This will be updated during Autumn 2001.

Young people have special needs and Diabetes UK produce excellent general diabetes educational books targeted at children, with a separate one for teenagers. Carers of children with diabetes are in particular need of support and knowledge.

With teenagers, it must be recognised that a non-critical approach, which will permit open discussion of, issues such as drug and alcohol interactions are particularly important. There may also be a role for peer education in this group.

Many barriers including language, cultural beliefs and attitudes, and length of residency in a country hinder the provision of health care. Recruitment for breast and cervical screening programmes in Australia has shown consistently lower participation rates for groups from culturally diverse backgrounds (Lee et al., 2000). Also, it must be recognised that it may be difficult to encourage the homeless, those living in institutions, people with mental health problems or learning difficulties to attend screening and methods for particular involvement of these patients should be considered.

Basch et al., (1999) recognised that certain groups may be less likely to attend screening visits and that focussing on high-risk subgroups is a good strategy for improving overall attendance rates. Consequently they performed a randomised study evaluating the effect of education in African Americans in 1993-1995. The outcome was attendance for a digital retinal examination (with mydriasis) within 6 months of randomisation. The study included 280 people with diabetes from 5 medical clinics in New York who had not received a retinal examination within the previous 14 months and were not blind or had advanced eye disease in both eyes. Each clinic provided patient education services and printed diabetes patient education materials, and three of the clinics had certified diabetes educators. Randomisation was stratified by clinic and sex. The control group received the routine medical education provided by their clinic. The intervention group received, in addition, a 3 component educational program: a low literacy, 9-page colour booklet, a motivational video and semi structured telephone education and counselling. The booklet and video were posted at randomisation. The telephone component was initiated approximately 1 week after randomisation. The health educator worked to identify reasons for and/or barriers to having a dilated retinal examination. Focussed problem solving then guided the subject to make an informed choice about receiving the screening examination. Follow up calls were made and individually tailored mailings of tip sheets provided practical strategies for overcoming specific barriers. The median number of calls made was 4 and the median time spent per patient was 53 minutes. When a patient attended for screening a congratulatory letter was sent and they were encouraged to go for an examination annually. After 6 months the control

### Assessment Report 3: Draft for Consultation

group were sent the intervention booklet along with a cover letter urging them to attend a digital retinal examination if they had not attended one in the previous 12 months.

In this study, 273 of the 280 (98%) patients were followed to the 6 month outcome. The mean age was 55 years and approximately 70% were unemployed. The intervention was completed by 130 of the 137 patients in the intervention group (95%). The most common reason for not scheduling or keeping a screening appointment was an acute health problem. Other reasons included family problems, lack of time and inclement weather.

Within the 6 month period, 55% of patients in the intervention group had attended digital retinal examination compared to 27% in the control group. A stepwise logistic model was fitted evaluating several possible predictors including sex and clinic. The odds ratio for examination status associated with receiving the intervention was 4.3, with 95% CI (2.4, 7.8). This highly significant result indicates that a patient-targeted educational intervention can substantially increase rates of diabetic retinopathy screening in African Americans. The authors note that this intervention may have significance for a wider population and the relative costs and effectiveness associated with each component of the intervention should be studied in a wider clinical setting.

#### 7.3.3 *Patient Information Leaflets*

A range of communication tools will be required to provide information about the national screening programme. These will need to be tailored to a variety of target audiences. They should be pre-tested in representative samples of patient groups and integrated with established and trusted communication channels.

One common form of communication is a patient information leaflet. Such leaflets should be drafted for the national scheme, with local modification as required and used in conjunction with other promotional materials. Circulation of the leaflets could include public libraries, health promotion units, family planning clinics, and pharmacies. They may be made available for passive collection or used by health professionals as a tool to aid discussions with patients. For the more general areas, a general leaflet about diabetes would probably be sufficient, with specific diabetic retinopathy screening leaflets available on request.

A selection of patient information leaflets to inform about diabetic retinopathy screening services is presented in Appendix 16. These are specific to local schemes and would need to be adopted for the Scottish national scheme, with sufficient space to permit inclusion of local information about the screening scheme.

For the national screening programme, key issues to present in a leaflet are:

- The importance of screening - the benefits and limitations
- The reasons that these screening tests are different from standard eye examinations
- The possible treatment modalities
- The need for eye drops and affects that may be experienced (see section ??)
- If retinopathy is detected, the treatments possible and expected outcomes
- Channels for further help and support
- Data Protection rights and Confidentiality controls to ensure individual privacy while obtaining public interest benefits. (The importance of quality assurance and clinical audit which needs record linkage of individual records prior to anonymisation.)

### Assessment Report 3: Draft for Consultation

In the case of diabetic retinopathy, provision of material for the partially sighted, in large, clear print in line with RNIB guidance, is particularly important. Furthermore, as the prevalence of diabetes, is between 3 and 4 times higher in communities of Asian and African-Caribbean origin than in those of white origin (Scottish Diabetes Framework Working Group, 2001) patient information leaflets should be available in relevant languages. Diabetes UK issues documents for the Chinese and for South Asian people in Urdu, Gujarati, Bengali, Hindi and Punjabi. Gaelic, Urdu and Punjabi texts will be particularly relevant for Scotland.

#### *7.3.4 Other Methods to Improve Screening Attendance*

Advertising campaigns can be used to improve education and encourage screening visit attendance. In 1998, Greater Glasgow NHS Board (GGHB, 1998) ran an advertising campaign over an 8 week period to promote their breast screening service. During this period, 506 women completed questionnaires about the service and advertising campaign. Forty three percent of the women were aware of the advertising campaign and 86% felt that breast screening should be advertised more. They found the campaign images and messages reassuring, supportive and credible, and felt that advertising could be used to raise awareness of the service, make women more conscious of the benefits of screening and change public perceptions of the screening process. In 2000, it was recommended that the Scottish breast screening service should adopt standard branding on all stationary and publications and that invitation letters should be made clearer and shorter to make them more user friendly. Learning from their experience will be important when the national diabetic retinopathy screening programme is established.

The potential of web-based technology has been discussed in section 6.7 and this includes important possibilities for patient education and interaction. All information should be presented in formats that are internationally recognised as suitable for the visually impaired (BOBBY compliant). For mobile screening units, the ability to provide accurate information about the location and timing of mobile screening sessions over the World Wide Web will be particularly valuable.

Legorreta et al. (1997) studied the effect of a 'reminder' intervention for a diabetic retinopathy screening programme in California, USA, in 1995, comparing attendance to that in the previous 2 years. The study identified 19,397 people with diabetes aged 18 years or older who were sent educational materials and a report of their current diabetic retinopathy status. In 1995, 26% of patients received a diabetic retinopathy examination, this was significantly higher than the previous two years (approximately 20% in each of the previous two years). This result is somewhat difficult to interpret given the low overall rate of those attending for screening and the non-randomised design.

Prela et al. (2000) performed a study in Montana, USA on 6546 Medicare beneficiaries with diabetes. A reminder letter was sent to a random selection of two thirds of these patients to attend diabetic retinopathy screening at the beginning of 1996. The median age of patients was greater than 75 years old. Three months after the letters were issued there was a significant increase in the percentage of patients attending screening in the group that received the reminder letter (19.4% vs. 17.2%), but at 6 months this benefit was lost, with 32.9% of those receiving the letter attending screening compared to 32.4% of those who hadn't received a letter. This randomised study did not demonstrate the benefit of a reminder letter in this predominantly elderly population, in which the overall screening rate was again very low.

### Assessment Report 3: Draft for Consultation

This short lived effect of mailed patient reminders has also been demonstrated in other studies (Brooks et al., 1996). Halbert et al. (1999) performed a randomised study of 23,740 people with diabetes during 1996-1997 in California, USA. They selected a population of people with diabetes who had no record of a digital retinal examination. Patients were randomised to a single intervention or multiple intervention group. All patients then received the first communication, which included educational materials and a report of their previous diabetic retinal examination. The multiple intervention group then received additional reminders at 3, 6 and 9 months. The median age of patients was in the range 56-64 years. The results showed that after the first communication a similar percentage of patients attended for screening. After the second reminder was sent to those in the multiple intervention group a higher percentage attending screening in this group, but the effect was small. For the third and fourth reminders, no differences between the single and multiple interventions could be demonstrated. At the end of the study 35.4% of patients in the single intervention group had attended screening, compared to 37% in the multiple intervention group. This difference was statistically significant, but it is a very small difference clinically, and the cost effectiveness of issuing multiple reminders beyond the second reminder is questioned. Consequently, the authors state that it may be more appropriate to direct resources into other avenues of improving screening rates, such as telephone follow up and increased involvement of physicians.

Livingston et al. (1998), report the outcome of focus groups involving health professionals and people with diabetes (21/50) in Australia. Five groups of 10 members were established. They emphasized the benefit of local networks to promote the benefits of early detection and local screening programmes, the need for GPs to distribute educational material to patients and the importance of reminders. As a result of these focus groups, Lee et al., 2000 performed a pilot study to identify strategies to encourage people with diabetes to attend a community based non-mydratic diabetic retinopathy screening programme in Australia. Screening occurred at a local venue, with a local number to call for day or evening appointments and transportation was provided. Two urban and two rural sites were studied. In the rural areas, the camera was portable permitting wide geographic coverage with seven towns visited in each area over four and five week periods. In the urban areas the screening took place over two and three week periods. In order to complement existing screening services, the 45% of the population with diabetes who did not have their eyes examined regularly were targeted to attend screening.

In this study, promotion for each site started 3 months prior to screening. In all sites, the GP was sent a letter of introduction and brochures, and asked to people with diabetes into the programme. This was followed up with a personal visit from a member of the programme staff. Articles were published in local and national newspapers before and during screening. The recruitment strategies were modified with experience at each site. The targeted recruitment strategies are presented in Table 7-1.

## Assessment Report 3: Draft for Consultation

**Table 7-1 Recruitment strategies used for diabetic retinopathy screening (Lee et al., 2000)**

	Rural 1	Rural 2	Urban 1	Urban 2
Community Networks <sup>1</sup>	+	+	+	+
Visits to all GPs	+	+	+	+
Flier	+			
Print media	+	+	+	+
Brochure		+	+	+
Postal distribution of brochure to people with diabetes <sup>a</sup>		+	+	+
Broadcast media		+	+	+
Translation of brochures			+	+
Presentations to community leaders			+	
Recruitment of ethnic groups via migrant resource centres			+	+
Ethnic print and broadcast media			+	+
Poster			+	+
Presentations to senior citizen and culturally diverse background groups with interpreters				+
Recruitment of ethnic groups via bilingual support workers				+
'Block' appointments at screening centre for groups from culturally diverse backgrounds with interpreter				+

<sup>1</sup> GPs, pharmacists, Diabetes Australia, Lions Clubs, church groups, senior citizens club, Rotary, diabetes clinics and educators

<sup>a</sup> Lists obtained from GPs, diabetes clinics, Veterans Affairs, and the National Diabetes Supply Scheme

A total of 1197 people with diabetes were examined at the screening sites. This represented 15% of people with diabetes (compared with the 45% targeted). In the rural communities, 91% were English speaking, compared to only 52% in urban communities. In rural communities 21% had never been checked for retinopathy compared to 30% in urban communities. This screening programme was able to screen an additional proportion of the diabetic population, increasing attendance at screening from 55% to 70%.

During the course of screening, participants mentioned that they had seen the programme promoted often three or four times before they scheduled an appointment. This supports the marketing strategy call the Three Hit Theory seeing an advertisement three times marks the starting point of the advertisement's effectiveness. A heavy influx of calls to book screening appointments was noted directly after the mail-out at each site. Thus the importance of this form of invitation and the need for good registries is noted.

Although the study of Lee et al. (2000) is not randomised, it presents an interesting variety of methods for encouraging screening attendance (see Table 7-1). Evaluation of the clinical and cost effectiveness of these in the Scottish national screening programme would be worthwhile.

### 7.3.5 Professional Educational Initiatives

A variety of professionals will be involved in provision of care to people with diabetes. A sensitive approach is required by all professionals to increase patient awareness and

## Assessment Report 3: Draft for Consultation

understanding, encourage patient self-management and ongoing commitment to screening and other healthcare initiatives.

Unlike other screening programmes that screen otherwise healthy patients, people with diabetes are more likely to discuss health management issues with their local pharmacist. Hence pharmacists have an important role to play in patient education. This has been recognised by the Royal Pharmaceutical Society of Great Britain in their report: Practical Guidance for Community Pharmacists on the Care of People with Diabetes (RPSGB, 2001). The RPSGB report notes that education does not necessarily lead to improvement. A pharmacist may provide additional motivational support, which with education, leads to behavioural change and improvement.

The RPSGB report notes that diabetes education is often poor in the elderly Type 2, particularly those who live in residential and nursing homes (where between 7 and 10% have diabetes) and so pharmacist involvement in such communities may be particularly beneficial. The report provides specific guidance on education about complications, however the current information about screening for diabetic retinopathy is unclear and could be updated in line with this HTBS Assessment. It is important to assist pharmacists in their interactions with diabetic patients and special leaflets may be appropriate for pharmacist distribution. Also, local pharmacists should be informed when a mobile unit is in the area, to encourage attendance of diabetic patients.

The National Pharmaceutical Association is drafting a report, which highlights that community pharmacists see people with diabetes up to five times more than any other health care provider (RPSGB, 2001). The NPA report promotes the role of the community pharmacist in providing appropriate individual health promotion messages and education for people with diabetes. HTBS will work with the NPA to ensure that their educational material takes account of this HTA.

The College of Optometrists places great emphasis on the role of optometrists in patient education and care in relation to diabetic retinopathy screening (as discussed in section 6.13.5). This service is valued by patients and should be utilised in the Scottish national screening programme.

A multi-professional group including doctors, pharmacists, nurses, dieticians and podiatrists has been brought together by the National Board for Nursing, Midwifery and Health Visiting for Scotland. The group remit is to identify core competencies for a broad range of health care professionals working in diabetes in each of their professions.

### **7.3.6 Patient Views**

#### *7.3.6.1 NSC Patient Expert Group*

Three people with diabetes were involved in the NSC expert panel on diabetic retinopathy screening. They visited six different diabetic retinopathy screening programmes (National Screening Committee, 2000). Following these visits, their recommendations were:

1. Screening should take place in an environment that is easily accessible and friendly to the patient.

### Assessment Report 3: Draft for Consultation

*In the programme that used mydriatic digital photography in a van, the limited clearance (six feet) and lack of wheelchair access was noted. One of the major concerns of the three people with diabetes were that patients were not always informed directly of results, or that GPs were not routinely informed of results within a reasonable timeframe. The ethos that 'no news is good news' is not acceptable.*

2. Patient information should be in large print. It should discuss treatment, the facts that proliferative retinopathy is symptomless and ensure clear instructions are given for appointments and locations. The use of other media (*local radio, audio and video tapes*) should be considered.

*The importance of explaining that effective treatment, which could be given as an outpatient, is available should be explained.*

3. Patient education is vital in order to ensure responsible self-care. Patients should be given information and allowed to make their own choices. Continuing professional support and encouragement are essential.

The NSC expert panel also summarised a visit to test the Panoramic200 non mydriatic laser scanning ophthalmoscope. The benefits of the laser scanning ophthalmoscope in capturing an image of the whole retina in a patient friendly manner without the need for mydriasis were clearly understood by the group. They also noted that with a five minute per patient turnaround time this method had the highest throughput of any system they considered.

Unfortunately, limited scientific evidence is currently available about the accuracy of the laser scanning ophthalmoscope for diabetic retinopathy screening. However, new studies are underway comparing it with standard screening techniques in a diabetic clinic, which will elicit patient preferences and provide information regarding turnaround time, accuracy and failure rates. This information should be evaluated as it emerges.

#### 7.3.6.2 Breast Screening Survey

The Scottish Breast Screening programme has undertaken a survey of patient preferences in relation to the provision of a mobile screening unit in South East Scotland (Fraser, 2000). Invitations were sent out to 469 women who had not responded to an earlier invitation to attend a hospital screening visit. They were invited to attend a mobile unit and 109 women returned questionnaires about the service.

The main reasons for not attending the hospital unit screening visit were

Centre too difficult to get to	49%
Nervous/anxious about having a breast x-ray	27%.

Main reasons for attending the mobile screening visit were

Mobile screening in local area easier to get to	74%
Doctor's letter stressed importance	43%
Friends/family encouragement	25%.

Very likely to attend next screening appointment

At mobile unit	84%
At hospital unit	25%.

## Assessment Report 3: Draft for Consultation

### 7.3.6.3 Mydriasis

Patients find the lower flash intensity of the digital camera more comfortable than Polaroid cameras (Taylor et al., 1999). However, the study of patient preferences (Klein, 1992) shows that some patients are distressed by the instillation of eye drops and would not return for screening. As the benefit of mydriasis (and thus the need for eye drops) is questionable, the proposal of allowing a patient to have a non-mydriatic retinal examination, then a mydriatic retinal examination if a technical failure occurred, is likely to improve screening attendance. As a technical failure cannot be predicted, the implications of using eye drops should be clearly communicated in advance to all patients (see section 5.3.6.1 of report).

### 7.3.6.4 Research

Research should be undertaken to establish patient preferences for diabetic retinopathy screening in Scotland considering issues such as:

- Location of screening (including travel time)
- Choice and convenience of appointment time
- Whether screening outcome is reported at the time of the visit
- Opportunities for advice from professional
- Factors that encourage and discourage attendance.

## 7.4 Conclusions

Patient empowerment is needed for all people with diabetes. An understanding of the different needs of the wide range of people who have diabetes (young, old, culturally diverse, etc) is essential and a variety of educational materials should be made available. For diabetic retinopathy screening, the fear of going blind must be recognised and handled sensitively. The benefits of attending regular screening visits and the procedures involved need to be explained. The technologies and techniques used in the screening programme should be described and those technologies that are still under study for diabetic retinopathy screening (e.g. the Panoramic200 ophthalmoscope) should be identified. The possible need for eye drops and transient effects on vision should be communicated prior to the screening visit indicating that driving is not recommended for at least 2 hours after mydriasis.

Patient education is essential and innovative motivational initiatives should be considered to encourage attendance at screening because it is recognised that standard educational approaches do not always engage motivations or promote cognitive reappraisal (i.e. create sufficient motivation to attend screening).

The research into the effectiveness of patient reminders suggests that more than 2 reminders is not effective and a wide range of methods may be needed to encourage attendance of defaulters including written reminders, advertising campaigns, use of educators and local community groups. This supports theories of learning, which imply that iterative communication processes can achieve the cognitive and behavioural learning required for change (awareness of problem and understanding of how it can be handled). The value of consultation with facilitators (counsellors) may be particularly valuable to allow discussion and clarification of sensitive issues that may be creating barriers to screening attendance.

### **Assessment Report 3: Draft for Consultation**

Patients have identified that they and their treating physicians must be informed of results within a reasonable timeframe. This is an important step to reduce patient anxiety and production of written results should be integrated as an objective into the quality assurance program (section 6.14).

## 8 ECONOMIC EVALUATION

### Conclusions

- With digital retinal cameras, non-mydriatic screening costs less than mydriatic screening.
- For efficiency, no more than ten regional screening offices are required in Scotland.
- From a costing perspective, the use of one staff member is more efficient than two staff.
- Key drivers in the economic evaluation are patient turnaround time and for mobile units, average distance travelled per day.
- Exploratory cost effectiveness analyses show that when a national non-mydriatic screening programme is compared to the current pattern of opportunistic screening in Scotland, cost savings are achieved.

### 8.1 Search strategy

For the economic evaluation of diabetic retinopathy screening, a scoping search was undertaken to gauge the quantity and quality of the existing literature, with particular attention being paid to finding studies by other HTA organisations, systematic reviews and research in progress. Following this, a wide range of databases (see Appendix 5) and web sites were selected to carry out a full literature review. Three databases (NHS and Econlit) were chosen specifically for economics information, and the web sites searched included those of the world's major health economics research units. Efforts were made to capture unpublished data by searching databases such as SIGLE and Dissertation Abstracts and by scanning appropriate web sites. No date limits were imposed. All databases were searched from their starting date until the latest material available, during July 2001. The only restriction put on the search was that, due to time and cost considerations, foreign language documents were excluded. In all cases however, where the search strategy did retrieve foreign language documents, an English language abstract was available and this was scanned for important information.

The topic was split into three concepts namely: diabetic eye disease; screening; cost-effectiveness. A search for all the probable synonyms for each concept was carried out, and then the results from each concept were added together. Searches were performed using the available subject headings (e.g. MeSH, Emtree etc.) and free text terms.

The full list of sources searched and a copy of the Medline search strategy are given in Appendix 5. The Medline strategy was adapted to search the other databases. A complete listing of all the search strategies can be obtained by contacting HTBS. Also contained within Appendix 5 is a flowchart showing the number of studies identified then included in each stage of the review process.

### 8.2 Data Extraction

The key studies used in the economic evaluation are summarised in Appendix 17.

### 8.3 Methodology

#### 8.3.1 Objectives

Several screening modalities could be envisaged in the national screening programme using combinations of the various screening components (optical device, use of mydriasis, mode of provision and professional resources). Clinical effectiveness results and organisational issues have resulted in the recommendation to use retinal cameras, but the efficiency associated with other components, when used in combination, needs to be assessed. This will be evaluated in a multi-stage economic analysis and should help NHS Boards to determine which method (or combination of methods) is suitable for their region, taking account of their own unique regional issues.

The objectives of the economic evaluation are to:

- Calculate the cost of imaging and grading per patient for a variety of diabetic retinopathy screening modalities.
- Perform exploratory analyses of patient benefits (and cost per QALY) in moving from the current Scottish system of opportunistic screening to a national programme, for a mydriatic model and a non mydriatic model.
- Calculate the overall cost (budget impact) of establishing and sustaining a national screening programme, taking account of the costs associated with national coordination facilities.

#### 8.3.2 Basis for Economic evaluation

Due to the need for a very high level of accuracy and the necessity for a robust quality assurance scheme within a national screening programme, the digital retinal camera is recommended as the optimum device for screening. Furthermore, as reported in the clinical effectiveness section, there is currently little evidence that the sensitivities and specificities achieved with a retinal camera differ with or without mydriasis. While the uncertainty surrounding these estimates differs for referable or sight threatening retinopathy, greater harmony is shown between them for any retinopathy (Appendix 7). As patients will be treated in the same manner within the national screening programme once referable retinopathy is detected, screening accuracy is a surrogate for patient benefit.

The economic evaluation is undertaken with the assumption that the accuracy of screening (patient benefit) is similar for non-mydriatic photography and mydriatic photography. It is recognised that the greater uncertainty around the central estimates of sensitivities and specificities for non mydriatic photography (see 95% confidence intervals in Appendix 7) is likely to lead to greater uncertainty around the cost effectiveness of non mydriatic photography compared to that for mydriatic photography (Briggs and O'Brien, 2001).

To allow for technical failures within digital screening, a mixture of services (including indirect ophthalmoscopy) will be required to achieve acceptable coverage and patient

### Assessment Report 3: Draft for Consultation

compliance. There are many ways in which such a screening service based mainly upon digital cameras can be provided.

The screening modalities considered in the Assessment Report are:

#### Mydriatic

- Mobile mydriatic, two field per eye operated by a single photographer within GP premises
- Mobile mydriatic, two field per eye operated by a single photographer within van
- Mobile mydriatic, two field per eye operated by a photographer and nurse
- Hospital based mydriatic, two field per eye operated by a single photographer
- Hospital based mydriatic, two field per eye operated by a photographer and nurse
- Hospital based examination by slit lamp for those not amenable to photography
- Grading of mydriatic, two field per eye including quality assurance.

#### Non-mydriatic

- Mobile non-mydriatic, single field per eye operated by a single photographer within van
- Hospital based non-mydriatic, single field per eye operated by a single photographer
- Grading of non-mydriatic, single field per eye including quality assurance.

The base case assumptions associated with these modalities are presented in Appendix 18.

The main economic analysis seeks to identify the least cost mode of a formal screening programme, taking account of these examples of service provision from across the UK. This is compared to the cost of an opportunistic screening programme, which is the current standard in Scotland, within an exploratory cost effectiveness analysis to derive the net economic cost of establishing a formal screening programme.

The breakdown and percentage coverage of opportunistic screening is taken from the Inter-College Audit as reported by the NSC (Grimshaw et al., 1999). The unit cost of opportunistic screening by GPs is taken as the average of the best and worst case estimates reported in James & Turner (1997) and adjusted to 2001 prices, though the move to a formal screening programme is unlikely to result in financial savings from this source.

The likely least cost options identified in the main economic analysis can be combined with the following to give the budgetary impact:

- National coordination within the CSA
- Screening office establishment and operation
- Referrals for assessment by ophthalmologists, both true and false positives
- Laser treatment episodes.

While implementation will spread initial costs over a number of years, it is difficult to project exact implementation timetables. Consequently, the gross and net costs (budgetary analysis) of establishing a national screening programme are presented for a single year, together with an estimate of annual recurrent costs and an estimate of annualised capital and recurrent.

## Assessment Report 3: Draft for Consultation

### 8.3.3 Cost measurement

Within the formal screening programme, capital costs are presented as annualised figures for the cost effectiveness analysis and summed with recurrent costs. For the budgetary analysis lump sum investments and recurrent costs are presented alongside annualised figures.

The cost of opportunistic screening by optometrists using slit lamps varies across NHS Boards. According to the HTBS baseline survey, optometrist fees range from £5 to £25 in Scotland, with median of £25. The basis for the fee differs across Scotland, with some covering the entire eye examination and others for screening alone, with the remainder of the examination paid for by the General Ophthalmic Service (GOS).

An unpublished survey shows that fees paid to optometrists for diabetic retinopathy screening in 1998 vary across the UK from £10 to approximately £40, with a mean of £26. This is consistent with Scottish data. However, these optometrist fees are for use of a slit lamp where there is no national coordination. In a national programme, the overheads for call-recall will be handled centrally. However, the other overheads an optometrist will face in the Scottish national screening programme are unclear. Hence for the base case economic analysis, a figure of £20 is tentatively assured for the optometrists imaging fee. This estimate is used for simple comparisons to NHS modalities and so can be easily substituted, if another fee is agreed locally.

The cost of hospital based opportunistic screening is taken from this report's costing for hospital based slit lamp examination within a formal screening programme.

Coordination and screening office establishment draws on experience from the breast cancer screening programme, with both the cost based upon establishment within hospital and the cost based upon establishment within commercial office space being presented. Screening offices are based upon a population of between four and five hundred thousand, with appropriate allowances for extra staffing and consumables for larger populations. NHS Boards with significantly smaller populations are assumed to be covered by other screening offices, with ten screening offices established. This is a pragmatic model and other regional groupings may also be appropriate. This avoids the possibility of dropping below a minimum efficient size of screening office, though. If screening offices are further consolidated further savings may be possible, though the main cost elements of staffing and consumables are likely to remain relatively constant.

The cost of the development and maintenance of a call/recall database and IT system is based upon an indicative costing from those operating a similar system within the breast cancer, cervical cancer and colorectal cancer screening programmes. This is not a formal quote and would be required to go out to tender if provided by the private sector. Indications from the Topic Specific Group suggest that significant costs could be saved if the IT system for call/recall could be developed within NHSScotland. Figures for this of £80,000 initial and £20,000 recurrent have been indicated, a breakdown of these being presented in Appendix 19.

There is no allowance for image capture software, as this has been developed and piloted within NHSScotland so avoiding potential copyright and encryption problems. This assumption will be verified during consultation.

### Assessment Report 3: Draft for Consultation

Throughout the UK there are a number of ways in which screening using digital photography is delivered. Within the analyses it is important to ensure comparability. Consequently, a common staff grade for the photographer is assumed, together with a common staff grade for nursing assistance where this applies. Equipment costs are derived from manufacturer quotes and the experience of current digital photography within NHSScotland and the NHS in England.

It has not been possible to allocate an administrative overhead for mobile modalities, this being assumed to be minor and subsumed within the operation of screening offices. Similarly, the mobile mydriatic photography option as operated by Grampian requires that the camera be transferred to a room within GP practices for operation. No allowance has been made for the opportunity cost of accommodation within GP surgeries. If visits of a couple of days to GP surgeries result in little or no displacement of activity ignoring this opportunity cost is justifiable. However, indications from the Topic Specific Group are that in certain areas, particularly urban areas, GPs are experiencing increasing pressures for the accommodation of services within their surgeries. Consequently, an indication is given of the opportunity cost for GP accommodation that would be required for mydriatic mobile screening within GP accommodation to be more costly than examination by optometrists.

The Newcastle mydriatic mobile screening option is also explored briefly as a possible alternative, as this screens patients within a suitably converted van obviating the need for GP surgery accommodation. In similar fashion, non-mydriatic mobile screening occurs within a suitably converted van, hence there is no allowance for GP accommodation.

Administrative costs for screening options within hospitals are taken from Scottish Health Service Costs 2000 (National Health Service in Scotland. Information and Statistics Division, 2000) PAM section on allocated overheads for eye examinations by hospital opticians.

The cost per screen is derived from an assumption of two hundred operational days per year coupled with reported patient turnaround times. Capital utilisation could be increased through the application of whole time equivalent staffing costs with an allowance for days during which maintenance occurs, but it remains unclear to what extent full time operation of screening units is possible.

Grading of images is assumed to follow the method established within the Welsh and Aberdeen screening programmes, with three levels of grading (section 6.9). These costs are added to the cost of screening for each screening modality to give a cost per graded screen. While opinion as to automated grading appears to be that systems are not yet ready for clinical practice, there is the potential for automated grading to substitute for level one grading with significant cost savings. Optometrist screening will be initially graded outwith NHSScotland, and as such is assumed not to be subject to level one grading within NHSScotland.

Summing screening costs and grading costs gives an overall cost per graded screen. However, within this there is no allowance for those not amenable to digital photography being examined by slit lamp. If this proportion were the same for mydriatic and non-mydriatic photography it would not affect their relative cost per graded screen. However, expert opinion and the clinical effectiveness review suggest that these rates may differ and that an allowance should be made for this. For mobile screening options it is assumed that patients not amenable to photography are examined by optometrists. For hospital based

### **Assessment Report 3: Draft for Consultation**

screening options it is assumed that they are examined within hospital. Note that it is not assumed that an individual presents for digital photography but is then referred to slit lamp examination, but rather that the screening system can distinguish those who require slit lamp examination based upon prior experience and so book appointments appropriately.

The costing of referrals to ophthalmologists follows similar principles to that of the costing of screening options. It is not suggested that ophthalmologists will be employed full time examining referrals from the screening programme. Rather it is assumed that referral costs are directly proportionate to the time spent examining referrals. While this method may marginally understate capital costs this will not markedly affect the analysis given the preponderance of staff costs.

The cost of laser photocoagulation treatment is taken from that reported by the Centre for Health Planning and Management within the NSC report (UK NSC, 2000), based upon data from the Royal Liverpool University Hospital.

Within the cost effectiveness and budgetary analysis there is no allowance for the costs of referrals to diabetologist for non-sight threatening reasons or for the costs of the treatment of those who have gone blind.

#### ***8.3.4 Estimation of Net Benefits and Budgetary Impact***

Given the likelihoods of transferring between different retinopathy states, and the likelihood of blindness with and without treatment, the anticipated numbers of years of sight, years of blindness and discounted Quality of Life Adjusted Years (QALYs) can be calculated for people with diabetes of type 1 and type 2. Given sensitivities and specificities of screening techniques, cohorts of people with diabetes can be flowed through the model, giving the anticipated number of referrals and treatments. The net benefits of moving from an opportunistic screening programme to a systematic screening programme can then be calculated.

However, given uncertainty around both the age distribution and the distribution of different stages of retinopathy within age cohorts this does not yield a prediction of the annual number of referrals and treatments. Consequently, the budgetary analysis adopts a simpler methodology. Reported sensitivities and specificities are coupled with the reported prevalence and incidence of treatable sight threatening diabetic eye disease to yield the predicted number of referrals and laser treatment episodes. These are then fed into the budgetary analysis to give an anticipated downstream treatment cost.

#### ***8.3.5 Discounting***

Costs are discounted at 6.0% with benefits discounted at 1.5% in the base case, as recommended by the Scottish Executive Health Department.

#### ***8.3.6 Sensitivity Analysis***

A key cost driver for all screening modalities within NHSScotland is patient turnaround time. In addition, for mobile screening options the amount of time spent travelling significantly affects the number of patients that can be screened. For hospital based screening modalities the allocated hospital charge for outpatient appointments drives costs to a significant extent.

## Assessment Report 3: Draft for Consultation

The effect of varying these is explored within sensitivity analysis, as is the effect of varying the number of operational days per year.

The effect of varying the fee charged by optometrists upon optimal service structure is explored, as is the effect of varying the percentage of patients screened by optometrists.

The anticipated impact upon people with diabetes depends upon the age at diagnosis and, critically, upon the effectiveness of photocoagulation treatment. A range in the relative risk reduction of blindness upon treatment is explored within the examination of anticipated patient benefits. The discount rate used for patient benefits also has a significant impact upon cost effectiveness, and is varied to include 0% and 6%.

The effect of wrongful referrals and those correctly referred for treatment depends upon the annual incidence of treatable sight threatening retinopathy within the diabetic population. The effect of varying this upon downstream examination and treatment costs is explored in the budgetary analysis.

### 8.3.7 Assumptions

Those who are not amenable to digital photography are identified within the screening database and booked slit lamp examinations as appropriate. Screening costs will be increased by the extent that this does not occur and secondary slit lamp examinations are required within the same screening cycle. This will be most significant during establishment of the screening programme but will diminish in the longer term.

This will slightly understate screening costs particularly during the establishment phase. If all patients not amenable to photography were always booked into photographic screening prior to being referred on to slit lamp examination this would increase the costs of screening exclusive of grading and other costs by a percentage approximately equal to the numbers not amenable to photographic examination.

No allowance has been made for training costs associated with the adoption of the new technology. The NSC report estimate of training costs is based almost exclusively on the cost of staff time during attendance. An allowance has been made for this within the base case number of operational days assumed per year. This may marginally understate the relative requirement of ophthalmologist time and ignores minor items such as room hire.

## 8.4 Economic Evaluation Results

### 8.4.1 Costs of Screening Modalities

All cost comparisons are on the basis of recurrent costs plus capital costs annualised at six percent. The results for mydriatic photography are presented first, followed by non-mydriatic photography.

#### 8.4.1.1 Mydriatic Photography Cost Calculation

Both mobile and hospital based mydriatic photography can be single staffed by the camera operator. The camera operator is responsible for both the administration of eye drops and the taking of photographs, patients being photographed while others wait for their eyes to fully

### Assessment Report 3: Draft for Consultation

dilate from the administered drops. Given this dual role, patient turnaround time in the base case analysis is taken as being 20 minutes<sup>2</sup>.

Using two staff members enables the camera operator to concentrate upon photography, with a nurse providing patient information and administering eye drops. This increases staffing costs, but also increases patient throughput so making better use of capital equipment. Patient turnaround time in the base case analysis is taken as being 15 minutes.

In the costings, camera operators were assumed to be MTO Grade 3. Nursing assistance is assumed to be Grade D. Where a single member of staff is used, it has recently been confirmed that the single member of staff must satisfy the Patient Group Directions (Appendix 8), to be able to administer eye drops. This would imply one person of at least nursing Grade D. However, as an MTO Grade 3 salary is higher than that of a Grade D nurses, this is not going to have a significant impact on the costings.

Camera equipment costs have been taken from supplier quotes<sup>3</sup> and NHSScotland experience. A 15 pence allowance per screen has been given, which together with eye drops at 5 pence gives a consumables cost of 20 pence per screen<sup>4</sup>. An additional allowance for flash tube renewal has assumed a flash tube life of 20,000 photographs as advised by the supplier.

All capital equipment is assumed to be purchased, with the necessary mobile van conversions and annual servicing being undertaken by suppliers<sup>5</sup>. For the mobile options fuel costs are taken as being a function of the daily drive time with an assumed average of 35mpg and 45mph for screening within GP surgeries, while screening within a suitable converted van takes a figure of 30mpg.

Grading of photographs is assumed to be hospital based and coordinated by one full time A&C Grade 5. Level one grading is performed by an MTO Grade 3 with a third of screens being passed to an MTO Grade 5 for level two grading. Level three grading reviews a third of level two gradings and is performed by an ophthalmic consultant who also reviews 5% of all screens for quality assurance. Each grading incident is assumed to take five minutes.

Slit lamp examination is assumed to be required for 5% of patients<sup>6</sup>, which can be undertaken within hospital or by optometrists. As reported below, the cost per slit lamp examination within hospitals is approximately £12. This is significantly less than current optometrist fees. Consequently, in the analysis of hospital based photographic screening it is assumed that the 5% requiring slit lamp examinations are seen in the hospital setting. However, for community based mobile screening it is assumed that optometrists perform slit lamp examination. As discussed below, hospital based screening appears the less expensive option from the NHS perspective. But acceptable patient travel times<sup>7</sup>, access and attendance is likely to require additional mobile or community based provision, giving rise to the assumption that for mobile screening options slit lamp examinations are performed by community optometrists.

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<sup>2</sup> Based upon Newcastle screening programme of eight years and a pilot within Elgin, Grampian of 300 patients.

<sup>3</sup> TOPCON UK

<sup>4</sup> HERU costing of Gloucestershire Screening Service

<sup>5</sup> Costs quoted by A.M. Phillips

<sup>6</sup> Expert opinion and clinical review section

<sup>7</sup> Sculpher (1991) reports the costs of patient travel and time, but these vary significantly between locations and it is difficult to draw conclusions as to likely patient travel times and costs for screening by different methods within NHS Scotland and optometrist practises.

### Assessment Report 3: Draft for Consultation

In order to compare photography delivered within NHSScotland with that delivered by optometrists, it has been assumed that optometrists photography is not subject to level one grading but that level two grading, level three grading and quality assurance is still performed within NHSScotland.

#### 8.4.1.2 Mydriatic Photography Costing Results and Sensitivity Analysis

Table 8-1 presents the annualised cost per screen by screening modality for the base case. The base case assumption is that all capital equipment has little or no resale value. Given the assumed five-year life of vans within mobile options, this is pessimistic. Consequently, the annualised cost per screen is also presented for a 20% resale value for vans, and for a 20% resale value for vans and camera related equipment.

**Table 8-1 Annualised cost per screen by screening modality (£)  
Base case**

	Mydriatic Mobile 1 Staff GP Prem.	Mydriatic Mobile 1 Staff Van Base	Mydriatic Mobile 2 Staff GP Prem.	Mydriatic Hospital 1 Staff	Mydriatic Hospital 2 Staff	Optometrist Photography
Cost/Screen	15.10	15.32	16.87	12.30	14.35	20.00
Grading	3.29	3.29	3.29	3.29	3.29	1.49
Slit Lamp All.	0.23	0.22	0.15	0.17	-0.12	..
<b>Total</b>	<b>18.62</b>	<b>18.83</b>	<b>20.30</b>	<b>15.76</b>	<b>17.52</b>	<b>21.49</b>
20% van resale	18.39	18.49	20.13	..	..	..
20% van & camera resale	18.00	18.11	19.84	15.51	17.32	..

It is clear that given the base case assumptions, there is only a small cost increase associated with screening patients within a van compared to screening patients within GP accommodation. Given that the above does not make any provision for the opportunity cost of GP accommodation, where pressures exist on GP accommodation it is likely to be cheaper to provide screening within a van along the lines of the Newcastle programme where this proves feasible.

Given the base case assumptions, the additional benefit of increased patient throughput from using two staff members is more than outweighed by the increase in staffing costs. As the sensitivity analysis of Appendix 21 shows, for mobile options this applies regardless of the daily drive time. Double staffing is dominated for both mobile and hospital based options in the base case. While a difference in the cost per screen of around two pounds may appear minor, this rapidly multiplies up with the number screened to around £17k per 10,000 screened.

As reported in the methodology section, the base case assumes a patient turnaround time of 15 minutes and 20 minutes for one staff members and two staff members. As shown in Appendix 21, reducing these by 20% narrows the difference in the cost per screen between the mobile and hospital based options, as the effect upon throughput is proportionally greater for mobile options given setting up and drive times.

### Assessment Report 3: Draft for Consultation

**Table 8-2      Annualised cost per screening modality (£)  
20% Reduction in Patient Turnaround Times**

	Mydriatic Mobile 1 Staff GP Prem.	Mydriatic Mobile 1 Staff Van Base	Mydriatic Mobile 2 Staff GP Prem.	Mydriatic Hospital 1 Staff	Mydriatic Hospital 2 Staff	Optometrist Photography
Cost/Screen	12.15	12.32	13.56	10.71	12.35	20.00
Grading	3.29	3.29	3.29	3.29	3.29	1.49
Slit Lamp All.	0.37	0.37	0.31	0.09	-0.02	..
<b>Total</b>	<b>15.81</b>	<b>15.97</b>	<b>17.16</b>	<b>14.09</b>	<b>15.61</b>	<b>21.49</b>

Retaining the assumed 20 minute patient turnaround time for the one staff member options, a one way sensitivity analysis can be performed to determine what improvement in patient turnaround times for two staff members modalities would be required to equate costs per screen. This suggests that patient turnaround times would have to fall to 12 minutes within the two staff members options for their cost per screen to be equal to that of the one staff member options; i.e. two staff members would be required to increase patient throughput by 67%. It should also be noted that an increase in the percentage of unfilled slots above the base case assumption of 5% further widens the cost differential between the one staff member and two staff members options.

The base case analysis shows hospital based screening to be cheaper than mobile provision for the base case, though allocated hospital overheads of £4 (National Health Service in Scotland. Information and Statistics Division, 2000) do contribute significantly to this conclusion. Concentrating upon the single staffing options, there is no obvious reason for patient turnaround times to differ between mobile and hospital-based provision. Consequently, the sensitivity analysis focuses upon hospital overheads and capacity utilisation, and the daily drive time involved in mobile provision.

As the cost per screen is linear in hospital overheads, they would have to increase by 70% for the cost per screen to be equal between hospital based and mobile provision. But given its fixed location, hospital based provision may have a limited population to draw on within an acceptable catchment area. Capital equipment purchased for photographic screening may lie unutilised for much of the time. Provided that the camera operator can be usefully employed during this down time and hospital overheads remain constant at £4 per attendee, capital equipment would need to be under-utilised by 45% within hospital based screening before the cost per screen was equated with mobile provision. Level one grading would be the obvious use of any spare MTO Grade 3 capacity. Yet even if the staff member is wholly inactive other than when performing photography, capacity under utilisation could rise to as much as 25% before the cost per screen is equated with mobile provision.

The base case analysis assumes a total daily drive time of two hours for mobile options; i.e. one hour each way. This significantly affects the number of patients that can be seen each day. Given the base case assumptions for hospital provision, the total daily drive time would have to fall to only one hour for the cost per screen of mobile and hospital provision to be equated.

The impact of total daily drive times and patient turnaround times is explored in greater detail in Appendix 21. Comparing single staffed mobile provision with optometrists, under base

### Assessment Report 3: Draft for Consultation

case assumptions the total daily drive time would have to increase to 2hr40min to equate costs per screen. Alternatively, retaining a two-hour daily drive time, the capital involved in mobile provision could be inactive for 35% of the time if the operator is engaged in grading or for 17% of the time if the operator is entirely inactive when not taking photographs. These percentage under utilisation rates equate the cost per screen from mobile provision and optometrist provision.

On a similar basis, if the optometrist fee were £15 the total daily drive time would be required to fall to only 1hr20min for mobile provision to remain cost effective. For an optometrist fee of £25 the total daily drive time can rise to 3hr30min and mobile provision still remain cost effective. However, the base case costing of mobile provision within GP premises makes no allowance for the opportunity cost or financial cost of using these premises. Given the base case differential of £2.87 between this and optometrist provision and a 20 minute patient turnaround time, accommodation charges of around £8.61 per hour would see mobile provision within GP accommodation and optometrist provision be of equal cost in the base case. An optometrist fee of £25 would require these accommodation charges to rise to £23.60 per hour to equate cost per screen. In areas where GP accommodation is heavily utilised and screening is likely to displace activity, the Newcastle model of screening within a suitably converted van is likely to provide the least cost mobile solution.

The above suggests a default of hospital-based provision where this is acceptable to patients, patient travel times not proving to be a deterrent and reasonable attendance rates being maintained. However, provision for areas outwith major urban centres may be more effectively served by a combination of mobile and optometrist coverage. The main drivers of overall cost and cost per screen under such circumstances will be the percentage seen in hospital, the drive time involved with mobile provision, any GP accommodation fees, optometrist fees and the balance struck between mobile and optometrist provision.

As an example, if 45%<sup>8</sup> of people with diabetes are seen in the hospital setting the effect of the balance between mobile and optometrist provision can be examined as shown in appendix 22. As would be expected, where the optometrist cost exceeds that of mobile provision, the cost per screen rises as optometrist provision increases. The sensitivity analysis can, however, also be seen as an initial guide to the cost minimising structure of service provision.

For a NHS Board, given the population that can be reasonably covered by hospital-based provision with both acceptable capacity utilisation rates and patient attendance, the default provision for the remaining population is mobile provision within NHSScotland. Optometrist fees within the NHS Board will indicate what total daily drive time is acceptable for mobile provision to remain cost effective. Potential mobile unit bases can then be reviewed to determine the likely diabetic population within the catchment area implied by the daily drive time, these being geographically dispersed. If the catchment area of a potential mobile unit base provides sufficient capacity utilisation, the area should be served by mobile provision. If mobile units can be transferred between bases and NHS Boards, capacity considerations will ease. For areas outside acceptable catchment areas, optometrist provision of screening will reduce costs.

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<sup>8</sup> Based upon Argyll and Clyde, Forth Valley, Greater Glasgow, Lanarkshire and Lothian populations being reviewed within the hospital setting. This is only for presentational purposes and does not presume that all in such areas will be seen in hospital or that none in other health boards will be seen in the hospital setting.

### Assessment Report 3: Draft for Consultation

Given the size of the proposed programme, SHS may manage to negotiate discounts on camera equipment and its associated hardware and upon van purchase and its associated hardware. A 20% reduction in camera costs causes around a 50 pence reduction in the cost per screen for all mydriatic options. This reduction is slightly greater for the single staffed options given the lower patient numbers seen which implies a greater capital cost per screen. Similarly, a 20% reduction in van purchase cost causes around a 25 pence reduction in the cost per screen for mobile options.

#### 8.4.1.3 Non-Mydriatic Photography Cost Calculation

The principles underlying the calculation of non-mydriatic photography exactly parallel those for mydriatic photography. However, as eye drops do not have to be administered only single staffing options are considered. This quickens patient turnaround to ten minutes, but increases the proportion not amenable to photography to 8%. As mobile photography is performed within the van, a suitably converted transit is required, increasing fuel consumption slightly to 30mpg.

Given the results that follow, provision of screening with mobile units in large urban centres may be as or more cost effective than hospital based provision. Consequently, it may be inappropriate to assume that all those not amenable to photography under the mobile option will receive optometrist slit lamp examination. If urban provision is through the mobile option, those requiring slit lamp examination may be seen by optometrists or within the hospital setting. If such slit lamp examinations are within the hospital setting, this would further enhance the relative cost advantage of mobile provision.

#### 8.4.1.4 Non-Mydriatic Photography Costing Results

**Table 8-3 Annualised cost per screen by screening modality for base case (£)**

	Non Mydriatic Mobile	Non Mydriatic Hospital	Optometrist Photography
Cost/Screen	7.15	8.05	20.00
Grading	1.92	1.92	0.82
Slit Lamp All.	0.95	0.28	..
<b>Total</b>	<b>10.02</b>	<b>10.25</b>	<b>20.82</b>
20% van resale	9.90	..	..
20% van & camera resale	9.75	10.14	..

Under the base case analysis, there is minimal difference in cost between screening organised in hospital compared to that organised through mobile provision. Clearly, as the total daily drive time increases beyond two hours mobile provision becomes more expensive. But this is likely to be for provision in areas where patient travel times to hospital-based facilities may be unreasonable and likely to impact upon attendance rates. The more appropriate comparison under such circumstances is with optometrist provision.

The main result of the above is to highlight the potential savings that would result if mydriasis and two fields prove to be unnecessary for those attending screening. While the exact level of savings would depend upon the balance struck between hospital, mobile and optometrist provision, annualised reductions in costs in the order of £870,000 could be anticipated. Given that work is currently under way regarding the need for mydriasis and two fields, it would

### Assessment Report 3: Draft for Consultation

seem sensible to future proof the roll out of a systematic screening programme through investment in cameras capable of non-mydriatic photography.

Due to the increased patient numbers seen within non-mydriatic units, camera and van purchase price discounts have only a limited effect upon the average cost per screen. A 20% discount on camera costs results in around a 25 pence reduction in the cost per screen, while a similar reduction in the van purchase price would result in a 14 pence reduction in the cost per screen. Additional sensitivity analyses paralleling those for mydriatic photography are presented in the appendices.

#### 8.4.2 *Exploratory Cost Effectiveness Analyses*

To illustrate the anticipated benefits of moving from the current pattern of opportunistic screening undertaken in Scotland to a national systematic programme, the progression of people with diabetes through the different stages of retinopathy is modelled. Using the transition probabilities and mortality multipliers reported in Vijan et al. (2000) for people with type II diabetes, cohorts can be flowed through the opportunistic and systematic screening programmes.

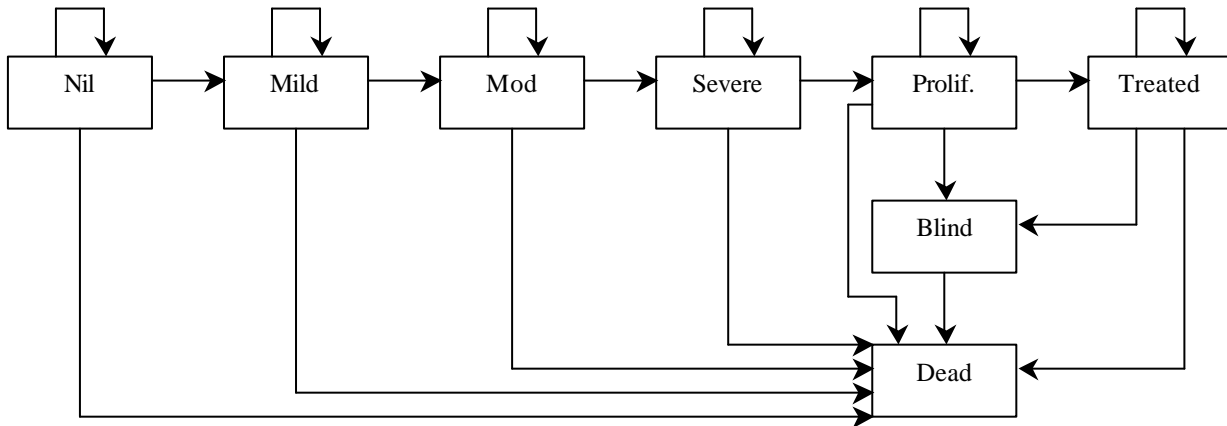
Opportunistic screening is assumed to be 50% by GPs, 30% by optometrists and 20% in hospital with a 60% attendance rate. The NSC report (UK NSC, 2000) also highlights that under opportunistic screening 80% of people with diabetes have been screened over two years, which suggests that 60% of people with diabetes present randomly each year for opportunistic screening<sup>9</sup>. The largest proportion of opportunistic screening is performed by GPs, which are typically reported as achieving around a 90% specificity (e.g. Sculpher et al, 1991). The specificities for opportunistic screeners are similarly taken as being 90%, with the associated sensitivities being taken from the clinical effectiveness review section. This results in sensitivities and specificities for GPs, optometrists and hospital-based diabetologists are taken as being 64% and 90%, 75% and 90%, and 82% and 90% respectively. Systematic screening is assumed to have an 80% attendance rate for people with diabetes again presenting randomly each year, with a sensitivity and specificity of 87% and 95%.

People with type 2 diabetes and no retinopathy pass through three background retinopathy states with no risk of blindness, transition probabilities between these being dependent upon the level of glycaemic control. Proliferative retinopathy then ensues which carries a risk of blindness. If proliferative retinopathy is detected patients are treated with photocoagulation that permanently reduces the risk of blindness. Not all will progress through the disease to blindness as all health states have an associated age related probability of death.

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<sup>9</sup> Note that simulations assume people with diabetes present randomly within each screening modality. In practise people with type 1 diabetes may have both higher opportunistic attendance rates and tend to be seen within the hospital setting, which may tend to reduce the effect of moving from opportunistic to systematic screening overall. However, it may also tend to increase the impact of the move to a formal screening programme upon people with type 2 diabetes.

**Assessment Report 3: Draft for Consultation**



The model structure for people with type 1 diabetes is as presented in this diagram, but with there only being one state for background retinopathy. Transition probabilities between no retinopathy to background retinopathy, and from background retinopathy to proliferative retinopathy are age related.

The details of the QALY calculations and associated discussion are presented in Appendix 23.

*8.4.2.1 Anticipated Cost Effectiveness of Moving to Systematic Screening*

*8.4.2.1.1 Mydriatic Photography*

Within each cohort the number of screens performed, false positives, true positives and treatments can be simulated for each year. These are then discounted to give the present value of QALYs and costs for the opportunistic and systematic screening programmes, from which the net cost/QALY can be calculated for the move from opportunistic to formal screening. This discounts costs at 6% and benefits at 1.5% as the base case. The discount rate used for benefits significantly affects the cost effectiveness for people with type 2 diabetes, results for discount rates of 0% and 6% on benefits being presented in Appendix 22 though the move to a formal screening programme for people with type 1 diabetes appears cost effective regardless of the benefit discount rate.

**Table 8-4 Cost per QALY of systematic screening relative to opportunistic screening: Mydriatic**

Age	RRR	Type II		Type I		
		9% A1c	7% A1c			
30	90%	£2,139	£4,655	15	90%	£826
	70%	£3,074	£6,694		70%	£1,222
	50%	£4,635	£10,168		50%	£1,947
40	90%	£3,808	£8,322	20	90%	£862
	70%	£5,328	£11,745		70%	£1,263
	50%	£7,836	£17,476		50%	£1,996
50	90%	£8,122	£17,603	25	90%	£991
	70%	£11,040	£24,509		70%	£1,432
	50%	£16,006	£35,130		50%	£2,232
60	90%	£21,397	£44,279	30	90%	£1,177
	70%	£29,151	£61,963		70%	£1,676
	50%	£42,719	£77,422		50%	£2,581

### Assessment Report 3: Draft for Consultation

Immediately obvious is the greater anticipated benefit among people with type 1 diabetes of the move from opportunistic to systematic screening. Even among the common age group of 30, the cost effectiveness among type 1 diabetic is much greater despite their lower life expectancy. People with type 1 diabetes progress through the disease much faster and the benefits accruing to them are correspondingly greater.

For people with type 2 diabetes, the pattern is very much as would be anticipated. Better glucose control lessens the likelihood of blindness, so lowering the relative benefit of a formal screening system. The greater effectiveness of treatment with photocoagulation, the more cost effective is the move to systematic screening, while age significantly reduces the anticipated cost effectiveness of such a move. Similar considerations concerning the duration of treatment benefits, distribution of retinopathy upon diagnosis and effect upon the detection of macular oedema as reported above for patient benefits apply to cost effectiveness.

Age is also a significant factor, though for a cohort aged sixty it may be unreasonably optimistic to assume that none will have severe or proliferative retinopathy and that 80% will have no retinopathy. It remains unclear quite what the likely cost/benefit is of screening those diagnosed at an advanced age, as unless they have severe background retinopathy they are relatively unlikely to progress to blindness. However, this result may be better interpreted as further querying the need for those with little retinopathy to be screened annually. Again, among people with type 2 diabetes there is little likelihood of developing severe background retinopathy or blindness within two or even three years, though this risk does rise with poor blood glucose control and is higher for people with type 1 diabetes. However, all people with diabetes will require initial screening to determine their initial retinopathy state. It would seem sensible to continue annual screening until an assessment of the need for annual screening of those with little or no retinopathy has been made. Note that this option is not available to opportunistic screening, hence any move towards less than annual screening if clinically justified would further benefit the cost effectiveness of systematic screening.

In the above, there is also no allowance for any increase in the healthcare costs of diabetic care which result from blindness. The significance of this has not been quantified, but will tend to increase the cost effectiveness of the move to a systematic screening programme. To the extent that cost savings may be realised through this route there may also be budgetary savings, though how likely it is that budgetary savings would result rather than the freed resources being used for other patient care is a matter of conjecture.

#### 8.4.2.1.2 *Non-Mydriatic Photography*

As reported in the clinical effectiveness section, there is currently little evidence that sensitivities and specificities differ between mydriatic and non-mydriatic photography. Consequently, for those who can be screened by either method throughout the progression of the disease, the patient impact can be taken as being the same.

However, it has been assumed that the number requiring slit lamp examination is higher for non-mydriatic photography than for mydriatic photography. Given the lower sensitivity of slit lamp examination as a general screening tool this would be anticipated to reduce the beneficial patient impact of a non-mydriatic screening system. Furthermore, the progression of conditions that make a person with diabetes unamenable to non-mydriatic photography may tend to coincide with a progression to sight threatening retinopathy. Consequently, the effect upon the relative patient impact of non-mydriatic screening versus mydriatic screening

### Assessment Report 3: Draft for Consultation

may be greater than would be suggested by a cursory examination of the difference in percentages requiring slit lamp examination and slit lamp sensitivities might suggest.

Yet it may be more realistic to assume that under a non-mydratic screening programme those amenable to non-mydratic photography will be screened as such. Those who present but are not amenable to non-mydratic photography may subsequently be dilated to check whether they are amenable to mydratic photography, and if not referred on to slit lamp examination. This model of screening would yield the same patient impact as outlined above for a mydratic screening programme, though with a slight increase in cost over the base case assumptions for a non-mydratic systematic screening programme.

Immediately apparent from this is that if non-mydratic and mydratic photography are as effective in terms of sensitivities and specificities, a non-mydratic systematic screening programme will dominate mydratic photography in terms of cost effectiveness. The additional expense of mydratic photography confers no additional patient benefits. Turning to the cost effectiveness of the move from an opportunistic screening programme to a systematic screening programme based upon non-mydratic photography, the cost per QALY will be lower than those reported for a mydratic screening programme above.

The average annualised cost per screen under a non-mydratic systematic screening programme is also slightly lower than that under an opportunistic programme. However, given that greater percentage assumed to attend a systematic programme, the total annual cost of screening under the systematic programme is slightly higher than that for the opportunistic programme. But this fails to take into account the cost of false referrals and true positives and treatments. Adopting the same procedure as for before yields cost effectiveness ratios as follows.

**Table 8-5 Cost per QALY of systematic screening relative to opportunistic screening: Non-mydratic**

Age	RRR	Type II		Age	RRR	Type I
		9% A1c	7% A1c			
30	90%	-£375	-£1,274	15	90%	£83
	70%	-£545	-£1,842		70%	£124
	50%	-£831	-£2,809		50%	£200
40	90%	-£728	-£2,356	20	90%	£127
	70%	-£1,026	-£3,336		70%	£189
	50%	-£1,519	-£4,977		50%	£303
50	90%	-£1,744	-£5,194	25	90%	£156
	70%	-£2,389	-£7,244		70%	£228
	50%	-£3,475	-£10,398		50%	£360
60	90%	-£5,311	-£13,684	30	90%	£199
	70%	-£7,246	-£19,132		70%	£286
	50%	-£10,634	-£23,957		50%	£445

When the cost of false referrals is taken into account, the move to a systematic programme based upon non-mydratic photography is cost saving for persons with type 2 diabetes. While reporting the cost per QALY under such circumstances is slightly unusual, it has been retained to illustrate the effect of screening those for whom the anticipated benefit is small. Among those diagnosed at an older age with little or no retinopathy, it is more cost effective

### Assessment Report 3: Draft for Consultation

to move from opportunistic to systematic screening than those of a younger age group. This results because the patient benefits for the cost saving are extremely small, questioning the need to screen older age groups at all if they have little or no retinopathy.

Given the greater speed of disease progression among persons with type 1 diabetes, the move to a systematic screening programme based upon non-mydriatic photography is not cost saving. However, it is not far from cost neutral and the cost per QALY is correspondingly extremely low. It should also be borne in mind that the simulations have not taken into account possible savings resulting from the reduction in treatments for blindness associated with diabetes.

#### 8.4.2.2 *Cost Effectiveness Analytical Assumptions*

The calculation of the patient impact of moving from an opportunistic screening programme to a systematic screening programme is critically dependent upon the probabilities and quality of life values used within the model. Vijan reports a range of probabilities around the central estimate, but unfortunately no such distributions are reported within Davies. Clearly, if the mortality risk is from diabetes and different degrees of retinopathy is higher than that reported and used in the model, the likelihood of a person with diabetes surviving to progress to blindness will be reduced. Similarly, if the transition probabilities are lower than reported people with diabetes will progress through the different retinopathy states at a slower rate, and the likelihood of blindness is again reduced.

Both these effects would tend to reduce the patient impact of the move from opportunistic to systematic screening in terms of the increase in years spent sighted and the decrease in the years spent blind. Conversely, if the mortality risk from diabetes is lower or the transition probabilities are higher, this will increase the likelihood of blindness and increase the impact of the move from an opportunistic to a systematic screening programme.

In addition to the above, the calculation of cost effectiveness ratios is critically dependent upon the values used for the quality of life in different health states. In particular, the quality of life value associated with a year of blindness drives the analysis to a significant degree. It is inevitable that there will be a degree of uncertainty around the estimation of such values, and this is reflected in the literature. Similarly, if for those blind the balance between well adjusted and poorly adjusted differs from the assumed equal balance, this will also affect the average quality of life value applicable to a year of blindness.

The simulations also assume that people with both types of diabetes present randomly to the screening modalities reported by the NSC for an opportunistic programme. This may be unrealistic, and a person with diabetes who was screened by his/her GP previously may be more likely to present at his/her GP again than to present at an optometrist or at hospital. This seems most likely to affect persons with type 1 diabetes who may be more likely to be seen within the hospital setting. Given that the sensitivity and specificity for opportunistic screening within hospital is significantly higher than that for opportunistic screening as a whole, this would tend to reduce the impact of the move from opportunistic to systematic screening for people with type 1 diabetes. Similarly, if opportunistic screening attendance rates for people with type 1 diabetes tend to be higher than for people with diabetes as a whole, this would again reduce the patient impact and cost effectiveness of the move to systematic screening for people with type 1 diabetes. However, it seems unlikely that this effect would worsen cost effectiveness ratios sufficiently to make the move to systematic

### Assessment Report 3: Draft for Consultation

screening for people with type 1 diabetes appear unattractive. Note that any such effect would also tend to improve cost effectiveness ratios for the move to systematic screening among people with type 2 diabetes.

#### 8.4.3 *Budgetary Considerations*

The overall cost of the screening programme will depend upon the balance between hospital based, mobile and optometrist screening, which is difficult to gauge a priori. There is also a degree of screening already occurring, which differs among NHS Boards. Consequently the cost estimates focused on here (Appendix 19) assume a complete absence of formal screening, and compare this with the cost of the opportunistic screening which may have been occurring prior to any moves towards formalised screening. Figures that deduct current budgetary allocations for diabetic retinopathy screening are presented in Appendix 20.

In calculating the indicative budget for the overall systematic screening programme it has been arbitrarily assumed that 45% of those screened are seen in hospital with the remainder being seen through mobile provision, though it is recognised that this will differ across NHS Boards and in particular that there may be areas of hospital capacity constraints in certain areas. Year one, recurrent and annualised gross costs of £4.79m, £2.52m and £3.03m can be anticipated for the establishment and operation of diabetic screening (Appendix 19). Local screening office establishment has assumed hospital-based offices. To the extent that these are integrated with community screening offices, savings on overhead allowances and some capital equipment may be realised.

This relates solely to providing the option of annual screening to diabetic with an assumed 80% acceptance rate. If early review is also provided within the screening system, annualised cost could increase by approximately £0.11m on the basis of 5% of those screened receiving early review.

For every 10% increase (decrease) in those being screened within the mobile setting, annualised costs will rise (fall) by approximately £35,300. These figures give little room for slack within mobile provision beyond the assumption of 200 operative days. Every additional 10% reduction in operating days can be anticipated to increase the annualised cost of mobile provision by approximately 4%.

There is no allowance within this calculation for photographic screening by optometrists. For every 10% of the total being screened who are screened by optometrists instead of within mobile units, an additional annualised cost of £58,000 would be anticipated given an optometrist fee of £20. This is clearly dependent upon the actual optometrist fee charged.

Note that the cost of grading adds significantly to the overall cost per screen. This is primarily driven by level one grading, staff costs for this approaching half the total annualised cost of grading. To the extent that automated grading could substitute for this, total grading costs could be significantly reduced in future.

However, the base case assumes a two-hour drive time for mobile screening. This may be unrealistic in that optimal service structure would suggest increasing the range of mobile provision until the marginal cost per screen of mobile provision rises to that of a graded optometrist screen, indicating a total daily drive time of 2hr40min. Under this assumption the

### Assessment Report 3: Draft for Consultation

cost per screen of those seen within mobile units would rise, but it is difficult to speculate as to what the impact upon the average cost per screen would be.

In terms of the cost of opportunistic screening, the UK NSC report (2000) suggests that in England around 60% of people with diabetes receive opportunistic screening in the absence of formal screening programmes. This is reported as being 50% GP, 30% optometrist and 20% hospital based. Taking the figures already presented together with the James et al. (2000) estimate for the cost of GP screening gives an annualised cost of £1.57m.

This suggests an additional annualised economic cost from the organisation of formal screening of around £1.46m. However, in terms of the overall budgetary effect it is unlikely that any savings would result from GPs and an annualised net budgetary impact of £2.24m would be predicted.

The downstream costs of referrals and treatment are outlined for various assumptions in appendix 24. This suggests that in the initial year downstream costs from referrals and treatment will be of the order of £1.3m as the backlog of previously undetected treatable sight threatening retinopathy is dealt with. With an incidence of 1.3% and a stable prevalence under opportunistic screening, around an additional 1,100 people with diabetes will require laser surgery in the first year compared to that which would be anticipated under opportunistic screening. However, this additional annual cost falls rapidly as the backlog of those with treatable eye disease is worked through. In the longer term an additional 150 laser treatments may be anticipated, with an annual downstream cost increase of £62,709.

This relates only to the direct downstream costs of false positives and the treatment of true positives, with no allowance for possible savings in terms of the reduction in treatment of those going blind. It also suggests that in the early years of screening programme establishment ophthalmology workloads may increase, as the backlog of treatable sight threatening eye disease is worked through. In the medium term workloads within ophthalmology may be reduced as referrals from false positives are reduced by around 3,000 with an increase of only a little over 150 in the numbers being treated. However, it should be stressed that these figures are quite speculative and sensitive to the base case assumptions that are used.

#### 8.5 Assumptions

Some of those not amenable to digital photography will still be given an initial photographic appointment, followed by slit lamp examination within the same screening cycle. This may arise with those newly diagnosed, and will arise for those developing eye problems that render them not amenable to photography between screening incidents. A worst case scenario of all those not amenable to photography being initially booked a photography appointment with a subsequent appointment for an optometrist slit lamp examination would cause screening costs to rise by the approximately these numbers multiplied by the cost of photographic screening. Where the principal screening modality is mydriatic photography this suggests an annual cost increase of between £100,000 and £116,000, while for non-mydriatic photography the cost increase would be £100,000.

It may be possible to increase capacity utilisation through staff rotation, and the adoption of whole time equivalent staffing. For instance, an assumption of fifty operative weeks per year would result in a fall of around eight percent in the cost per graded screen for the mydriatic

### Assessment Report 3: Draft for Consultation

mobile option with one staff member. However, an assumption of an annual number of operative days of 250 may be difficult to realise in practise, and while the reduction in the cost per graded screen is not insignificant it is less than a third of the percentage increase in operative days. Consequently, the base case analysis retains the assumption of 200 operative days coupled with full time rather than whole time equivalent staffing.

The economic analysis has not included patient travel times and costs, because they vary greatly depending on locality in Scotland. Patient travel times and costs are likely to impact significantly upon attendance rates, and so the optimal service design will be required to take these into account in each region.

#### 8.6 Conclusions

Non mydriatic diabetic retinopathy screening is associated with a lower cost than mydriatic screening. For non mydriatic screening, if the base case assumption of an average daily drive time of 2 hours in the van is appropriate, there is little difference in the cost of screening given in hospital or given by mobile unit. The components that have most influence on these costs are the patient turnaround time and drive time of the mobile unit. Consequently the possibility of hospital vs mobile screening provision vs optometrist provision should be considered in each region, given the density of the population, travel requirements and hospital and optometrist availability.

For those people with diabetes living on the islands, it is likely that mobile provision (shared with other areas) or optometrists will provide optimal provision. The range covered by a mobile unit should be based on the density of the diabetic population (number and drive time) and may cross NHS Board boundaries, so the possibility of mainland Boards sharing vans should also be considered.

Given the diabetic population in Scotland, a maximum of 10 regional screening centres should be established and for organisational purposes co-ordination of a smaller number e.g. 6 may be more feasible.

Decisions regarding optimal screening modality in each NHS Board or region will depend critically upon the fee rates charged locally by optometrists for diabetic retinopathy screening and any fees or opportunity cost charged for the use of accommodation for mobile provision.

Exploratory cost effectiveness analyses demonstrate cost savings when a national non-mydriatic screening programme is compared to the current situation in Scotland of opportunistic screening.

### 9 TOPICS FOR FURTHER EVALUATION

During this Health Technology Assessment, the following areas of research, audit and development have been identified. These will test assumptions made in this report and allow improvement in the national programme in the light of experience:

#### Clinical effectiveness:

- Investigate the role of mydriasis and multiple/single fields in screening by retinal photography (study underway by Leese et al, 2000)
- Estimate failure rates in the proposed system
- Test quality assurance measures for slit lamp evaluation to ensure that they reach a high and uniform quality standard.
- Evaluate the role of automatic grading by computer.
- Assess the role of laser scanning ophthalmoscopy.

#### Organisational issues:

- Investigate the possibility of less frequent screening in some patient groups
- Develop a training and accreditation scheme for retinal graders
- Develop a national treatment protocol for the administration of the mydriatic agent tropicamide
- Establish a robust quality assurance scheme
- Examine use of compressed JPEG images, lossless compression and laptop screens for grading
- Use current expertise to equip mobile retinal screening units in the national programme, ensuring facilities allow disabled access.

#### Patient issues:

- Ascertain patient preferences for
  - Location of screening
  - Timing of appointment
  - Whether screening outcome is reported at the time of the visit
- Evaluate factors that encourage screening attendance (and those most/least likely to be influenced by the intervention)
  - Educational material (leaflets, videos, media for a variety of sub-groups)
  - Written reminders (benefits of multiple reminders and style of invitation)
  - Advertising campaigns (press, television and radio)
  - Use of Educators
  - Peer education (particularly for teenagers)
  - Dissemination points.

#### Economic evaluation:

- Monitor attendance rates geographically and for different modalities
- Estimate initial levels of diabetic retinopathy
- Estimate net effect upon both referrals and treatments for diabetic retinopathy
- Estimate net effect upon both referrals and treatment for MO
- Estimate net effect upon registered blind within diabetic population.

## 10 RECOMMENDATIONS FOR THE NATIONAL SCREENING PROGRAMME FOR DIABETIC RETINOPATHY

In designing the national screening service for diabetic retinopathy in Scotland the best current data on clinical effectiveness and economic aspects have been taken into account. Equally important, however, has been the considerations of patient preferences and organisational issues. Giving these factors appropriate weight has resulted in recommendations that differ significantly from previous Health Technology Assessments of diabetic retinopathy screening.

Section 10.1 of this chapter explains how evidence from these different areas was combined to determine the main clinical components of the proposed screening service. Section 10.2 covers structural components of the service.

### 10.1 Technical components of the screening service

**The primary screening method will use non-mydriatic, digital retinal cameras and images will be graded by staff trained and specialising in this task.** The clinical effectiveness data show that this is a sensitive and specific method with acceptable rates of technical failure. Digital imaging is overwhelmingly preferred to other imaging methods because it allows transmission of images and storage for quality control and review purposes.

**A single image of the macula with a 45-50 degree angle of view is sufficient for screening purposes.** New clinical evidence has shown that one digital image per eye provides similar screening accuracy to two images. Although a single study cannot provide complete confidence this study represents the strongest available evidence. In combination with issues related to mydriasis (below) this study shows that the balance of current evidence favours a single image. The storage capacity and processing times for single images are lower than those for multiple images.

**Mydriasis should not be used unless clear evidence exists that an image of adequate quality cannot be obtained in a particular patient without it. This evidence may either be a current technical screening failure or past screening history. In the latter case the necessity for mydriasis should be taken into account when planning the screen.** Clinical evidence shows that mydriasis is unnecessary in the majority of patients to obtain a single retinal image. Patient preference reveals that mydriasis is uncomfortable and inconvenient and may increase the probability of non-attendance for screening. The cost per patient of non-mydriatic screening is less than that for mydriatic screening.

**If non-mydriatic retinal screening fails then digital photography with mydriasis should be offered immediately or arranged. If this also fails then examination using a biomicroscope should be offered or arranged.** The use of digital photography will allow a trained operator to make an immediate decision regarding the adequacy of the image. Fallback methods of screening are essential to allow for technical failure of non-mydriatic digital photography.

**The retinopathy grading system must be clearly defined and consistently applied.** A standard grading nomenclature for diabetic retinopathy is essential for consistent grading, for internal and external quality assurance purposes, for ease of exchange of data between clinical information systems, and for agreement on referral thresholds. Quality assurance requires

### Assessment Report 3: Draft for Consultation

that grading decisions can be independently validated and this requires a uniform grading system. A system based on single retinal images adapted from the CRAG grading system is recommended. Grading can be performed by any suitably trained and accredited individual.

#### 10.2 Structural components of the screening service

**Diabetic retinopathy screening should be organised with robust quality assurance and fully integrated with routine diabetes care.**

**A national coordinating centre should be established.** Certain features of the service will require coordination across NHS Boards. In the implementation phase clear guidance is required on the aims and objectives of the programme and the quality standards required for individual components of the programme and for the programme as a whole. On a continuing basis quality assurance and higher level grading could be done at a national level to ensure efficient use of trained staff, consistent standards, and minimisation of the burden on local ophthalmology services. Research into service improvements should also be commissioned and coordinated centrally.

**Six to ten regional screening offices should be established, linked to the national coordinating centre and each NHS Board to facilitate local delivery of the screening, within the national framework.**

**Each NHS Board will be responsible for ensuring its participation in the national programme. Named individuals should be identified to lead the process locally: addressing the best approach to meet local access needs but using technologies and system organisation that fits within the national programme.** The HTBS economic evaluation allows NHS Boards to make judgements about the optimal modalities for its area (hospital based, van or optometrist) and provides guidance on staffing issues to be considered locally, within a framework that provides clear guidance about the form of technology to be used (digital retinal cameras, IT, etc).

**A variety of educational materials should be used to inform people with diabetes about the retinopathy screening programme and patient preferences should be elicited to determine barriers to screening attendance.**

## **Assessment Report 3: Draft for Consultation**

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