

The Royal College of General Practitioners  
Effective Clinical Practice Unit, University of Sheffield

# Clinical Guidelines for Type 2 Diabetes

## **Diabetic retinopathy: early management and screening**

A Collaborative Programme between:

The Royal College of General Practitioners

Diabetes UK

The Royal College of Physicians

The Royal College of Nursing

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# Authorship

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Hutchinson A, McIntosh A, Peters J, Home P, Feder G, Baker R, Forrester J, Alexander W, Eltringham-Cox A, Greenwood R, Grimshaw G, Hine C, Khunti K, Wilson A, Woodward G, (2001) *Clinical guidelines and evidence review for Type 2 diabetes: Diabetic retinopathy: early management and screening*. Sheffield: ScHARR, University of Sheffield.

This document is also available at <http://www.shef.ac.uk/guidelines/>

## **Partner Organisations**

The Royal College of General Practitioners

Diabetes UK

The Royal College of Physicians

The Royal College of Nursing

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# Preface

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Type 2 diabetes is affecting increasing numbers of people in the United Kingdom. Although its management can sometimes seem straightforward, the burden of serious complications and their sequelae may be considerable both for the individual concerned and for the health care services in general.

Nevertheless, many aspects of these complications can be ameliorated, even prevented in some instances, with good management of the condition. The aim of the Type 2 diabetes guideline series is to provide guidance about managing Type 2 diabetes for the whole range of clinical staff who work in primary and secondary care. This guideline and evidence review on the early management and screening of diabetic retinopathy is part in a series that also addresses other key aspects of Type 2 diabetes care: foot care, renal care, lipids management; management of blood pressure; and blood glucose management. Summary guidelines will be published by the National Institute for Clinical Excellence (NICE). The foot care guideline has already been published by the Royal College of General Practitioners.

This document comprises the clinical practice recommendations and the evidence review undertaken to support the development of the early management and screening of diabetic retinopathy guideline. It also contains several recommendations for areas of research, identified by the retinopathy working group. For whilst the scientific literature contains a vast amount of research conducted about diabetes, relatively little of that research was found to be useful in addressing key clinical questions that health care professionals and patients ask about retinopathy management and screening in people with Type 2 diabetes.

These national guidelines have brought, in an explicit way, the available international research evidence together with the experience of a considerable number of health care professionals and patient representatives with substantial experience of managing Type 2 diabetes. This combination of scientific literature, professional and patient experience has produced both an evidence base and set of recommendations that can be used as they stand, or can provide the starting point for local adaptation of the guidelines.

The clinical guidelines and evidence review were constructed by a multi-professional, multi-agency collaboration. The process was led by the Royal College of General Practitioners Effective Clinical Practice Programme at its Unit based in the School of Health and Related Research at the University of Sheffield. It would not have been possible to undertake this project without the very considerable work of all the individual health care professionals and university staff, patients and their representatives who took part in the project. The support of the National Institute of Clinical Excellence and the various collaborating organisations and agencies was also a key element of allowing this work to be undertaken. I would like to thank them all.

Professor Allen Hutchinson  
Programme Director

# 1. Method of guideline development

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# The national clinical guideline for Type 2 diabetes

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The national clinical guideline for Type 2 diabetes is comprised of a series of six inter-related guidelines that deal with different aspects of Type 2 diabetes. Throughout this document the entire series of guidelines is referred to as ‘the national guideline’. The aim of the national guideline is to provide recommendations to assist health care professionals in their management of people with Type 2 diabetes and is aimed at all health care professionals providing care to people with diagnosed Type 2 diabetes in primary and secondary care, irrespective of location. Depending on the type, stage and severity of clinical problem, the guidelines may also be valuable to those who work in the tertiary sector of diabetes care.

The constituent guidelines deal with the following areas within Type 2 diabetes:

- ◆ foot care: prevention and management (Hutchinson et al, 2000a)
- ◆ retinopathy (diabetic retinopathy: early management and screening)
- ◆ renal care (renal disease: prevention and early management)
- ◆ lipids management
- ◆ blood pressure management
- ◆ blood glucose management, including patient education

This section outlines the methodological approach that is taken to develop the national clinical guideline for Type 2 diabetes. The overall approach is the same for each constituent guideline (renal care, retinopathy etc). Where any variation in the process has occurred then this will be noted.

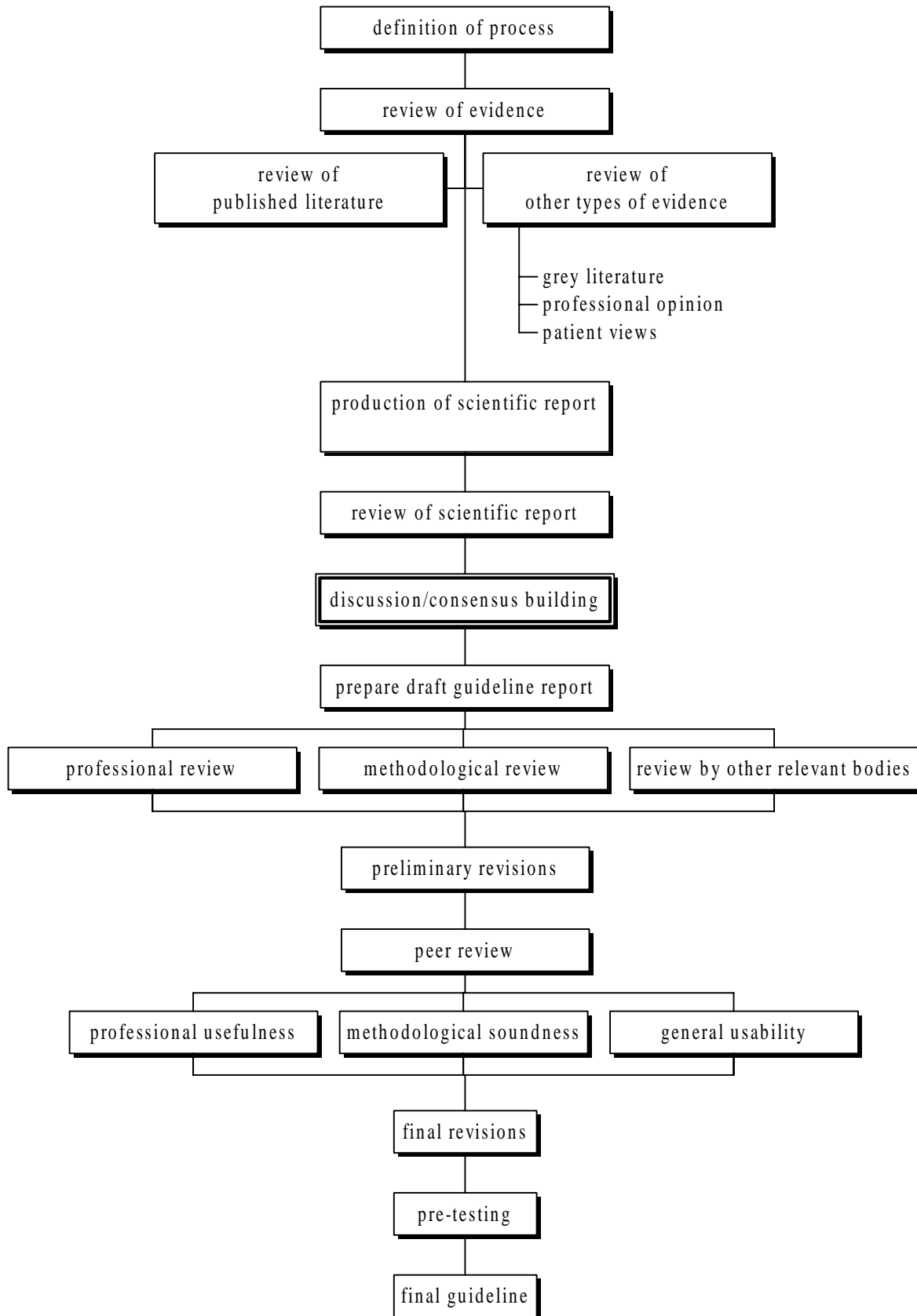
Each constituent guideline is developed and presented in such a way that they can stand as independent guidelines as well as part of the complete series that make up the national guideline.

Key features of the national guideline include:

- it is evidence based, where evidence is available
- in areas where evidence is lacking this is made clear, and the consensus methods used to derive recommendations are clearly described
- recommendations are explicitly linked to evidence where it is available
- the recommendations, methods and conclusions in the guideline are explicit and transparent.

The key steps taken to develop a guideline are outlined in Figure 1.

# Figure 1: Outline of guideline development process





# Scope of the national guideline for Type 2 diabetes

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The national guideline aims to cover the clinical care and management of people with diagnosed Type 2 diabetes. It does not cover people who have not been diagnosed as having Type 2 diabetes, for example those in a pre-diabetic state or people with impaired glucose tolerance or care in pregnancy. Nor does it cover issues concerned with screening for undiagnosed cases of Type 2 diabetes.

In each of the clinical areas covered by the national guideline, scoping exercises were undertaken in order to:

- develop pathways of care for the clinical areas in Type 2 diabetes
- develop key clinical questions for the constituent guidelines to address
- provide a useful mechanism for checking that all areas considered relevant were covered

For foot care, retinopathy, renal disease and glucose management, the pathways were initially developed by members of the Recommendations panel. These were further developed and refined by the Clinical working groups in each concerned area. For lipids and raised blood pressure, the pathways were developed from the outset by the Clinical working groups in each of these areas.

## Note on nomenclature

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Throughout the guideline documents we have used the classifications recommended by the World Health Organisation (WHO) (1999) and the American Diabetes Association (2001). Diabetes UK has recommended adoption of this classification (Diabetes UK, 2000, [www.diabetes.org.uk](http://www.diabetes.org.uk)).

Type 2 diabetes is described by the WHO Consultation as follows:

Type 2 (diabetes) is the most common form of diabetes and is characterised by disorders of insulin action and insulin secretion, either of which may be the predominant feature. Both are usually present at the time that this form of diabetes is clinically manifest. By definition, the specific reasons for the development of these abnormalities are not yet known.

The WHO Consultation document goes on to say:

Diabetes mellitus of this type previously encompassed non-insulin dependent diabetes, or adult onset diabetes. It is a term used for individuals who have relative (rather than absolute) insulin deficiency. People with this type of diabetes frequently are resistant to the action of insulin. At least initially and often throughout their lifetime, these individuals do not need insulin treatment to survive. This form of diabetes is frequently undiagnosed for many years because the hyperglycaemia is often not severe enough to provoke noticeable symptoms of diabetes. Nevertheless such patients are at increased risk of developing macrovascular and microvascular complications.

Where journal papers and other works are discussed in this guideline, the nomenclature that has been used in the original papers has been left unchanged. Therefore most papers cited in these guidelines refer to non-insulin dependent diabetes (NIDDM) and insulin dependent diabetes (IDDM), rather than Type 2 or Type 1 diabetes.

We acknowledge that it is now recognised that some children suffer from Type 2 diabetes (Fagot-Lampagna et al 2000). However, these guidelines refer only to the management of adults with Type 2 diabetes.

# Responsibility and support for the guideline

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## Responsibility

The national clinical guideline was developed under the direction of the Royal College of General Practitioners Effective Clinical Practice Programme, Director: Professor Allen Hutchinson, ScHARR, University of Sheffield.

## Funding

The guideline was developed with funding from the National Institute for Clinical Excellence (who took over responsibility for the National Health Service Executive, Guidelines Development Programme, with whom funding was originally agreed). Additional funding was provided by Diabetes UK (formerly British Diabetic Association).

The National Institute for Clinical Excellence is associated with the National Clinical Guideline for Type 2 Diabetes, produced by The Royal College of General Practitioners Effective Clinical Practice Unit through a funding contract. This arrangement provides the Institute with the ability to secure value for money in the use of the NHS funds invested in this organisation's work and enables the Institute to influence topic selection, methodology and dissemination practice. The Institute considers the work of this organisation to be of value to the NHS in England and Wales and recommends that it be used to inform decisions on service organisation and delivery.

This publication represents the views of the authors and not necessarily those of the Institute.

## Using the guideline

Guidelines are only one type of information that health care professionals may use when making decisions about patient care. It is assumed that this guideline, like all guidelines, will be used by health care professionals who will also bring to bear their clinical knowledge and judgement in making decisions about caring for individual patients. It may not always be appropriate to apply either specific recommendations or the general messages in this document to each individual or in every circumstance. The availability of resources may also influence decisions about patient care, including the adoption of recommendations.

The review date of this guideline is three years from publication date, by which time new, relevant results may be available that may affect the recommendations within the guideline.

# Project structure

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There were many groups and individuals involved in the development of the national clinical guideline (see Figure 2, Project Structure page 13). Some groups were concerned with clinical areas (the working groups), others were concerned with the management and quality assurance of the guideline development process or with other important aspects related to the guideline such as implementation and patient involvement. Different groups were involved in the stages outlined in Figure 1 to different amounts and their roles are described below.

## Recommendations panel

The Recommendations panel had ultimate responsibility for ensuring that a valid, relevant and rigorous national clinical guideline is produced as a result of the guideline development process. It had the key role in ensuring that all areas are covered, both in those areas covered by the Clinical working groups and also in areas of care which do not neatly sit in any particular group. The Recommendations panel also ensured that issues pertinent across all Clinical working group areas, for example issues of risk for people with Type 2 diabetes, were adequately covered. The working groups in the clinical areas presented their recommendations, comments and views to this group, who had to ensure that recommendations were consistent in terms of the overall wording, presentation and clinical coherence. They were also responsible for agreeing the final grading of the recommendations. The Recommendations panel also had a central role in shaping what the overall national guideline looked like and, as such, the panel also acted as a quality control mechanism.

## Clinical working groups

Six groups were concerned with specific clinical areas within Type 2 diabetes care. The six Clinical working groups were:

- foot care (prevention and management of foot problems)
- retinopathy (early management and screening )
- renal care (renal disease: prevention and early management)
- lipids management
- management of raised blood pressure
- blood glucose management

The Clinical working groups consisted of members of the project team (guideline methodologists, small group facilitators and systematic reviewers) together with practitioners and content experts. The chair of each group was also a member of the Recommendations panel. The groups were given remits to:

- formulate the key questions to be considered by both the evidence reviews, and the guideline, in their clinical area
- consider the evidence (both that which is presented to them and any additional evidence that the group identifies as relevant and meeting quality criteria)
- consider and comment on the evidence review (undertaken by project team members)
- draft recommendations in their clinical area, for consideration by the Recommendations panel
- consider comments from the recommendations panel (and other internal reviewers) and review their recommendations if necessary
- consider external feedback from the development process, particularly from the NICE stakeholder reviews, and to make any necessary amendment proposals to the Recommendations panel

## Project management group

The project management group oversaw the progress of the development of all the constituent guidelines (and thus the overall national guideline), and the whole project in general. This group dealt with management and policy issues within the project.

## Advisory group

The advisory group consisted of representatives from the concerned professions, Diabetes UK, Royal Colleges and similar bodies. It offered advice and assistance on the general direction, quality and policy issues surrounding the development of the guideline. It met approximately every 6 months.

## Systematic reviews group

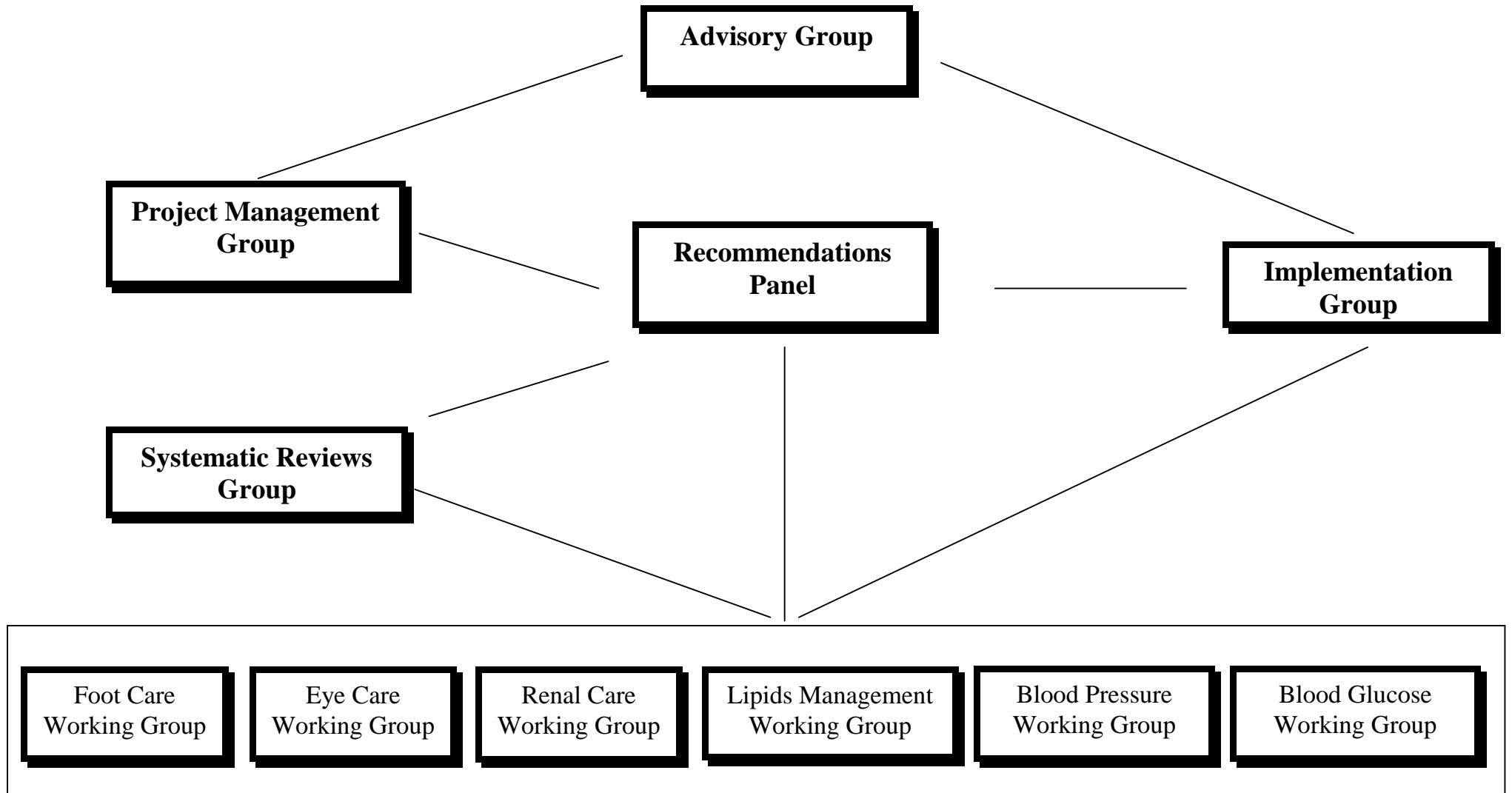
The systematic reviews group offered advice and comment on the systematic reviews being undertaken for the guideline, ensuring that rigorous methodology was employed. It was therefore a quality assurance mechanism.

## Patient organisation involvement

Diabetes UK had representation on the Advisory Group and Recommendations panel. It also had representation on individual Clinical working groups, and is represented in the review process.

## Figure 2: Project structure

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# Aim and scope of the retinopathy guideline

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This guideline is aimed at all health care professionals providing eye care to people with diagnosed Type 2 diabetes in primary and secondary care, irrespective of location of care facilities. The guideline is not primarily aimed at health care professionals working in the tertiary care sector of diabetes eye care, although it may be useful to them.

The initial scope of this guideline was defined by the retinopathy working group, which identified clinical areas and issues that it considered important in the early management of diabetic retinopathy.

The recommendations are:

- ◆ evidence based wherever possible;
- ◆ explicitly linked to evidence where available;

and in some areas, where evidence is not available;

- ◆ recommendations are based on consensus of the development group(s). These are clearly stated as such.

The retinopathy management guideline focuses on the primary detection and early management of retinopathy, especially the sight threatening forms of the disease which require action, in particular, referral. It does not cover areas of surgical management for proliferative retinopathy and severe macular oedema, such as laser treatment.

## Note on classification of retinopathy

The terms used in describing retinopathy, such as background, proliferative and preproliferative are not defined by every individual and organisation/association in exactly the same way. Whilst there is some level of agreement it is not total. A new classification and grading system is currently under consideration.

In this document we have used the terms given by the authors in the papers identified and extracted. In some instances only a term was given, in other instances details (such as presence of cotton wool spots) were given and in yet other instances a classification system (e.g. Airlie House) was cited. We have also tried to give descriptions of signs (e.g. presence or absence of exudates) in recommendations and other instances where more details are required.

We recognise that the adoption of a new classification system may help these anomalies of terminology in the future. However, currently several classification systems are used and that this may continue at least for a time after any new system is introduced.

# Areas of care considered by the evidence review

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These were

- ◆ **Screening method**
  - ◆ effectiveness
  - ◆ cost
  - ◆ patient preference
- ◆ **Professional performing screening method**
  - ◆ effectiveness
  - ◆ cost
  - ◆ patient preference
- ◆ **Location of screening**
  - ◆ effectiveness
  - ◆ cost
  - ◆ patient preference
- ◆ **Classification of patient on result of screen**
- ◆ **Screening interval**
  - ◆ risk factors
- ◆ **Risk factors and speed of progression**

In the construction of this guideline the structuring of the evidence review is primarily based on the screening/review methods and on the type of health professional undertaking the task.

Where available, evidence on cost and patient preference, training standards for screening and population coverage are taken into account in the recommendations, although these issues relate principally to population screening programmes rather than to the individual clinical practice issues which this guideline addresses.

# Evidence identification and grading

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## Search strategies

The search strategies attempted to locate systematic reviews and meta analyses, randomised trials, other comparative studies, quality of life studies and economic studies using a combination of subject heading and free text searches. Extensive use was made of high quality recent review articles and bibliographies, as well as contact with subject area experts. The search strategy was also backed up by the expert knowledge and experience of group members. Searches were limited to English language citations.

The following bibliographic databases were searched using an optimally sensitive search strategy of subject headings and text words:

- ◆ Cinahl
- ◆ Cochrane Trials Register
- ◆ Embase
- ◆ Healthstar
- ◆ Medline
- ◆ Psyclit
- ◆ Science Citation
- ◆ Social Science Citation
- ◆ HEED
- ◆ NHS Economic Evaluation Database for Economic Evaluations
- ◆ ECRI HTAIS

Trial registers were searched for ongoing and unpublished trials and conference proceedings were examined using the Index to Scientific and Technical Conference Proceedings (ISI). Access to 'grey literature' was through HMIC database and SIGLE.

Studies covering both Type 1 and Type 2 diabetes were eligible for inclusion if they specifically addressed screening for, and early management of, diabetic retinopathy. Studies were included:

1. if they were prospective in design;
  2. compared at least one screening method in a blinded fashion with a reference standard
- and
3. all patients included in the study had the reference standard examination.

All databases were searched from 1983 onwards and the main review was completed by July 1999, although some more recent cost utility papers on screening methods have been included.

Assessment and grading of papers retrieved was conducted independently by two reviewers and disagreements were resolved by discussion. The papers were graded according to their study design, using the AHCPR grading hierarchy (AHCPR 1992). For the purposes of this review manuscripts awaiting publication have been excluded. Full details of the search strategies are available from the authors.

# Evidence grading

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Evidence grading (and consequent recommendation grading) is particularly problematic in the assessment of the retinopathy screening papers identified in the review, since the use of the AHCPR evidence grading framework (*see below*) must result in a maximum grading level of III for screening (non-experimental, descriptive) studies, no matter what their quality or appropriateness.

## Classification of Evidence

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Evidence level	Description
<b>Ia:</b>	evidence from meta-analysis of randomised controlled trials
<b>Ib:</b>	evidence from at least one randomised controlled trial
<b>IIa:</b>	evidence from at least one controlled study without randomisation
<b>IIb:</b>	evidence from at least one other type of quasi-experimental study
<b>III:</b>	evidence from non-experimental descriptive studies, such as comparative studies, correlation studies and case-control studies
<b>IV:</b>	evidence from expert committee reports or opinions and/or clinical experience of respected authorities

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Adapted from Agency for Health Care Policy and Research (1992) *Acute Pain Management: Operative or Medical Procedures and Trauma* Agency for Health Care Policy and Research / US Department of Health and Human Services, Public Health Service, Rockville, MD

# Recommendation grading

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By current convention a level III evidence study must attract a recommendation grading of C or D (see below).

## Grading of Recommendations

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- A** directly based on category I evidence
  - B** directly based on category II evidence, or extrapolated recommendation from category I evidence
  - C** directly based on category III evidence, or extrapolated from category I or II evidence
  - D** directly based on category IV evidence, or extrapolated from category I, II or III evidence
- 

From Eccles M et al (1998) North of England Evidence Based Guideline Development Project: guideline for angiotensin converting enzyme inhibitors in primary care management of adults with symptomatic heart failure *BMJ* **316**: 1369

This direct linking of recommendation grade to evidence level may not be helpful in clinical practice terms since important clinical practice issues may be graded, for instance, C or D, and this might be mistaken by the occasional reader as a recommendation *weighting* rather than as the resultant of evidence grading. An example of this in the retinopathy guideline is the strongly held view in the Recommendations panel and the Clinical working group on the classification of eye care as routine, early review or referral. This is thought to be clinically important but the evidence grading is IV and the recommendation grading is D.

## Synthesis of the studies

Overall, and with one or two notable exceptions, the studies included were generally of small numbers of cases or professionals, as can be seen from the individual evidence tables. Furthermore, there was considerable variation in the outcome measures used by the authors of the different studies identified in the review process, these being: any retinopathy, background (or non-proliferative) retinopathy, sight threatening retinopathy, referable retinopathy, proliferative retinopathy and serious retinopathy. Although an initial attempt was made to regroup the studies into a classification framework such as background or proliferative retinopathy, or as background, sight threatening or referable retinopathy, the individual studies did not usually provide enough information to support reclassification. The original study classifications are therefore used in the results of the review.

Studies of screening and early detection would normally have a reference standard against which to assess the effectiveness of the test in question. Such reference standards against which to assess the effectiveness of screening methods for detecting retinopathy would ideally be a 'gold standard' test such as seven-field stereoscopic fundus photography or fluorescein angiography (Bachmann and Nelson 1996), but these tests are not usually feasible in clinical practice. Moreover, there proved to be a variety of reference standards used in the studies that made comparison of results between studies difficult. For example, some studies included a standard of ophthalmologists using ophthalmoscopy, retinal photography or a combination of both. Other reference standards included assessment by diabetes physicians, whose level of experience in screening for retinopathy may have been considerable but was unreported, or trained graders of retinal photographs working from reading centres. For these reasons, a quantitative meta-analysis of the studies was deemed inappropriate.

Because the great majority of the studies included in the review were screening studies it was necessary to decide on a standard for an acceptable level of sensitivity and specificity for the screening tests for diabetic retinopathy. Although no formal standard exists, the British Diabetic Association (1997) (now Diabetes UK) has proposed levels of at least 80% sensitivity and 95% specificity and the Recommendations panel agreed that these were appropriate. This standard is used in the review as the basis for assessing the effectiveness of the screening/monitoring tests used in the management of diabetic retinopathy.

At the time of going to press there are active discussions in the UK on proposals for a new classification system for diabetic retinopathy. No formal proposals have yet been agreed nationally.

## Areas without consensus

There may be areas where the group was unable to reach consensus on an area, no matter whether evidence is available or not. Where this has happened there is scope to report that a consensual recommendation could not be reached, to present the opposing views, and leaving the final view to the user of the guidelines

## Review of the guideline

This guideline was reviewed in two rounds through public stakeholder consultation, after the methods proposed by the National Institute for Clinical Excellence. In addition, external content expert review was sought from 5 national and one international expert. These responses were collated and important issues of evidence and clinical practice were considered by the retinopathy working group.

## Acknowledgements

The developers would like to acknowledge the help received from the Section of Information Resources, ScHARR, University of Sheffield for their substantial contribution to the systematic reviews undertaken in the development of the diabetic retinopathy: early management and screening.

Additional reviewing by the NHS Centre for Reviews and Dissemination, University of York for their Effective Health Care Bulletin, Complications of diabetes: screening for retinopathy; management of foot ulcers, was also used in this evidence document. We are grateful for their help with this.

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# 2. Principal recommendations

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## Early management

### Eye care for all people with diabetes

- ◆ Arrange recall and annual review of all people with Type 2 diabetes (D)
- ◆ Maintain good blood pressure control (at or below 140/80mm Hg) (A)
- ◆ Maintain good blood glucose control (preferably below HbA<sub>1c</sub> 6.5% - 7.5% according to individual's target) (A)
- ◆ Examine eyes at the time of diagnosis and at least annually thereafter (including in people who are registered blind and partially sighted) (D)
  - ◆ check visual acuity, corrected with glasses or pinhole (D)
  - ◆ examine for diabetic retinopathy following dilation of pupils with tropicamide (B)
- ◆ Refer patient for opinion if cataracts are interfering with vision or the retina is obscured (D)
- ◆ Classify eye care as: **routine care required** or **early review** required or **referral** required (D)

### Routine care

#### *Review annually if:*

- ◆ there is no retinopathy present (D)
- ◆ there is only minimal or mild background retinopathy/ low risk background retinopathy (D)

### Early review

#### *Review every 3 to 6 months if:*

- ◆ there is occurrence or worsening of lesions since the previous examination (D)
- ◆ there are scattered exudates more than 1 disc diameter from the fovea (D)
- ◆ a person is at high risk of progression  
(that is, where there is rapid improvement in blood glucose control, or the presence of hypertension or renal disease) (D)

# Referral

## Referral within four weeks

*Refer for opinion within 4 weeks if:*

- ◆ there is an unexplained drop in visual acuity (D)
- ◆ there are hard exudates within 1 disc diameter of the fovea (D)
- ◆ macular oedema is present (D)
- ◆ there are unexplained retinal findings (D)
- ◆ pre-proliferative or more advanced (severe) retinopathy is present (D)

## Urgent referral to ophthalmology specialist within one week

*Refer within one week if:*

- ◆ there is new vessel formation (D)
- ◆ there is evidence of pre-retinal and/or vitreous haemorrhage (D)
- ◆ rubeosis iridis is present (D)

## Emergency referral to ophthalmology specialist on the same day

*Refer on the same day if:*

- ◆ there is sudden loss of vision (D)
- ◆ there is evidence of retinal detachment (D)

# Detection and screening

## Detection of diabetic retinopathy

- ◆ Use tests that have been demonstrated to achieve:
  - ◆ sensitivity of 80% or higher
  - ◆ specificity of 95% or higher
  - ◆ technical failure rate of 5% or lower (C)
- ◆ Use either:
  - ◆ mydriatic retinal photography as the first choice, when undertaken and when photographs or images are evaluated by trained personnel (C) *or*
  - ◆ mydriatic slit-lamp indirect ophthalmoscopy, when used by trained personnel (C)
- ◆ Use tropicamide to achieve mydriasis, unless contraindicated (C)

## Screening for diabetic retinopathy

- ◆ Arrange recall and annual review of eyes of people with Type 2 diabetes (D)
- ◆ Perform an appropriate and acceptable retinopathy screening test for all people with Type 2 diabetes (D)
- ◆ Participation in opportunistic screening should not be regarded as an adequate substitute for participation in a formal screening programme. It is an option only if formal screening is not possible (D)

The full recommendations together with accompanying evidence statements are re-presented on pages 44 – 49.

### 3. Screening and early detection of diabetic retinopathy

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# Summary review of evidence

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## Introduction

Diabetic retinopathy is a highly specific microvascular complication of diabetes and the leading cause of blindness in people under the age of 60 in industrialised countries (Williams 1994). It is also a major cause of blindness in older people. After 20 years from the onset of diabetes, over 90% of people with Type 1 and more than 60% of people with Type 2 will have diabetic retinopathy (Klein et al 1984a, Klein et al 1984b). Because of the sight threatening potential of the disease and the availability of methods to slow down the rate of progression of the disease, the UK National Screening Committee has recommended screening for diabetic retinopathy as a national priority (Garvican et al 2000).

The mechanisms underlying diabetic retinopathy are unclear, but the progression of the disease is well known and may take several forms:

The initial stage is background retinopathy which is characterised by capillary microaneurysm formation, dot and blot intraretinal haemorrhages, and lipid exudates. This stage of the disease does not cause visual impairment.

The next stage of the disease process is preproliferative retinopathy, which is characterised by capillary and arteriolar closure.

Finally, proliferative retinopathy develops and is characterised by the growth of new blood vessels from the optic nerve head, or from elsewhere, which may lead to progressive visual impairment caused by scarring and bleeding (Singer et al 1992, Bachmann and Nelson 1996).

A previous review of the literature concluded that there was inconsistent and inconclusive evidence on the most effective methods for screening (Mason et al 1996). More recently, Bachmann and Nelson (1998) pooled the data from many of the available screening studies up to 1996 in their modelling project on the effectiveness of diabetic retinopathy screening programmes, and determined that retinal photography was the screening test of choice. The findings of these previous reviews were updated by a systematic review of the published evidence (Hutchinson et al 2000b), using the framework of clinical questions outlined by the retinopathy working group.

A summary of the evidence is presented here, together with clinical practice recommendations and evidence statements. Further details of the evidence base are presented in Section 6.

# Diabetic retinopathy: screening tests

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In this section are presented the reported sensitivities and specificities extracted from the papers deemed to be of sufficient quality for the review. However, the papers used a number of different reference standards against which the various screening methods were compared and direct comparisons are therefore problematic in some instances (see also page 19).

Full details of the reference standards used for each paper are reported in the tables of results presented in Section 6.

## Ophthalmoscopy

Ophthalmoscopy may be undertaken by either the direct method (used by most doctors in everyday practice) or by the indirect method, used mainly by doctors in more specialist practice and by optometrists/opticians. Figure 3 presents the reported sensitivities, with 95% confidence intervals where available, for different health professionals using ophthalmoscopy to detect various stages of retinopathy in patients with Type 2 diabetes. Figure 4 presents the related specificities. Details on the reference standard against which ophthalmoscopy has been compared for the same studies, the location of the screening, population coverage, and sensitivity and specificity, are to be found in Section 6.

### General practitioners

Overall, results showed that general practitioner test sensitivity levels in the detection of referable, sight threatening, pre-proliferative, proliferative or serious retinopathy were lower than the 80% standard, ranging from 33% to 66%. Analysis is complicated by the fact that the two UK based studies identified (O'Hare et al 1996, Gibbins et al 1998) used different scales for classifying retinopathy from those based in New Zealand and the Netherlands (Lienert 1989, Reenders et al 1992), making direct comparison of the findings impossible.

In a larger study population examining the effectiveness of screening methods (Buxton et al 1991), where a total of 2350 patients were screened in three centres by 318 general practitioners, sensitivity for detecting sight threatening retinopathy ranged from 41% to 67%. However over 70% of the general practitioners did not participate in two of the study centres.

### Opticians and optometrists

Three studies evaluated the effectiveness of screening by opticians or optometrists using dilated ophthalmoscopy (O'Hare et al 1996, Gibbins et al 1998, Buxton et al 1991) while a fourth evaluated the effectiveness of undilated ophthalmoscopy (Klein et al 1985). In two further studies, ophthalmoscopy (including indirect) was used with dilated pupils (Kleinstejn et al 1987, Burnett et al 1998). Sensitivity of detection of referable, proliferative or sight threatening retinopathy ranged from 48% - 100%.

## **Ophthalmologists**

The performance of ophthalmologists using ophthalmoscopy was evaluated in five studies (Kinyoun and Fujimoto 1988, Schatata et al 1993, Pugh et al 1993, Moss et al 1985, Harding et al 1995), four of which included indirect ophthalmoscopy (Kinyoun and Fujimoto 1988, Schatata et al 1993, Pugh et al 1993, Moss et al 1985) and two of which (Kinyoun and Fujimoto 1988, Schatata et al 1993) used any retinopathy as their sole outcome. For sight threatening and proliferative retinopathy, sensitivity of detection was 65% and 79% respectively. The studies evaluated individual ophthalmologists and therefore the generalisability is limited.

## **Other professionals**

The effectiveness of ophthalmoscopy to detect retinopathy in the hands of a number of other health professionals, such as diabetologists, nurses, junior doctors, hospital physicians, and technicians has been examined in a number of studies. One limited study evaluated the effectiveness of a single diabetologist carrying out ophthalmoscopy (type not stated) (Forrest et al 1987), while a second evaluated diabetologists using dilated ophthalmoscopy (Lienert 1989). Sensitivities ranged from 27% to 81% in detecting serious or proliferative retinopathy.

Buxton et al (1991) evaluated the effectiveness of hospital physicians undertaking retinopathy screening using dilated ophthalmoscopy. Although this was a multi-centre study, hospital physicians were only used as screeners in one centre so any potential variation in screening performance between centres could not be measured. Junior hospital physicians were reviewed using dilated ophthalmoscopy in another study (Lienert 1989). In neither study did sensitivity reach the 80% level.

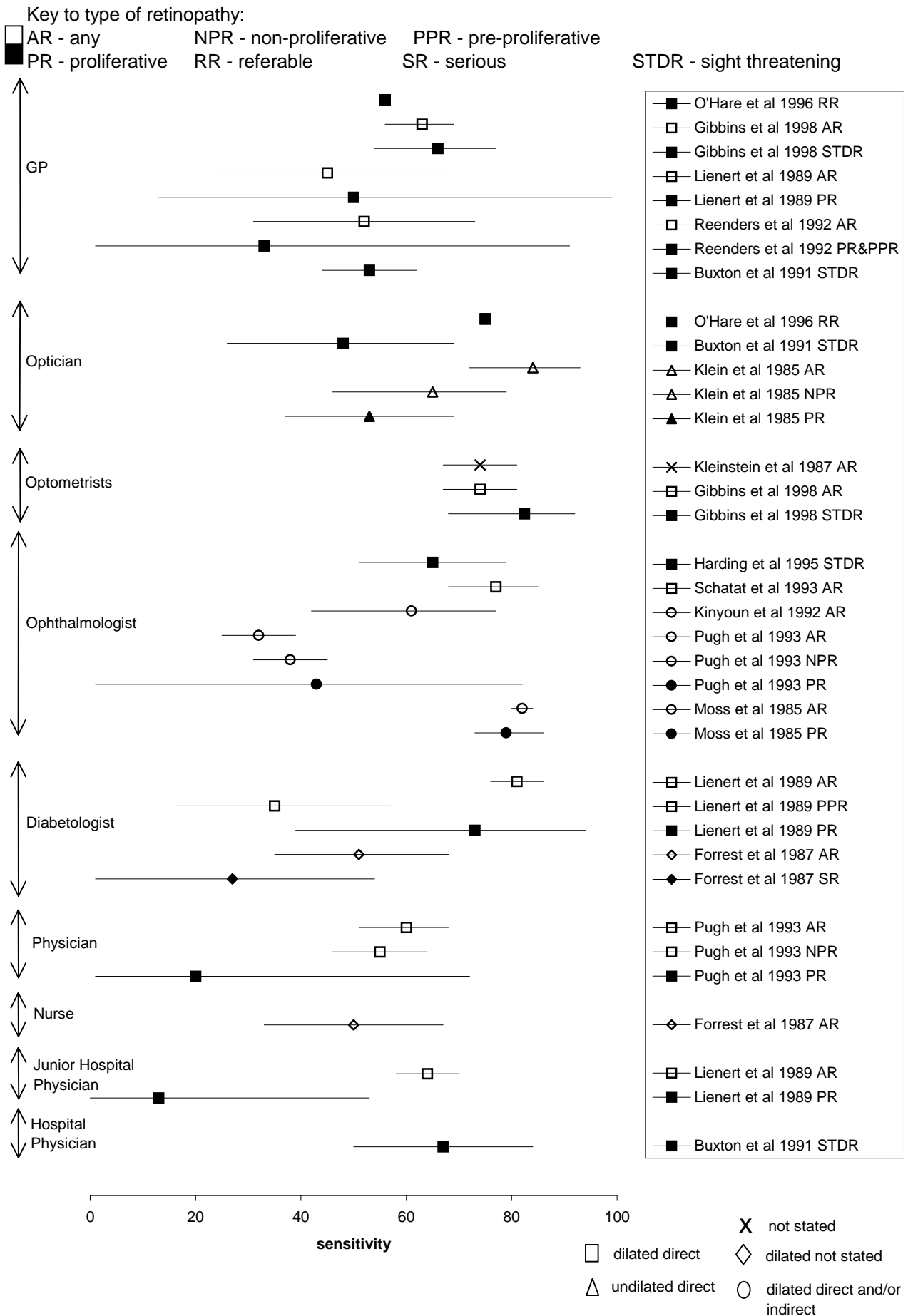
Nurse practitioners or technicians using dilated ophthalmoscopy, when screening for the combined outcome of moderate to severe non proliferative retinopathy and proliferative retinopathy, had very low sensitivity at 14% (Pugh et al 1993). In another study (Forrest et al 1987) the sensitivity of a single nurse practitioner using ophthalmoscopy (type not stated) to detect serious retinopathy was 55%.

## **Summary**

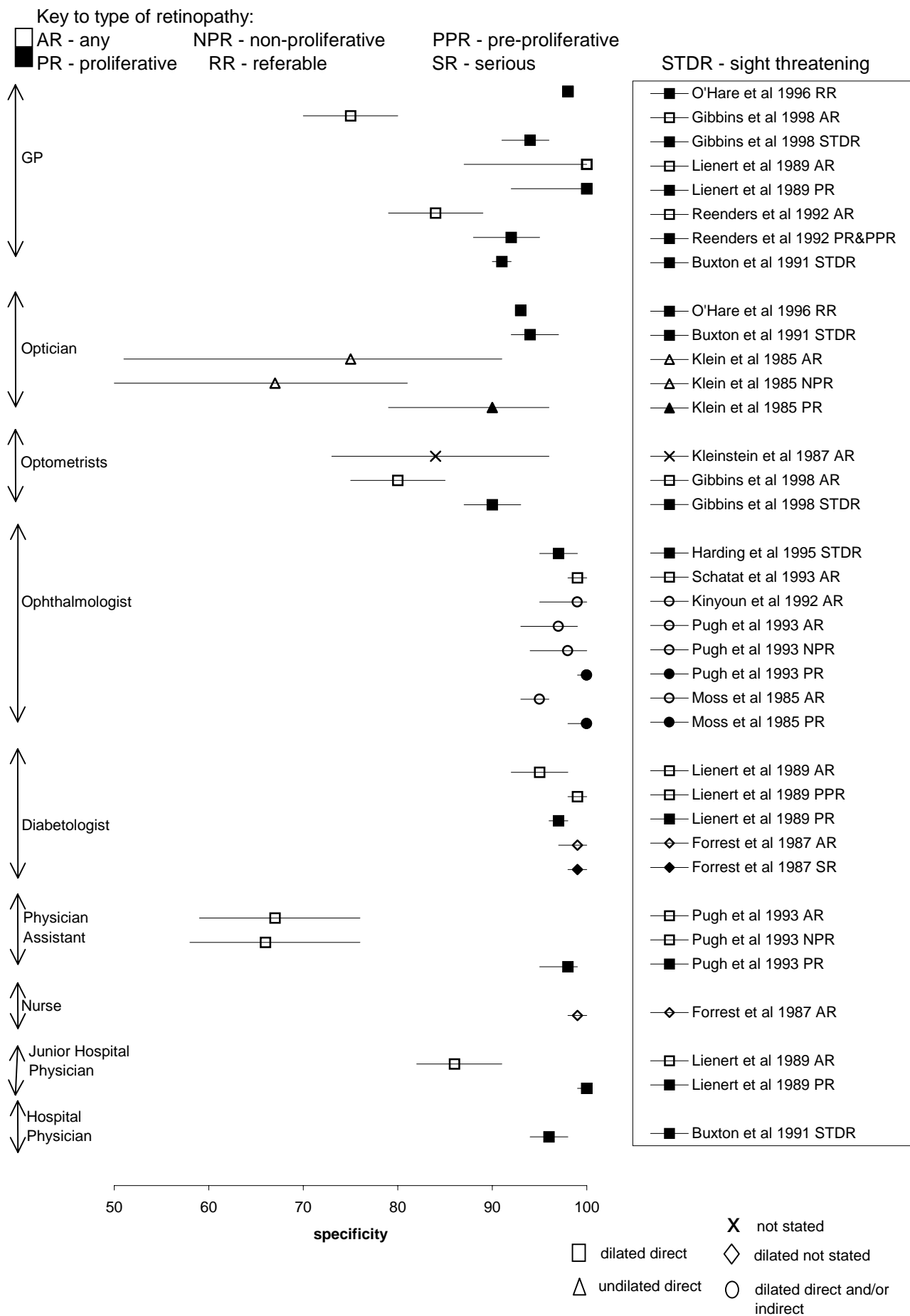
In screening for any sight threatening retinopathy, using outcomes of proliferative, or serious, referable, or sight threatening, the specificities achieved were higher than 91% (review standard 95%), while there was a much greater spread for sensitivity with only one study reaching the 80% sensitivity standard.

Overall, the studies demonstrate that direct ophthalmoscopy does not usually meet the required standards for retinopathy screening and review. There is some limited evidence that professionals using indirect slit-lamp ophthalmoscopy can achieve the required standards.

**Figure 3: use of ophthalmology: reported sensitivities**



**Figure 4: use of ophthalmology: reported specificities**



## 45 degree retinal photography

Figure 5 presents the reported sensitivities, with 95% confidence intervals where available, from a range of studies examining the effectiveness of different professionals using retinal photography, or reading or using the results from retinal photographs, in the detection of a number of retinopathy outcomes. Figure 6 (page 35) presents the specificities for the same studies. Details of the reference standard against which the retinal photographs were compared, the location used and the population coverage are to be found in Section 6.

In general, for retinal photography, the specificities achieved are lower than those obtained with ophthalmoscopy. However, the reported sensitivities are higher than those seen for ophthalmoscopy and it is the absolute level of sensitivity and the balance between sensitivity and specificity which are the important constituents of the decision on effectiveness and cost effectiveness of the screening/review method.

### General practitioners

Of the three studies that assessed general practitioners reading mydriatic retinal photographs (Gibbins et al 1994, Gibbins et al 1998, Van der Kar et al 1990), one used instant film photographs (Van der Kar et al 1990) while the other two used 35mm film (Gibbins et al 1994, Gibbins et al 1998). Sensitivity ranged from 87% to 100% between the three studies in the detection of proliferative, sight threatening or referable retinopathy. There were no studies of general practitioners using non-mydriatic 45 degree retinal photographs.

### Opticians/optometrists

In a single study (Gibbins et al 1998), mydriatic 35mm photographs were taken at general practices and later assessed by optometrists, who achieved a level of sensitivity of greater than 91% in the detection of sight threatening retinopathy.

### Ophthalmologists/ophthalmologist assistants

Two UK studies evaluated the sensitivity and specificity of photographs read by ophthalmologists or their clinical assistants. In the first, non-mydriatic photographs were used with instant colour film or 35mm photographs read by two ophthalmologist assistants (Williams et al 1986). In the second study, mydriatic 35mm retinal slides were read by an ophthalmology clinical assistant but 14% of photographs were ungradeable (Harding et al 1995). Little variation was found in sensitivity between the two studies (89% to 93%).

### Other professionals

A number of other professionals including independent graders and diabetologists have also been evaluated in screening for retinopathy using retinal photography. Three studies evaluated non-mydriatic retinal photography assessed by trained independent graders (Penman et al 1998, Klein et al 1985, Pugh et al 1993) whilst in two of the same studies, mydriatic 35mm photographs were also read, although the outcomes used were different in the latter two studies (Klein et al 1985, Pugh et al 1993). The type of film was not stated in one of the studies (Penman et al 1998) and nor was the location stated in two (Penman et al 1998, Klein et al 1985). Furthermore, in the study by Penman et al 1998, 22% of the photographs were classified as ungradeable. Sensitivities for the detection of sight threatening or proliferative retinopathy in two of the studies (Penman et al

1998, Klein et al 1985) ranged from 60% to 98%, while in the third (Pugh et al 1993) sensitivities ranged from 25% to 50%.

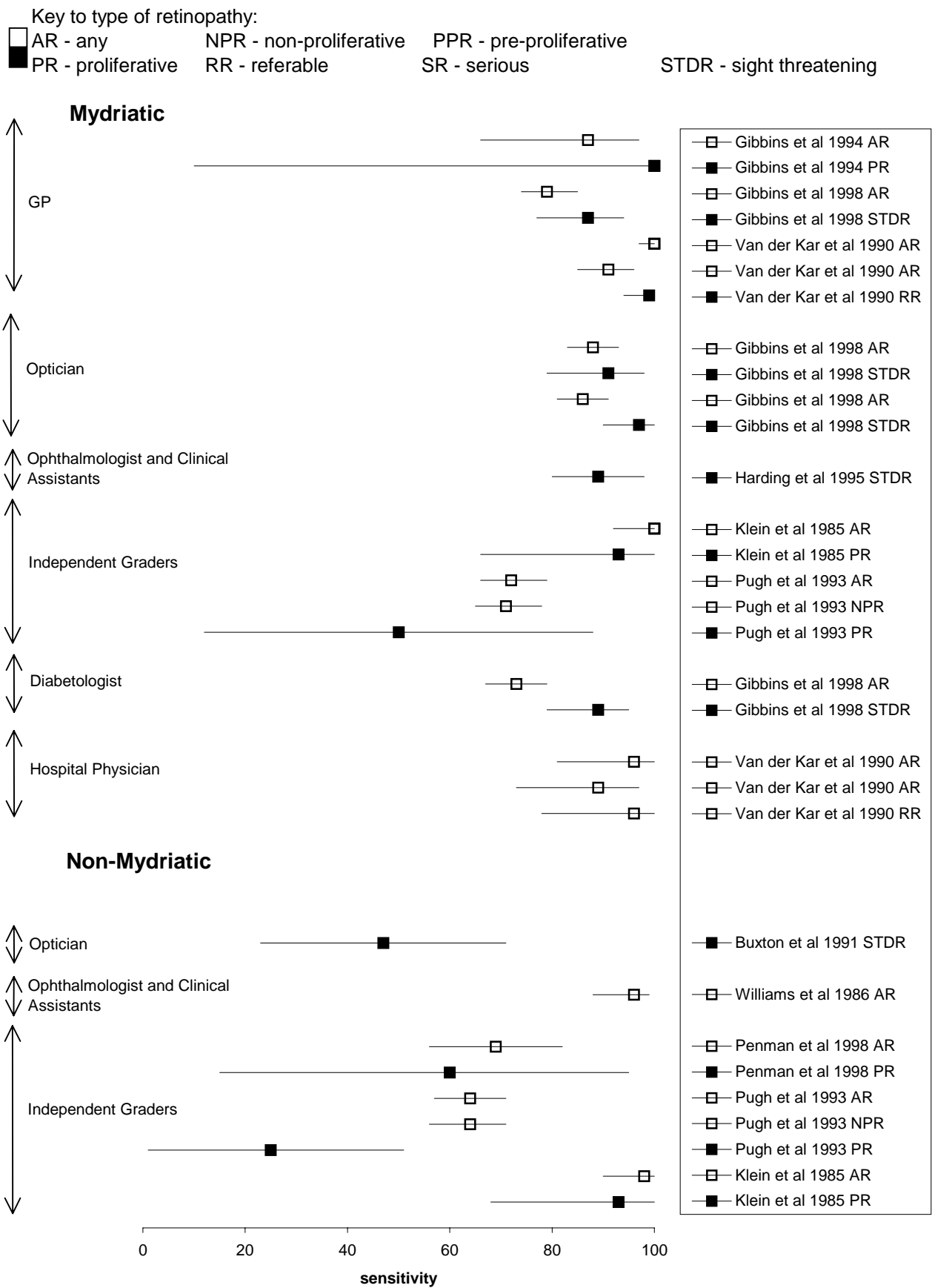
Mydriatic retinal photography with 35mm film was assessed by four diabetes specialists in one study (Gibbins et al 1998), which achieved sensitivities for the detection of sight threatening retinopathy of 89%.

Retinal cameras are now being developed that use digital imaging techniques to produce an instant enlarged retinal image on a computer monitor screen. Good agreement in grading non-sight threatening retinopathy and sight threatening retinopathy was found between digital images and 35mm colour transparencies, both read by a diabetes physician, in 40 patients with known diabetic retinopathy (George et al 1998). There was complete agreement in grading retinopathy between the two methods, in 93% of eyes.

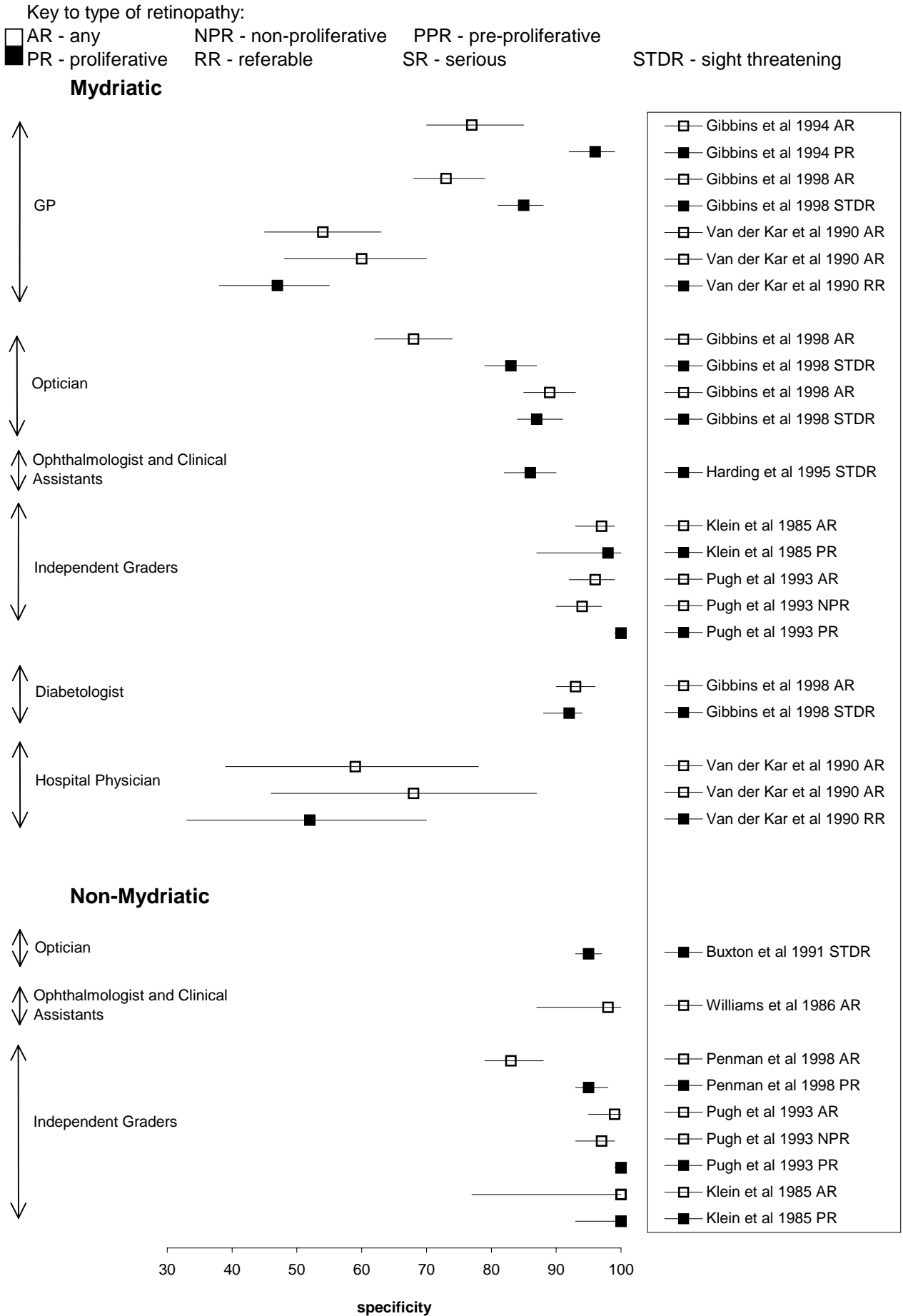
In the detection of sight threatening retinopathy Ryder et al (1998a) compared digitized optical images with instant film prints, both read by a diabetes physician experienced in grading photographs. Digital images, when read by an experienced observer, detected 34 eyes with sight threatening retinopathy, compared to 24 using instant film prints. This study lacked a reference standard to compare the accuracy of the diagnoses.

Both studies provide promising evidence about digital imaging, but they are small and further evaluation is needed against acceptable reference standards.

**Figure 5: retinal photography: reported sensitivities**



**Figure 6: retinal photography: reported specificities**



## Ophthalmoscopy combined with 45 degree retinal photography (non-mydriatic or mydriatic)

Figure 7 shows the reported sensitivities and specificities for different professionals using ophthalmoscopy combined with 45 degree retinal photography in the detection of one or more retinopathy outcomes. Details on the reference standard used, the location and the population coverage are to be found in Section 6.

In one study (Sculpher et al 1991) the accuracy of general practitioners using ophthalmoscopy and 45 degree non-mydriatic photography read by an ophthalmologist, compared with general practitioners using ophthalmoscopy alone, was assessed by classifying a positive result from either method as a positive diagnosis. Sensitivity for the combined methods improved from 53% for general practitioners using ophthalmoscopy alone to 80% using the combined method. In a second study (O'Hare et al 1996), a small improvement in sensitivity from 56% to 60% was demonstrated by general practitioners in detecting referable retinopathy using ophthalmoscopy in combination with 45 degree mydriatic retinal photography, in contrast to direct ophthalmoscopy alone.

Screening by opticians using ophthalmoscopy and non-mydriatic photographs read by an ophthalmologist also resulted in greater sensitivity for detecting sight threatening retinopathy, at 67% compared to 47% for opticians using ophthalmoscopy alone (Sculpher et al 1992).

Finally, two studies assessed opticians or optometrists using ophthalmoscopy and mydriatic retinal photography (O'Hare et al 1996, Ryder et al 1998b). O'Hare et al 1996 evaluated a combined method of opticians using ophthalmoscopy and mydriatic 45 degree retinal photography. In the detection of sight threatening retinopathy the combined method had higher sensitivity at 88% than that for opticians using ophthalmoscopy alone, at 73%. In the study by Ryder et al (1998b), a single hospital-based specialist optometrist examined mydriatic retinal instant film photographs combined with ophthalmoscopy except where the photographs were perfect and definitely showed no retinopathy. The sensitivity of detection of sight threatening retinopathy was 100%.

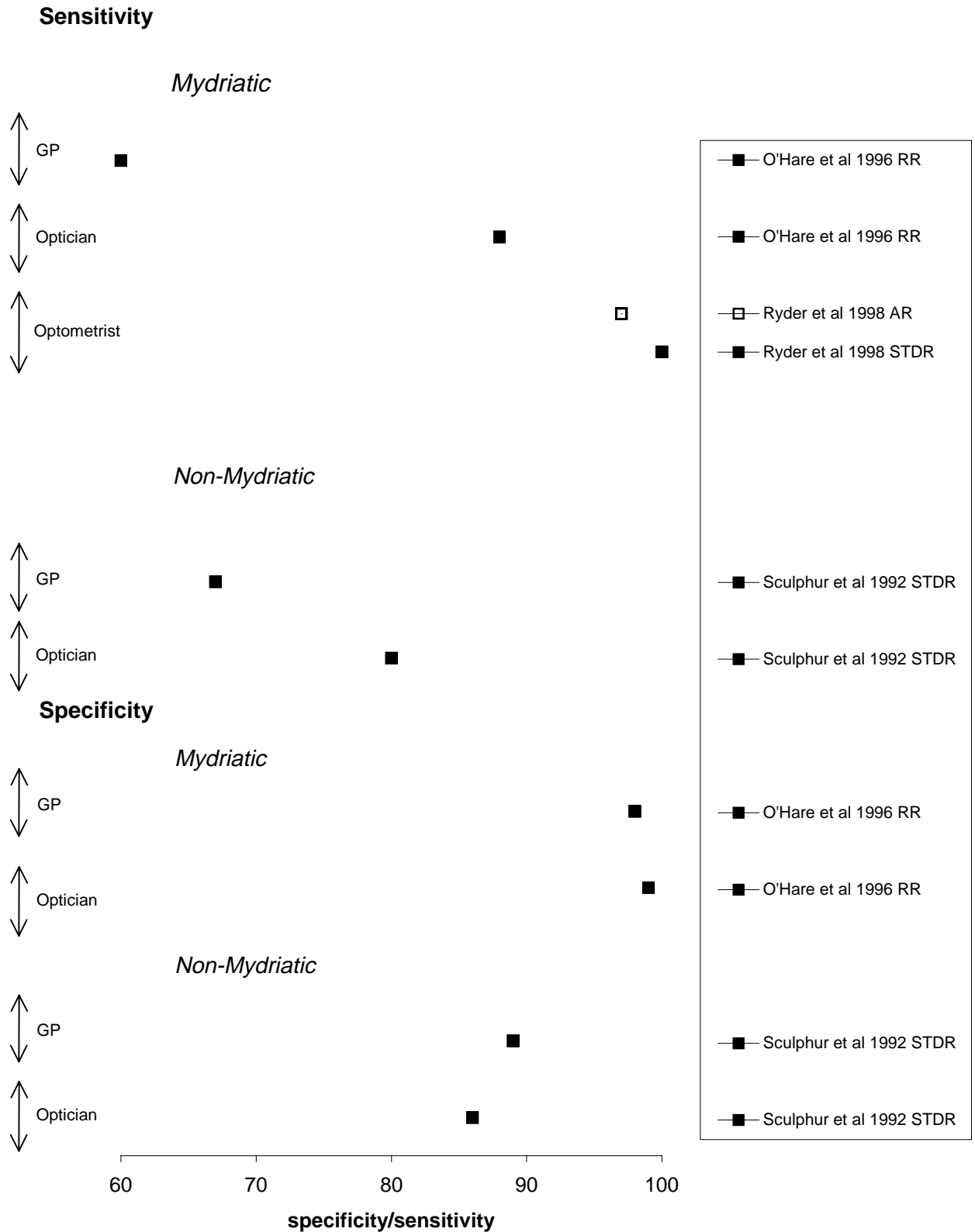
### Summary

Studies of the use of 45 degree retinal photography, and subsequent reading of films by trained staff, demonstrate that it is possible to reach an acceptable standard of clinical practice with such methods. These results are not dependent on the type of professional involved but do emphasise the need for training in reading the photographs or images. Studies of ophthalmoscopy used in conjunction with retinal photography show that in some hands, although retinal photography reaches an acceptable standard of sensitivity and specificity, direct ophthalmoscopy reached by the user is still below standard. Ophthalmoscopy should not therefore be the method of choice of most professionals for screening/review of retinopathy.

**Figure 7: ophthalmoscopy combined with 45° retinal photography**

Key to type of retinopathy:

- AR - any                      NPR - non-proliferative                      PPR - pre-proliferative
- PR - proliferative            RR - referable                      SR - serious                      STDR - sight threatening



## Effectiveness of screeners and screening methods

### Comparison of health professionals

Of the two studies comparing general practitioners and optician or optometrists using ophthalmoscopy (O'Hare et al 1996, Gibbins et al 1998), neither stated whether any differences found in sensitivity between the two groups of practitioners were statistically significant.

In a larger study of general practitioners and opticians using ophthalmoscopy (type not stated) (Buxton et al 1991), no statistically significant differences in sensitivities were found between general practitioners (53%) and opticians (47%) in detecting sight threatening retinopathy. However, the opticians only screened patients in one centre, whereas the general practitioners' result was a mean sensitivity from three centres.

### Comparison of ophthalmoscopy and non-mydriatic retinal photography

Two studies compared ophthalmoscopy (both types) versus non-mydriatic retinal photography (Buxton et al 1991, Pugh et al 1993). In the study by Buxton et al (1991) the differences in sensitivities between these two methods were not statistically significant ( $p=0.1$ ). In detecting moderate to severe and proliferative retinopathy, assessment of non-mydriatic retinal photographs by a reading centre had higher sensitivity (61%) than ophthalmoscopy (both types) by ophthalmologists (33%), but again the difference was not statistically significant. Conversely, direct/indirect ophthalmoscopy by ophthalmologists showed significantly higher specificity than non-mydriatic photographs in the second study ( $p<0.0001$ ) (Pugh et al 1993).

### Comparison of ophthalmoscopy (both types) and mydriatic retinal photography

In each of three studies comparing relative effectiveness (Gibbins et al 1998, Pugh et al 1993, Harding et al 1995), mydriatic retinal photographs achieved better sensitivity than ophthalmoscopy, regardless of who was reading the photographs or using the ophthalmoscope. For sight threatening retinopathy, retinal photographs assessed by an experienced ophthalmic clinical assistant achieved higher sensitivity than ophthalmologists using ophthalmoscopy (both types) (89% versus 65%) (Harding et al 1995).

Similarly, for detection of moderate to severe and proliferative retinopathy, assessment of mydriatic retinal photographs by trained graders in a reading centre was significantly more sensitive than ophthalmoscopy by an ophthalmologist (84% versus 33%;  $p<0.0001$ ) (Pugh et al 1993).

Finally, in the detection of sight threatening retinopathy, general practitioners reading 35mm colour retinal photographs achieved sensitivities of 87% compared to 66% when they used ophthalmoscopy (Gibbins et al 1998). In the same study, community optometrists reading 35mm colour retinal photographs achieved sensitivities of 91% compared to 82% with ophthalmoscopy in the identification of sight threatening retinopathy.

### Comparison of mydriatic and non-mydriatic retinal photography

Pugh et al (1993) reported that mydriatic retinal photographs were significantly more sensitive than non-mydriatic photographs (sensitivities 81% versus 61%;  $p<0.0001$ ) for the detection of moderate non proliferative, severe non proliferative and proliferative retinopathy. Klein et al (1985) found similar levels of sensitivity for non-mydriatic and mydriatic camera use. Each method achieved 93% sensitivity for the detection of proliferative retinopathy.

If the results of the three studies evaluating mydriatic photographs alone (Gibbins et al 1994, Gibbins et al 1998, Harding et al 1995) are compared with the two studies evaluating non mydriatic photographs alone (Penman et al 1998, Buxton et al 1991), a trend towards higher sensitivity in the detection of sight threatening retinopathy and proliferative retinopathy can be seen for the mydriatic method, regardless of who is reading the photographs. Mydriatic retinal photographs read by ophthalmological clinical assistants, general practitioners and optometrists achieved sensitivities of 87%, 91% and 89% respectively in detecting sight threatening retinopathy (Gibbins et al 1994, Gibbins et al 1998, Harding et al 1995). Non-mydriatic retinal photographs read by an ophthalmologist or trained graders achieved sensitivities of 56% and 60% respectively (Penman et al 1998, Buxton et al 1991). There was no evidence from these five studies to allow comparison of cost effectiveness.

## **Summary**

Mydriatic 45 degree retinal photography/imaging appears the most effective test when screening for, or when reviewing established, diabetic retinopathy.

## **Visual acuity testing**

Reduction of visual acuity is an important indicator of diabetic maculopathy, which is difficult to detect by means other than of screening or clinical examination. While there may be other causes of a drop in visual acuity, the prospect of unmanaged diabetic maculopathy alone is a reason for considering its value.

One study was found which evaluated visual acuity in the detection of people with diabetic retinopathy (Harding et al 1985). This study measured the effectiveness of mydriatic retinal photography and direct ophthalmoscopy in the detection of sight threatening retinopathy in 358 patients from four general practices in Liverpool, who were tested in hospital settings. Measuring visual acuity alongside mydriatic photography increased sensitivity of photography from 89% to 91%, although specificity fell from 86% to 76%. For direct ophthalmoscopy measuring visual acuity increased sensitivity from 65% to 74% although specificity fell from 97% to 77%.

## **Summary**

There is a lack of direct evidence about the role and usefulness of visual acuity testing in retinopathy screening. The recent report from the National Screening Committee (Garvican et al 2000) has as a result not included a recommendation for its use in systematic screening programmes. However there is broad expert consensus that examination of visual acuity (including testing of visual fields) is an essential element of the overall approach to eye care for people with diabetes, and is therefore an important part of clinical practice. This is reflected in documents such as the Royal College of Ophthalmologists (1997) clinical practice guideline on retinopathy management, which recommends visual acuity testing as part of the overall eye care approach. The retinopathy working group supports this view.

## Macular oedema

Clinically significant macular oedema is an important complication of diabetes leading to reduced visual acuity if untreated. Diagnosis of this complication rests on the use of stereoscopic, slit lamp, indirect ophthalmoscopy in expert hands (Royal College of Ophthalmologists 1997).

There was consensus in the Recommendations panel that the presence of macular oedema requires referral within four weeks. Because of the difficulty of determining the difference between non-significant macular oedema and clinically significant macular oedema, the panel recommends that visual acuity testing be used as a screening test for this complication in routine practice. Reduced visual acuity is an indication for specialist referral within four weeks.

## Mydriasis

A recent systematic review (Pandit and Taylor 2000) concluded that mydriasis using tropicamide (0.5-1%) was safe. They found that when tropicamide alone was used the risk of inducing acute glaucoma was close to zero. Stronger or combined mydriatics had an overall risk of between 1 in 3300 and 1 in 20000 of inducing acute glaucoma.

The authors' conclusion that mydriasis using tropicamide was safe applied to an analysis of studies that included general populations; patients already known to have chronic glaucoma; patients who had mydriasis in the fellow eye of those with acute glaucoma in one eye and patients who had previously had iridectomy for acute glaucoma.

Additionally they also concluded that the use of pilocarpine to reverse mydriasis was potentially harmful and should be discouraged.

Dosages and cautions on use are to be found in the British National Formulary (42, 2001).

## Cost issues

Two studies undertook secondary cost analysis of data collected in two of the larger studies of the effectiveness of screening/review modalities. Sculpher (1992) re-analysed the data from the study by Buxton et al (1991). Lairson (1992) undertook a cost analysis within the US study by Pugh et al (1993). Both of these studies contrasted costs of different types of practitioner undertaking a screening programme, usually describing outcomes in terms of relative costs per true positive case identified.

While these studies provide some useful background reading for bodies wishing to commission a diabetic retinopathy screening programme (such as the NHS National Screening Committee), they are less useful in a clinical practice guideline which gives guidance on the methods to be used for individuals rather than the economics of a major screening programme.

A recent cost analysis concluded that the replacement of existing opportunistic screening practice by systematic screening programmes was justified in cost effectiveness terms. The authors concluded that the costs of systematic screening programmes (which in their analysis found the incremental cost effectiveness of replacing opportunistic screening with systematic screening was £32) were justified. They argued that opportunistic costs could be feasibly diverted. Costs and cost effectiveness were very dependent on features such as sensitivity and specificity of the screening tool, compliance and levels of prevalence (James et al 2000).

Vijan et al (2000), in an economic modelling paper, argued that those with worst HbA<sub>1c</sub> levels were those who might benefit from being screened more often – but recognised that this group was often most difficult to get to participate in screening programmes (and other aspects of their care). Overall they argued that annual screening for most patients with Type 2 diabetes produced little benefit over and above that which could be gained from screening every second to third year according to their model (see clinical practice overview pages 42-43).

For a further discussion on cost effectiveness see also Section 8 (Appendix 1).

# Clinical practice overview

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This synthesis of the evidence is concerned with the development of a clinical practice guideline rather than a national retinopathy screening programme. Thus although service structure and configuration are important to health service professionals providing direct care for patients, the conclusions from the review, the evidence statements and the recommendations all relate to care for individuals. This is a singular issue for this particular national guideline because much of the data relates to screening and early detection and it is sometimes difficult to disentangle discussion about which tests are appropriate for which patients, from discussion about whether and how the National Health Service should set up early detection and monitoring systems.

For example, clinical practice guideline recommendations should not enter the debate about which clinical professions might be involved in the running of a screening programme and this guideline does not do so. In the UK, that is the domain of the NHS National Screening Committee and the evidence base for this guideline has been made available to the Committee in its deliberations on whether to recommend a national screening programme on diabetic retinopathy and on how it might be structured. It is, however, the place of the guideline to determine the level of sensitivity and specificity of the tests which health professionals require in order to make appropriate clinical decisions, and on which they themselves should decide in undertaking screening and review tests.

Conclusions from the studies included in this review must be based principally on the general trend of the results rather than the quality of individual studies, since the majority of studies contain small numbers of cases and potential selection bias could limit their individual generalisability. Equally, other biases such as experience, training and motivation may be present, given the limited numbers of personnel taking part in many of the studies. Nonetheless, it has been possible to use the results of the review (Hutchinson et al 2000b) to make evidence based recommendations on the management of diabetic retinopathy.

Despite the methodological problems of the individual papers, the review confirms that mydriatic retinal photography provides the most sensitive screening and monitoring test for detection of retinopathy that is sight threatening. Furthermore the evidence demonstrates that sensitivities of 80% should be feasible within a screening programme or in early detection monitoring of known, low risk retinopathy. Mydriasis is best achieved by the use of tropicamide in dosages recommended by the British National Formulary (BNF 2001).

The clinical practice implication of these findings is that test methods used for screening and early management of diabetic retinopathy, whatever they are and whichever type of health professional carries out the test, must attain 80% sensitivity standard. Thus if methods of screening/monitoring other than mydriatic retinal photography are used, such as indirect ophthalmoscopy, these must also match the 80% sensitivity standard. There is no clear evidence to show in whose hands the methods work best, since sensitivities greater than 80% in the detection of proliferative, sight threatening, or referable retinopathy were achieved in different studies by general practitioners, optometrists, diabetes specialists and independent graders using retinal photography.

In only one study did the use of direct ophthalmoscopy meet the required 80% sensitivity standard. Indirect ophthalmoscopy in the hands of trained clinicians can be used with caution to detect diabetic retinopathy.

Increasingly, the attainment of an 80% sensitivity standard and 95% specificity standard are the requirements of training (certificated) courses in diabetic retinopathy screening for optometrists using indirect ophthalmoscopy (personal communication from Professor E.G. Woodward).

Although location may be dictated by the choice of screening method and resources available, there is no clear evidence to show in which location screening works best. Digital imaging photography will have an impact on choice of location if the potential of this method seen in two small studies (George et al 1998, Ryder et al 1998a) is realised.

Ophthalmoscopy still has a place in clinical practice in the non-routine surveillance test. However, quality assurance of the technique in routine use is difficult and the method, on its own, does not achieve adequate sensitivity. If repeated retinal photographs are ungradeable then the patient should be referred for expert opinion. It is important to acknowledge that ophthalmoscopy may have a place as an opportunistic diagnostic test for those who fail to be captured by formal screening programmes.

There was no evidence in the papers which supported decisions on the review frequency for a particular type of retinopathy or to assist with decisions of what type of problem should be referred for specialist opinion, and with what urgency. Under the circumstances the Recommendations panel developed explicit consensus from which the various time intervals were derived. While the panel agreed that some emerging evidence suggests that a review interval of 2 years would be cost effective for those people who have no evidence of retinopathy, a decision was made to recommend a 1 year review interval. This pragmatic decision was in line with the recommendations from the UK National Screening Committee and was also based on the practicalities of managing a regular review process in the clinical setting. In the view of the Recommendations panel this 1 year review interval should be adopted as standard practice until primary research evidence becomes available that might identify sub-groups who might safely have longer review periods, (see also Section 4, Research issues).

The full clinical practice recommendations from the review, together with evidence statements and consensus panel recommendations, are to be found on the following pages.

# Clinical practice recommendations and evidence statements

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## Early management

### Eye care for all people with diabetes

#### Recommendation

Arrange recall and annual review of all people with Type 2 diabetes (D)

#### Evidence statement

*There was explicit consensus in the Recommendation panel and Clinical working group that annual review was the most practical and appropriate interval and that a proactive recall system was required to prompt patients and staff (IV)*

#### Recommendation

Examine eyes at the time of diagnosis and at least annually thereafter (including in people who are registered blind and partially sighted) (D)

- ◆ check visual acuity, corrected with glasses or pinhole (D)
- ◆ examine for diabetic retinopathy following dilation of pupils with tropicamide (C)

#### Evidence statements

*There was explicit consensus in the Recommendations panel and Clinical working group that both eyes of all people with Type 2 diabetes should be examined at diagnosis to assess retinopathy status and that annual follow-up was essential for all, irrespective of the level of visual acuity (IV)*

*The Recommendations panel and Clinical working group considered that the measurement of visual acuity is an essential part of screening/review in retinopathy care (IV)*

*Irrespective of screening test performed, results are better following mydriasis (III)*

*Tropicamide is the drug of choice in mydriasis (Ib)*

## Recommendation

Classify eye care as: *routine care* required or *early review* required or *referral* required (D)

## Evidence statement

*There was strong explicit consensus in the panel that clinicians should take positive steps to classify, through stratification of risk, the type of management plan required for each patient (IV).*

## Recommendation

Refer patient for opinion if cataracts are interfering with vision or the retina is obscured (D)

## Evidence statement

*There was explicit consensus in the panel that expert ophthalmological opinion on management is required if cataracts are interfering with vision or the retina is obscured (III)*

## Recommendation

Maintain good blood pressure control (at or below 140/80mm Hg) (A)

(for information on levels of control see the guidelines in this series on raised blood pressure management)

## Evidence statement

*The United Kingdom Prospective Diabetes Study found that*

- ◆ *a smaller proportion of patients in the tight blood pressure group showed deterioration in retinopathy from baseline at median follow up of 4.5 years. By a median follow up of 7.5 years the reduction in risk was 34%. At nine years a reduction in risk of 47% for visual deterioration was found.*

## Recommendation

Maintain good blood glucose levels (preferably below HbA<sub>1c</sub> 6.5% to 7.5%, according to individual targets) (A)

(for information on levels of control see the guidelines in this series on blood glucose management)

*The United Kingdom Prospective Diabetes Study found that*

- ◆ *a decrease of 0.9% in haemoglobin A<sub>1c</sub> (from 7.9% to 7.0%) was associated with a 21% decrease in risk for any end point and a 37% reduction in risk of microvascular complications.*

## Routine care

### Recommendation

Review annually if there is no retinopathy present or there is only minimal or mild background retinopathy or low risk background retinopathy (D).

### Evidence statement

*There was explicit consensus in the panel that a review interval of one year was appropriate for people in whom no retinopathy was detected or who had only minimal or mild background retinopathy or low risk background retinopathy (IV) (for further discussion see page 43)*

## Early review

### Recommendation

Review every three to six months if

- ◆ there is occurrence or worsening of lesions since the previous examination *or*
- ◆ there are scattered exudates more than 1 disc diameter from the fovea *or*
- ◆ a person is at high risk of progression, categorised by rapid improvement in blood glucose control or existence of hypertension or renal disease (D)

### Evidence statements

*There was explicit consensus in the panel that earlier review to identify possible progression of early retinopathy signs was required for those in whom there is occurrence or worsening of lesions since the previous examination, or there are scattered exudates more than 1 disc diameter from the fovea, or a person is at high risk of progression, (categorised by rapid improvement in blood glucose control or existence of hypertension or renal disease) (IV)*

# Referral

## Referral within four weeks

### Recommendation

Refer for ophthalmological opinion within 4 weeks if

- ◆ there is an unexplained drop in visual acuity or
- ◆ there are hard exudates within 1 disc diameter of the fovea or
- ◆ macular oedema is present or
- ◆ there are unexplained retinal findings or
- ◆ pre-proliferative or more advanced (severe) retinopathy is present (D)

### Evidence statements

*There was strong explicit consensus in the panel that referral for ophthalmological opinion within 4 weeks was required if there is an unexplained drop in visual acuity, or there are hard exudates within 1 disc diameter of the fovea, or macular oedema is present, or there are unexplained retinal findings, or pre-proliferative or more advanced (severe) retinopathy is present (IV)*

## Urgent referral to ophthalmology specialist within one week

### Recommendation

Refer to an ophthalmology specialist within one week if there is new vessel formation, or there is evidence of pre-retinal and/or vitreous haemorrhage, or rubeosis iridis is present (D)

### Evidence statement

*There was strong explicit consensus within the panel that a patient should be referred to an ophthalmology specialist within one week if there is new vessel formation, or there is evidence of pre-retinal and/or vitreous haemorrhage, or rubeosis iridis is present (IV)*

## Emergency referral to ophthalmology specialist on the same day

### Recommendation

Refer on the same day if there is sudden loss of vision or there is evidence of retinal detachment (D)

### Evidence statement

*There was strong explicit consensus within the panel that a patient should be referred to an ophthalmology specialist on the same day if there is sudden loss of vision or there is evidence of retinal detachment (IV)*

# Detection of diabetic retinopathy

## Recommendation

Use tests that have been demonstrated to achieve sensitivity of 80% or higher, specificity of 95% or higher and a technical failure rate of 5% or lower (C)

## Evidence statements

*The standard required for retinopathy screening should be no less than specificity of 80% and sensitivity of 95% (IV)*

*Different levels of screening tests produce different sensitivities and specificities in the hands of different professional groups (III)*

*The opinion of the panel, supported by the views of various authors, is that a technical failure rate of less than 5% should be achieved for retinal photographic test programmes (IV)*

## Recommendation

Retinal photography is currently the most practical method, when conducted and evaluated by trained personnel (C)

## Evidence statements

*Retinal photography generally achieves levels of 80% sensitivity and 95% specificity when used by personnel trained in retinal photography, irrespective of health professional type performing the screening tests (III)*

*For 45 degree retinal photography, those using 35mm film appear better than those systems using instant film systems (III)*

*Digital image retinal photography may be better than instant film systems (III)*

## Recommendation

Use, as second choice, slit-lamp indirect ophthalmoscopy, when operated by trained personnel (C)

## Evidence statements

*In the hands of trained personnel, the use of slit-lamp indirect ophthalmoscopy can achieve levels of 80% sensitivity and 95% specificity (III)*

## Recommendation

Use tropicamide, with appropriate caution, to achieve mydriasis (B)

## Evidence statements

*Tropicamide is the drug of choice in mydriasis (Ib)*

*The panel supported the views on the efficacy and use of tropicamide as a mydriatic, published in the British National Formulary (IV)*

# Screening for diabetic retinopathy

## Recommendations

Arrange recall and annual review of people with Type 2 diabetes (D)

Perform an appropriate and acceptable annual retinopathy screening/review test for all people with Type 2 diabetes (D)

Participation in opportunistic screening should not be regarded as an adequate substitute for participation in a formal screening programme. It is an option if formal screening is not possible (D)

## Evidence statement

*There was strong agreement within the panel that a review on at least an annual basis is required to assess for retinopathy in all people with diabetes. This review should be planned and not opportunistic, except in those few individual cases where adherence to a planned programme is not possible (IV)*

## 4. Research issues

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There is now discussion in the United Kingdom about the possibility of establishing a national screening programme for retinopathy among people with diabetes. It is important to ensure that appropriate, high quality research studies on effective implementation methods are commissioned to support the decision-making process or, at least, to monitor the effectiveness of any programme, once established.

Well designed screening studies are required to determine that new tests of screening/early detection (such as digital camera retinal photography) meet the standards of 80% sensitivity and 95% specificity. There is a danger that 'technology creep' will allow developments in this field without the required assessments.

Studies needed to determine the appropriate intervals of screening and review, which are currently unclear. This would have a major impact on the benefits and costs of preventing and managing sight threatening retinopathy.

## 5. Clinical audit criteria for diabetic retinopathy

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# Introduction

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Each of the six parts of the Type 2 diabetes guideline will contain a set of clinical audit review criteria. These have been directly developed from the principal recommendations in the guideline, using some of the methods refined in The Royal College of General Practitioners Clinical Practice Evaluation Programme (<http://www.shef.ac.uk/~scharr/public/cpep/>). Because resources are limited it has not been possible to seek external review of these criteria, nor to test out their usability in everyday practice. They are process based rather than outcome based, since they are based on the evidence reviews.

Despite these developmental limitations, they are presented as part of the NICE commissioned programme of work in order that clinical teams may have the opportunity to select, test and refine them within the context of the team's clinical setting.

# Audit review criteria selected by NICE

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- ◆ The percentage of people with diabetes\* who have had their eyes examined in the previous 12 months.
- ◆ For those with lesions that have occurred since the preceding examination, the percentage who have had their eyes examined in the previous 3-6 months.
- ◆ For those at high risk of progression, the percentage of people who have had their eyes examined in the previous 3-6 months. (A high risk of progression is associated with rapid improved in blood glucose control, or presence of raised blood pressure, or renal disease.)
- ◆ For those with severe (sight threatening) retinopathy on examination, the percentage of people who have been referred for specialist opinion within 4 weeks of the finding.
- ◆ For those with new vessels found on examination, the percentage of people who have been referred to an ophthalmologist within 1 week.

\*Includes those who are registered blind or partially sighted.

# Additional review criteria

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## *Eye care for all people with diabetes*

- ◆ For those who have had their eyes examined in the previous 12 months, the percentage of people who were part of a formal annual screening programme.
- ◆ The percentage of patients who have had their eyes examined following diagnosis.
- ◆ The percentage of patients who have had their visual acuity checked as part of an eye examination.
- ◆ The percentage of patients who have been examined following dilation of pupils with tropicamide as part of an eye examination, unless contraindicated.
- ◆ The percentage of patients who have had their eye care requirements classified as either routine care, early review or referral required.
- ◆ For those with cataracts interfering with vision, the percentage of patients who have been referred for opinion.
- ◆ For those with the retina obscured, the percentage of patients who have been referred for opinion.

## *Routine care*

- ◆ For those with no retinopathy present, the percentage of patients who have had their eyes examined in the previous 12 months.
- ◆ For those with minimal background retinopathy present, the percentage of patients who have had their eyes examined in the previous 12 months.
- ◆ For those with mild background retinopathy present, the percentage of patients who have had their eyes examined in the previous 12 months.
- ◆ For those with low risk background retinopathy present, the percentage of patients who have had their eyes examined in the previous 12 months.

## *Early review*

- ◆ For those with lesions that have worsened since the preceding examination, the percentage of patients who have had their eyes examined in the previous 3 to 6 months.
- ◆ For those with scattered exudates more than 1 disc diameter from the fovea, the percentage of patients who have had their eyes examined in the previous 3 to 6 months.

## ***Referral***

- ◆ For those with an unexplained drop in visual acuity detected, the percentage of patients who have been referred for opinion within 4 weeks of finding.
- ◆ For those with hard exudates within 1 disc diameter of the fovea on examination, the percentage of patients who have been referred for opinion within 4 weeks of finding.
- ◆ For those with macular oedema on examination, the percentage of patients who have been referred for opinion within 4 weeks of finding.
- ◆ For those with unexplained retinal findings on examination, the percentage of patients who have been referred for opinion within 4 weeks of finding.
- ◆ For those with pre-proliferative retinopathy on examination, the percentage of patients who have been referred for opinion within 4 weeks of finding.

## ***Urgent referral***

- ◆ For those with preretinal haemorrhage found on examination, the percentage of patients who have been referred to an ophthalmologist within 1 week.
- ◆ For those with vitreous haemorrhage found on examination, the percentage of patients who have been referred to an ophthalmologist within 1 week.
- ◆ For those with rubeosis iridis found on examination, the percentage of patients who have been referred to an ophthalmologist within 1 week.

## ***Emergency referral***

- ◆ For those with sudden loss of vision, the percentage of patients who have been referred on the same day to an ophthalmologist.
- ◆ For those with retinal detachment, the percentage of patients who have been referred on the same day to an ophthalmologist.

## 6. Detailed evidence base

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# Reported sensitivities and specificities from studies

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## Key:

Outcome column: AR = any retinopathy, PR= proliferative retinopathy,  
STDR = sight threatening retinopathy, RR = referable retinopathy,  
NPR= non proliferative retinopathy

## General practitioners using ophthalmoscopy

Location	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
<b>Dilated direct ophthalmoscopy</b>						
gp practice with mobile screening unit	ophthalmologist dilated ophthalmoscopy	RR	56	98	data not provided	O'Hare et al 1996
gp practice	reading centre assessing 35mm slides	i) AR ii) STDR	i) 63 (56-69) ii) 66 (54-77)	75 (70-80) 94 (91-96)	67%	Gibbins et al 1998
hospital diabetes clinic	ophthalmologist dilated ophthalmoscopy	i)AR ii)PPR -PR	45 (23-69) 50 (13-99)	100 (87-100) 100 (92-100)	51%	Lienert 1989
gp practice	ophthalmologist-dilated ophthalmoscopy	i) AR ii) PR	52 (31-73) 33 (1-91)	84 (79-89) 92 (88-95)	68%	Reenders et al 1992
gp practice	ophthalmological clinical assistant ophthalmology	STDR	53 (44-62)	91 (90-92)	95%	Buxton et al 1991

## Opticians using ophthalmoscopy

Location	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
<b>Dilated direct ophthalmoscopy</b>						
optician practice	ophthalmologist dilated ophthalmoscopy	RR	75	93	data not provided	O'Hare et al 1996
optometrist practice	reading centre assessing 35mm slides	i) AR ii) STDR	74 (67-81) 82 (68-92)	80 (75-85) 90 (87-93)	68%	Gibbins et al 1998
optician practice	ophthalmological clinical assistant ophthalmology	STDR	48 (28-70)	94 (92-97)	96%	Buxton et al 1991
<b>Undilated direct ophthalmoscopy</b>						
not stated	3 field 30 degree stereoscopic colour photos	i) AR ii) NPR iii) PR	84 (72-93) 65 (46-79) 53 (37-69)	75 (51-91) 67 (50-81) 90 (79-96)	data not provided	Klein et al 1985
<b>Dilated direct and/or indirect ophthalmoscopy</b>						
university medical center	stereoscopic 7 field photography	RR	74 (67-81)	84 (73-96)	data not provided	Kleinstein et al 1987

## Ophthalmologists using ophthalmoscopy

<b>Dilated direct ophthalmoscopy</b>						
<b>Where</b>	<b>Reference standard</b>	<b>Outcome</b>	<b>Sensitivity % (95% CI)</b>	<b>Specificity % (95% CI)</b>	<b>Coverage (percentage of included patients screened)</b>	<b>Study</b>
hospital clinic	stereoscopic slit lamp biomicroscopy by consultant specialist	STDR	65 (51-79)	97 (95-99)	83%	Harding et al (1995)
hospital clinic	bilateral stereoscopic fundus photography	AR	77 (68-85)	99(98-100)	54%	Schachat et al (1993)
<b>Dilated direct and indirect ophthalmoscopy</b>						
hospital clinic	stereoscopic 7-field photographs	AR	61 (42-77)	99 (95-100)	34%	Kinyoun et al (1992)
primary care clinics	stereoscopic 7 field photographs	i) AR ii) NPR iii) PR	32 (25-39) 38 (31-45) 43 (1-82)	97 (93-99) 98 (94-100) 100 (99-100)	63%	Pugh et al 1993
<b>Dilated direct and/or indirect ophthalmoscopy</b>						
community (mobile van)	stereoscopic 7-field photographs	i)AR ii)PR	82 (80-84) 79 (73-86)	95 (94-96) 100 (98-100)	data not provided	Moss et al 1985

## Other health care professionals using ophthalmoscopy

Who	Location	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
<b>Dilated direct ophthalmoscopy</b>							
diabetologist	hospital diabetes clinic	ophthalmologist dilated ophthalmoscopy	i) AR ii) PPR iii) PR	81 (76-86) 35 (16-57) 73 (39-94)	95 (92-98) 99 (98-100) 97 (96-98)	47%	Lienert 1989
<b>Dilated ophthalmoscopy (indirect/direct not stated)</b>							
diabetologist	not stated	5 field non stereoscopic retinal photographs assessed by independent assessor	i)AR ii)SR	51 (35-68) 27 (1-54)	99 (97-100) 99 (98-100)	85%	Forrest et al 1987
<b>Dilated direct ophthalmoscopy</b>							
physician's assistant	primary care clinics	stereoscopic 7-field photographs	i) AR ii) NPR iii) PR	60 (51-68) 55 (46-64) 20 (1-72)	67 (59-76) 66 (58-76) 98 (95-99)	45%	Pugh et al 1993
<b>Dilated ophthalmoscopy (indirect/direct not stated)</b>							
nurse	not stated	5 field non stereoscopic retinal photographs read by trained grader	i)AR ii)SR	50 (33-67)	99 (98-100)	84%	Forrest et al 1987
<b>Dilated direct ophthalmoscopy</b>							
junior hospital physicians	hospital diabetes clinic	ophthalmologist dilated ophthalmoscopy	i)AR ii)PR	64 (58-70) 13 (0-53)	86 (82-91) 100 (99-100)	51%	Lienert 1989
hospital physicians	hospital clinic	ophthalmoscopy by ophthalmological clinical assistant	STDR	67 (50-84)	96 (94-98)	97%	Buxton et al 1991

## Various health care professionals using non-mydriatic retinal photography (45 degree camera)

Details of method	Who	Where	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
<b>Using 35 mm film</b>								
single photo	independent grader	primary care clinics	stereoscopic 7 field retinal photography	i) AR ii) NPR iii) PR	64 (57-71) 64 (56-71) 25 (1-51)	99 (95-100) 97 (93-99) 100(99-100)	63%	Pugh et al 1993
single photo	independent grader	not stated	3 field 30 degree stereoscopic colour photos	i) AR ii) PR	98 (90-100) 93 (68-100)	100(77-100) 100(93-100)	data not provided	Klein et al 1985
<b>Using Polaroid film</b>								
single photo	optician	hospital clinic	ophthalmoscopy by ophthalmological clinical assistant	STDR	47 (23-71)	95 (93-97)	56%	Buxton et al 1991
<b>Using 35 mm slides or Polaroid prints</b>								
single photo	ophthalmologist	hospital clinics	ophthalmoscopy by ophthalmologist	AR	96 (88-99)	98 (87-100)	data not provided	Williams et al 1986
<b>Type of film not stated</b>								
2 photos	independent grader	not stated	binocular indirect ophthalmoscopy	i) AR ii) STDR	69 (56-82) 60 (15-95)	83 (79-88) 95 (93-98)	94%	Penman et al 1998

## Various health care professionals using mydriatic retinal photography (45 degree camera)

Details of methods	Who	Where	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
<b>Using 35mm slides</b>								
2 photographs per eye	general practitioners	hospital	same photographs read by ophthalmologists	i)AR ii)PR	87 (66-97) 100 (10-100)	77 (70-85) 96 (92-99)	83%	Gibbins et al 1994
2 photographs per eye	general practitioner	GP premises	reading centre assessing 35mm slides	i)AR ii)STDR	79 (74-85) 87 (77-94)	73 (68-79) 85 (81-88)	67%	Gibbins et al 1998
2 photographs per eye	optometrists (community)	optometrist practice	reading centre assessing 35mm slides	i)AR ii)STDR	88 (83-93) 91 (79-98)	68 (62-74) 83 (79-87)	67%	Gibbins et al 1998
2 photographs per eye	optometrist (specialist)	optometrist practice	reading centre assessing 35mm slides	i) AR ii) STDR	86 (81-91) 97 (90-100)	89 (85-93) 87 (84-91)	67%	Gibbins et al 1998
Single non stereoscopic photo	independent grader	not stated	3 field 30 degree stereoscopic colour photos	i) AR ii) PR	100 (92-100) 93 (66-100)	97 (93-99) 98 (87-100)	data not provided	Klein 1985
3 photos	independent grader	primary care clinics	stereoscopic 7 field retinal photography	i) AR ii) NPR iii) PR	72 (66-79) 71 (65-78) 50 (12-88)	96 (92-99) 94 (90-97) 100 (99-100)	63%	Pugh et al 1993
3 colour photographs	ophthalmological clinical assistant	GP practices and mobile screening unit	slit lamp biomicroscopy by specialist	STDR	89 (80-98)	86 (82-90)	89%	Harding et al 1995
2 photographs per eye	diabetologist	at hospital	reading centre assessing 35mm slides	i)AR ii)STDR	73 (67-79) 89 (79-95)	93 (90-96) 92 (88-94)	67%	Gibbins et al 1998
<b>Using Polaroid film</b>								
bilateral colour fundus photos	general practitioner	photos taken at regional hospital	i) consensus by both ophthalmologists ii) consensus by one or both ophthalmologists reading same photos	i) AR iia) AR iib) RR	100 (97-100) 91 (85-96) 99 (94-100)	54 (45-63) 60 (48-70) 47 (38-55)	100%	Van der Kar et al 1990
	hospital physician	hospital	i) consensus by 2 ophthalmologists ii) consensus by one or both ophthalmologists	i) AR iia) AR iib) RR	96 (81-100) 89 (73-97) 96 (78-100)	59 (39-78) 68 (46-87) 52 (33-70)	100%	Van der Kar et al 1990

## Various health care professionals using direct ophthalmoscopy in combination with non mydriatic retinal photography

Who	Location	Reference standard	Outcome	Sensitivity % (95% CI)	Specificity % (95% CI)	Coverage (percentage of included patients screened)	Study
GP	gp practice	ophthalmoscopy by ophthalmological clinical assistant	STDR	80	86	69%	Sculpher et al 1991
optician	optician & gp practice	ophthalmoscopy by ophthalmological clinical assistant	STDR	67	89	12%	Sculpher et al 1991

## Various health care professionals using direct ophthalmoscopy in combination with mydriatic retinal photography (instant prints)

Who	Location	Reference standard	Outcome	Sensitivity	Specificity	Coverage (percentage of included patients screened)	Study
GP	mobile van	ophthalmologist dilated ophthalmoscopy	RR	60	98	data not provided	O'Hare et al 1996
optician	mobile van	ophthalmoscopy by ophthalmological clinical assistant	RR	88	99	data not provided	O'Hare et al 1996
optometrist	hospital diabetes clinic	diabetes physicians analysing retinal photographs with ophthalmologist	AR STDR	97 100	not provided	Data not provided	Ryder et al 1998b

# Cohort studies: comparing effectiveness of methods

Study	<b>Buxton et al 1991</b>					
<b>Population:</b>	Diabetic patients in the practices of the GPs who took part in the 3 study sites (Oxford, Exeter, Sheffield)					
	Patients in the hospital diabetic clinics in one site (Exeter)					
	People with diabetes on opticians list in one site (Oxford)					
<b>Study Comparisons:</b>	GPs screening patients		Ophthalmic opticians screening patients		} primary screeners	
	Physicians screening patients					
	All patients had ophthalmic examination by primary screener.					
	Patients in all five groups additionally had stet photographed by non-mydratiac camera using Polaroid film					
	Photography undertaken by:					
	/one ophthalmic clinical assistant	(Exeter)				
	/two clinical assistants	(Oxford)				
	/one specific nurse	(Sheffield)				
<b>Locations:</b>	Exeter: ophthalmic examination at GP premises or hospital clinic					
	- photograph taken at same appointment					
	Oxford: ophthalmic examination at place of GP or ophthalmic optician					
	- photograph taken at separate appointment, eye department					
	Sheffield: ophthalmic examination at place of GP					
	- photograph taken at separate appointment, eye department					
<b>Reference Standard</b>	Ophthalmoscopic examination by ophthalmological clinical assistant					
	Exeter: 1 individual, Oxford: 2 individuals, Sheffield: 3 individuals					
	Through dilated pupils, after retinal photograph, at same appointment					
<b>Blinding</b>	Yes					
<b>Other features</b>	Referral grades					
	1. normal					
	2. abnormal not referred					
	3. referred					
	mydriasis 1% eye drops					
	all screeners using ophthalmoscopy recorded for each patient examined whether or not any of 7 manifestations of STDR was present in each eye					
<b>Patient numbers:</b>	7098 patients identified					
	3318 remained after exclusions					
		<b>Exeter</b>		<b>Oxford</b>		<b>Sheffield</b>
		<b>hospital physician</b>	<b>GP</b>	<b>optician</b>	<b>GP</b>	<b>GP</b>
identified	656	2161	1095	978	2324	
excluded	229	954	680	350	1683	
included	427	1207	415	628	641	
male %	53%	59%	51%	52%	56%	
age years	49±18	66±13	60±17	61±15	65±12	
% on insulin						
treatment	75%	16%	23%	21%	5%	
duration (years)	11±10	8±8	8±7	7±7	7±6	

**Study**                      **Buxton et al 1991 (continued)**

Profession numbers:	Exeter		Oxford		Sheffield
	hospital physician	GP	optician	GP	GP
	not stated	160/180	not stated	85/280 47 screened 38 to ophthalmic optician	73/328

**Results**                      Performance of primary screener in terms of referral against reference standard of clinical assistant (95% CI shown for sensitivity and specificity).

	Exeter		Oxford		Sheffield
	hospital physician	GP	optician	GP	GP
included cases	427	1207	415	628	641
matched cases	416	1150	395	618	582
sensitivity	67% (50-84)	57% (45-69)	48% (26-69)	41% (25-56)	67% (45-88)
specificity	96% (94-98)	94% (93-95)	94% (92-97)	89% (87-92)	86% (83-89)
ppv	57%	37%	31%	19%	13%
odds ratio	50	21	15	6	12

Only photographs graded as "some retinal detail" or better were given a referral grade by the ophthalmologist.

Performance by primary screener group of screening using non mydriatic photography, in terms of referral, against reference standard of clinical assistants.

	Exeter		Oxford		Sheffield
	physician	GP	optician	GP	GP
included cases	427	1207	415	628	628
matched cases	398	1059	357	451	534
sensitivity	67% (50-84)	58% (46-70)	47% (23-71)	35% (16-53)	67% (45-88)
specificity	97% (96-99)	97% (96-98)	95% (93-97)	95% (93-97)	98% (97-99)
ppv	67%	57%	32%	29%	52%
odds ratio	73	48	17	10	92

**Conclusion**                      All the screening methods assess showed relatively poor sensitivities. Specificities were higher.

The routine use of any of these single screening methods will fail to detect a large proportion of cases of sight threatening diabetic retinopathy.

## Study **Forrest et al 1987**

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<b>Population:</b>	All patients registered with one group practice, Islington, London
<b>Study Comparisons:</b>	Diabetologist – no formal training in ophthalmoscopy SRN – given 2 week intensive course in ophthalmoscopy (by diabetologist) in using retinal photographs and clinical examination of diabetic and non-diabetic patients, in hospital wards and diabetic clinics  Fundoscopy carried out by diabetologist and SRN 5 field nonstereoscopic retinal photography by diabetologist photographs graded by independent assessor at Retinopathy Photography Unit
<b>Locations:</b>	Not Stated
<b>Reference Standard</b>	Retinal photography through dilated pupils
<b>Blinding</b>	
<b>Other features</b>	In known diabetics, some degree of retinopathy was present in 38.3% patients (36.8% eyes) – no relation of retinopathy to age, duration, treatment, smoking, levels of HbA <sub>1c</sub> (small numbers). In those not known to have diabetes, 12 eyes (3.4%) in 9 subjects were assessed as showing changes of diabetic retinopathy – 4 classed as diabetic on glucose tolerance test, 3 as impaired glucose tolerant and 2 as normal. Pupils dilated with 0.5% tropicamide drops unless contraindicated.
<b>Include/Exclude Criteria</b>	not explicitly stated
<b>Patient numbers:</b>	59 known diabetic patients (from 83 known diabetics) 223 without known diabetes (from random sample 1908 >40 years invited for health screen, 1644 eligible, 1084 attended, 347 recalled for glucose tolerance test, 223 attended – total 282.  282 subjects 246 right eye photographs available 236 left eye photographs available (missing = 18 each eye mislaid, 6 right 9 left cataracts, 5 right 6 left glaucoma, 3 right 11 left refusals)  482 photographs total  438 photographs could be assessed (90.9%) (2 not assessable due to ptosis, 8 due to cataracts repeated in 16 eyes of remaining 32, 11 yielded assessable)
<b>Profession numbers:</b>	
<b>Results</b>	407 eyes were examined by nurse and had photograph available <u>eye examination in which nurse allocated grade:</u>  sensitivity for any retinopathy = 50.0% ± 16.8% specificity = 99.2% ± 0.9%  if unclassified are included as position screening  sensitivity for any retinopathy = 56.4% ± 15.6% specificity dropped slightly  nurse, detected any changes in eyes with serious retinopathy  sensitivity = 54.5% ± 29.4% specificity = 92.4% ± 2.6%  neovasc not found in 6 eyes, found on photograph

**Study** **Forrest et al 1987 (continued)**

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**Results (continued)** Doctor examined eyes of 259 subjects  
517 eyes (one prosthetic)  
graded 494 (95.6%) (23 eyes remain, 18 cataracts, 2 ptosis, 3 non-cooperation)  
412 eyes examined by doctors and photographs available

sensitivity for any retinopathy 51.3% ± 15.7%  
specificity for any retinopathy 98.7% ± 1.2%

to detect any changes with serious retinopathy

sensitivity 72.7% ± 26.3%  
specificity 95.3% ± 2.0%

ability of doctor to detect serious retinopathy

sensitivity 27.3% ± 26.3%  
specificity 99.2% ± 0.8%

neovasc not found in 5 out of 6 cases

**Conclusion** Eye examination by experience diabetologist likely to miss }  
substantial proportion of retinopathy. } both miss  
Nurse is able to achieve almost equivalent levels of accuracy } circa 50%  
after only 2 weeks training, and training by ophthalmologist } of cases  
would produce even better results

Inaccuracies are likely to result from inexperience and not from intrinsic problems with staff or techniques.

<b>Study</b>	<b>Gibbins et al 1994</b>				
<b>Location</b>	Retinopathy screening clinic, local cottage hospital				
<b>Population</b>	All patients registered with rural group practice in Mid Wales and identified as having diabetes – 166 patients (2.2% of list)				
	Mean (SD)	SE	Median	Range	
Years since diagnosis	8 (8.16)	0.7	5.0	1-41	
Age (years)	65.4 (14.8)	1.3	68.0	16-96	
Height (cm)	116.5 (8.8)	0.8	165.0	150-191	
Weight (kg)	74.0 (12.3)	1.1	73.4	51-113	
Systolic BP	156.0 (24)	2.1	158.0	110-250	
Diastolic BP	85.0 (8.0)	0.7	84.0	68-110	
<b>Study comparison</b>	Mydriasis – 1% tropicamide drops, unless history of glaucoma fundus photographs, camera, 35mm (100ASA) colour transparency film), two 45° pictures per eye				
	Photographs assessed by GP from practice and ophthalmologist from University Hospital				
<b>Reference standard</b>	Ophthalmologists interpretation of results				
<b>Other features</b>	Picture grading				
	Normal: no diabetic lesions seen				
	Background diabetic retinopathy: microaneurysms and/or dot haemorrhage				
	Background with exudate: background and hard exudates				
	Proliferative: additionally cotton wool spots or venous abnormal				
	Preproliferative: any neovascular				
	Non diabetic changes noted separately				
<b>Inclusion/exclusion criteria</b>					
<b>Blinding</b>	Yes				
<b>Numbers in study</b>	166 identified patients				
	143 attended clinics				
	137 patients provided analysable fundal photographs				
	(23 of those 137, had diabetic retinopathy identified by ophthalmologist; 13 had background, 8 had back with exudates, 0 had preproliferative, 2 had proliferative. 6 with back and exudates had maculopathy. therefore total of 8 had sight threatening)				
<b>Non participants</b>	23/166 did not attend screening clinics				
<b>Results</b>	Using ophthalmoscopy as reference standard				
	GP - sensitivity for retinopathy 87% (95% CI = 66% - 97%), specificity for retinopathy 77% (95% CI = 70% - 85%)				
	Eight patients with agreed retinopathy were graded differently by the 2 observers.				
	Three patients with retinopathy missed by GP, 13% of those with retinopathy or 2% of all photographs taken and analysed				
	26 false positives by GP (8 poor picture quality, 10 with good quality had Drusen, 7 no retinal abnormality)				
<b>Conclusion</b>	Adequately trained GPs could act as first screener utilising fundal photography				

<b>Study</b>	<b>Gibbins et al 1998</b>
<b>Population</b>	All registered patients with diabetes in the study practices. Study practices – 4 Welsh group general practices. Practices had to have a known diabetes prevalence of at least 2%, computerised diabetes register and facilities for on-site clinical screening sessions.
<b>Study comparisons</b>	Direct ophthalmoscopy by GP. Direct ophthalmoscopy by specialist optometrist. Retinal photography. Direct ophthalmoscopy by optometrist (community)  Slides examined and graded for DR, STDR by: 6 GPs from participating practices. Specialist optometrist. 4 consultant physicians with special interest in diabetes, recruited from district and general hospitals in South Wales 11 community non specialist optometrists who conducted examinations  GPs and community optometrists only assessed slides of subjects on whom they had conducted direct ophthalmoscopy.  Specialist optometrist assessed all slides.  Diabetologist each examined 25% of the pooled slides.
<b>Reference standard</b>	External reference standard, Diabetic Retinopathy. Grading centre, London. 2 trained independent graders graded all slides. 1 senior grader as adjudicator when difference of opinion
<b>Other features</b>	Mydriasis using 1% tropicamide universally used, unless glaucoma or history of anterior lens implantation. Specialist optometrist had general optometric qualification and special training in identification and grading of diabetic retinopathy.  EURODIAB protocols used to obtain two 45° retinal fields per eye, 35mm colour transparencies (100ASA) as slides.  All assessors provided with standardised modular training. GPs optometrists received additional training according to specific needs. All used the same slide viewing boxes. WCDRS grading system used – derived from European protocols and agreed in advance with independent reference standard centre.  2 screening sessions (Phase 1, 2) over 3 year period.
<b>Location</b>	Testing in GP premises (ophthalmoscopy by GP, specialist optometrist). community optometrists not explicitly stated (imply own premises)
<b>Nos. in study</b>	Phase 1: 959 diabetic patients, from total study population of 4762 eligible 62 excluded on medical grounds 613 attended sessions 605 patients photographed, 343 (55.9%) male, 502 (81.9%) NIDDM.  Phase 2: 996 known diabetic patients 47 excluded on medical grounds 644 attended 640 photographed, 365 56.7% male, 513 79.7% NIDDM

**Study** **Gibbins et al 1998 (contd)**

**Results**

GPs + specialist optometrist from phase 1  
 diabetologist from phase 1  
 community optometrist from phase 2

Detection of any retinopathy – figures are mean (95% CI)

	GPs		Community Optometrist	
	ophthalmoscopy	35mm slides	ophthalmoscopy	35mm slides
Sensitivity	65.7 (56.0-69.2)	79.2 (73.7-84.6)	73.9 (66.9-80.8)	88.2 (83.1-93.3)
Specificity	75.0 (69.7-80.3)	73.5 (68.1-79.0)	79.8 (74.8-84.9)	67.8 (61.9-73.7)
PPV	67.2 (60.5-73.8)	71.0 (65.1-76.8)	69.8 (62.7-76.8)	63.7 (57.2-70.2)
	Spec optometrists		Diabetologist	
	ophthalmoscopy	35mm slides	ophthalmoscopy	35mm slides
Sensitivity	69.9 (63.6-76.1)	86.1 (81.4-90.8)		72.6 (66.5-78.7)
Specificity	61.7 (55.7-67.7)	88.9 (85.1-92.8)	Not assessed	93.3 (89.5-96.0)
PPV	60.1 (53.9-66.2)	86.5 (81.9-91.2)		89.9 (85.3-94.4)

Detection of sight threatening Retinopathy

	GPs		Community Optometrist	
	ophthalmoscopy	35mm slides	ophthalmoscopy	35mm slides
Sensitivity	65.7 (53.4-76.7)	87.3 (77.3-94.0)		88.7 (79.0-95.0)
Specificity	93.8 (90.9-96.0)	84.8 (81.3-88.4)	Not assessed	91.5 (88.3-94.1)
PPV	65.7 (53.4-76.7)	51.2 (42.3-60.1)		65.6 (55.2-75.0)
	Spec optometrists		Diabetologist	
	ophthalmoscopy	35mm slides	ophthalmoscopy	35mm slides
Sensitivity	79.2 (68.0-87.8)	97.2 (90.3-99.7)	82.2 (68.0-92.0)	91.1 (78.8-97.5)
Specificity	88.5 (85.3-91.6)	87.4 (84.1-90.7)	89.7 (86.6-92.9)	82.7 (78.7-86.7)
PPV	55.9 (46.2-65.5)	58.8 (50.0-67.7)	50.7 (38.7-62.6)	40.6 (31.0-50.2)

In phase 1: 78.0%

In phase 2: 78.4%

Slides assessed by reference centre as excellent or good quality and only the slides of excellent or good quality where available for macular fields of both eyes were used to calculate sensitivity, specificity, ppv.

**Conclusion**

Motivated and trained GPs and community optometrists using 35mm colour transparencies could provide an effective screening service – but at a lower level of performance than that provided by a specialist assessor.

Regular training and supervision to maintain quality is pre-requisite.

Role of Diabetologists may be as secondary screeners for intermediate grades of retinopathy.

Two field 35mm slides provide method of choice for community based screening, clear advantages over direct ophthalmoscopy by GPs and community optometrists. Best performance will be obtained by using dedicated photograph assessors, who do not need to be medically qualified.

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**Study**                      **Harding et al 1995**

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<b>Population</b>	General practice population (4 general practices) mean age 60.2 years, proportion treated with insulin 24.9%
<b>Study Comparison(s)</b>	Community based retinal photography versus direct ophthalmoscopy by ophthalmologist through dilated pupils
<b>Reference standard</b>	Slit lamp biomicroscopy carried out by a consultant specialist
<b>Other features</b>	Retinal photography through dilated pupils was performed in each eye of the patients by a trained technician in a mobile unit. Photographs were graded by an experienced ophthalmic clinical assistant. Retinopathy was graded on 8 levels according to a simplified protocol used in the Early Treatment Diabetic Retinopathy Study. Maculopathy was graded on 6 levels
<b>Location</b>	Inner city community clinics; hospital assessment clinic, tertiary centre in Liverpool
<b>Inclusion/Exclusion criteria</b>	All patients with diabetes attending 4 general practices with disease registers were examined. Patients attending an ophthalmologist already were included
<b>Blinding</b>	Yes
<b>Numbers in study</b>	358
<b>Non participants</b>	32 lost to follow up and 6 whose photographs were ungradeable due to poor quality. no differences between patients who completed study and those who did not in terms of age, type and duration of diabetes
<b>Outcomes/endpoints</b>	sensitivity and specificity in detecting sight threatening eye disease (>level 40 ETDRS classification) Retinal photographic screening: sensitivity: 89% (80%-98%) specificity: 86% (82%-90%) Ophthalmoscopy: sensitivity: 65% (51%-79%) specificity: 97% (95%-99%) Photographs were unobtainable in 12 (3.7%) patients and ungradeable in another 34 (9%) patients. Prevalence of sight threatening disease was higher in these patients. Only 7 patients were scored ungradeable by direct ophthalmoscopy. measuring visual acuity alongside the screening methods increased sensitivity of photography to 91% although specificity fell to 76% for direct ophthalmoscopy measuring visual acuity increased sensitivity to 74% although specificity fell to 77% prevalence of eye disease by reference standard 4.7% retinopathy =level 40 maculopathy =level 3 10.3% and sight threatening eye disease 14.1%

<b>Study</b>	<b>Kinyoun et al 1992</b>																
<b>Population</b>	Subjects enrolled in the Japanese-American Community diabetes study – in patients																
<b>Study comparisons</b>	Dilated indirect Ophthalmoscopic dilation examination by retina specialist. Dilated direct ophthalmoscopic dilation examination by retina specialist. Seven standard field fundus photographs taken of subjects with diabetes, 35mm film																
<b>Patient numbers</b>	393 subjects, 124 with diabetes mellitus (all type II) 393 initial exams, 135 had second dilation examination 1 or more years later  Total 528 examinations  124 diabetes patients had photograph taken  9 patients had repeat photograph 1 or more years later  Total 133 photographic examinations																
<b>Location</b>	ophthalmoscopic tests done in patients hospital room																
<b>Blinding</b>	Yes																
<b>Ref standard</b>	133 sets of photographic examinations to compare retina spec. reading with same specialist's ophthalmoscopic findings																
<b>Results</b>	percentage agreement (kappa stat) between retina specialist's ophthalmoscopic examination, (O) retina specialist reading of photograph (S) and trained graders (G) reading of photographs for 59 subjects.																
	<table border="0"> <thead> <tr> <th></th> <th>O vs. S</th> <th>S vs. G</th> <th>O vs. G</th> </tr> </thead> <tbody> <tr> <td>Presence of diabetic retinopathy</td> <td>90 (0.58)</td> <td>93 (0.79)</td> <td>86 (0.49)</td> </tr> <tr> <td>Grade of ref (right eye)</td> <td>92 (0.79)</td> <td>90 (0.69)</td> <td>86 (0.56)</td> </tr> <tr> <td>Grade of ref (Left eye)</td> <td>88 (0.69)</td> <td>92 (0.84)</td> <td>86 (0.62)</td> </tr> </tbody> </table>		O vs. S	S vs. G	O vs. G	Presence of diabetic retinopathy	90 (0.58)	93 (0.79)	86 (0.49)	Grade of ref (right eye)	92 (0.79)	90 (0.69)	86 (0.56)	Grade of ref (Left eye)	88 (0.69)	92 (0.84)	86 (0.62)
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Grade of ref (right eye)	92 (0.79)	90 (0.69)	86 (0.56)														
Grade of ref (Left eye)	88 (0.69)	92 (0.84)	86 (0.62)														

<b>Study</b>	<b>Klein et al 1985</b>
<b>Population</b>	99 people, from where, how chosen etc not stated
<b>Study comparisons</b>	1) direct ophthalmoscopy through undilated pupil 2) grading of non-stereoscopic 45° retinal photograph taken through pharmacologically undilated pupil 3) grading of nonstereoscopic 45° photograph taken through dilated pupils
<b>Reference standard</b>	Grading of stereoscopic retinal photograph taken with standard 30° camera
<b>Location</b>	Photograph not stated. Graded at University of Wisconsin Fundus Photography Reading Centre
<b>Other features</b>	Diabetic retinopathy described as 1) absent 2) i. very early (retinal microaneurysms) ii moderate to severe (microaneurysms and other abnormalities) 3) (fibrous, new vessel, preretinal or vitreous haemorrhage) 4) not determinable mydriasis with 2.5% phenylephrine + 1% tropicamide  35mm film as slides
<b>Blinding</b>	Yes
<b>Nos in study</b>	55 male, 44 female age range 15-84 years, median 54 71 had history of diabetes only one eye of each patient was used 198 photographs taken with non-mydriasis camera 61 lost                   36 pharm undilated pupil 25 dilated pupil  lost due to flash malfunction comparisons of grading of photographs standard 30° fundus camera (dilated pupil) vs. non-mydriasis camera (undilated camera) SP=63 pairs  standard 30° fundus camera (dilated) vs. non-mydriasis camera (dilated) SP=74 pairs  comparisons between grading photographs taken with non-mydriasis camera to those taken with standard 30° camera exact agreement between severity of retinopathy 82.5% grading of 45° and 30° stereoscopic, dilated 86.5%  Retinopathy status based on ophthalmoscopy (undilated) agreed with that based on 30° stereoscopic photograph 54.3% cases  Agreement between graders on severity of retinopathy was 85.1% for 45° photographs, undilated 85.1% for 45° photographs, dilated 90.0% for 30° stereoscopic photographs
<b>Conclusion</b>	Direct ophthalmoscopy through an undilated pupil was found to be both insensitive and nonspecific

**Study**                      **Kleinstein et al 1987**

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<b>Population</b>	
<b>Study comparison</b>	Validity of optometrists diagnosis compared to reference standard all optometrists performed fundus examination using direct or indirect ophthalmoscopy
<b>Reference standard</b>	Retinal specialist's diagnosis based on review of fundus photographs taken by two experienced photographers
<b>No. of patients</b>	25 eyes photographed 14 patients with different levels of retinopathy age range 18-79, equal numbers of men and women average duration diabetes 14.2 years (3-23)
<b>Nos. in study</b>	11 optometrists members of University of Alabama, Birmingham Medical Centre, 8b optometrists in private practice 11 UAB optometrists – average age 34.4, 6.3 years experience saw estimated 96 patients with diabetes/year 8 community optometrists - average 32.6 years, 3.6 years experience saw estimated 118 patients with diabetes/year
<b>Other features</b>	Classification of retinopathy based on grading using a modified Airlie House Classification Scheme patients examined on two successive Saturdays mydriasis – 1% tropicamide and 2.5% hydroxyamphetamine
<b>Results</b>	Error rate: comm opt 28%, faculty optometrists 19% statistically significant (diagnosis matching type and grade)  Sensitivity: community optometrists 73%, faculty optometrists 75%, overall 74% (95% CI 67-81)  Specificity: community optometrists 70%, faculty optometrists 94%, overall 84% (95% CI 73-96)  77% of eyes needing secondary or tertiary care would have been referred, 2% of eye not needing referral would have been required
<b>Conclusion</b>	Study found optometrists correctly diagnosed over 75% of eyes as to presence or absence of retinopathy from limited clinical information. Error rate for diagnosis was low

<b>Study</b>	<b>Lairson et al 1992</b>																				
<b>Population</b>	Half of study population were veterans receiving care at VA hospital. Half of study population were USAF personnel, dependants or retirees receiving care at USAF Medical centre																				
<b>Study comp.</b>	1) 45° photograph without pharm dilation, one photograph of each eye, taken by PA (physician assistant) or nurse practitioner with 45° camera read by internist at clinic + trained readers at Wisconsin Fundus Reading Centre  2) 45° photograph, pupils dilated, 3 photographs taken of each eye same field as 1. And in stereo, (3 <sup>rd</sup> photograph slightly different field)  3) all positive findings verified by photographs through dilated eyes with seven field stereoscopic 30° photographs of each eye taken by certified retinal photographer read by trained readers at Reading centre  4) ophthalmologist conducts both direct and indirect funduscopy examinations through dilated pupils technician – PA or nurse practitioner examines dilated eyes with direct ophthalmoscopy positive findings verified as 3																				
<b>Reference standard</b>	Photographs through dilated pupils, seven field stereoscopic 30° photograph of each eye taken by certified retinal photographer read by trained readers at Reading Centre																				
<b>Other feature</b>	Accuracy – by subjects sequentially screened by the 4 methods modification of Airlie House Classification used. examination added half way through. therefore not available for all patients																				
<b>No of patients</b>	351 cases for camera methods 347 cases for ophthalmologist examination 172 cases for technician examination (352 patients)																				
<b>Results</b>	45° photograph with dilation: sensitivity 81% ophthalmologist examination: specificity 99%  <table border="1"> <thead> <tr> <th></th> <th colspan="2">45° photograph</th> <th colspan="2">Examination</th> </tr> <tr> <th></th> <th>without dilation n=351</th> <th>With dilation n=351</th> <th>Ophthalmologist n=347</th> <th>Technician n=172</th> </tr> </thead> <tbody> <tr> <td>Sensitivity</td> <td>61%</td> <td>81%</td> <td>33%</td> <td>10%</td> </tr> <tr> <td>Specificity</td> <td>85%</td> <td>96%</td> <td>99%</td> <td>99%</td> </tr> </tbody> </table>		45° photograph		Examination			without dilation n=351	With dilation n=351	Ophthalmologist n=347	Technician n=172	Sensitivity	61%	81%	33%	10%	Specificity	85%	96%	99%	99%
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Sensitivity	61%	81%	33%	10%																	
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<b>Conclusion</b>	In this setting, medical care cost per true-positive case detected was lower for the 45° camera with dilation, this remains that case when patient costs were added																				

<b>Study</b>	<b>Lienert 1989</b>
<b>Population</b>	Patients attending a general diabetic clinic
<b>Study comparison</b>	Ophthalmoscopic examination by non-ophthalmic practitioner Ophthalmoscopic dilation examination by ophthalmologist
<b>Reference standard</b>	Ophthalmoscopy dilation examination by ophthalmologist using direct ophthalmoscopy
<b>Number of patients</b>	500 consecutive patients – 51.2% of patients attending during study period 260 (52%) male, 240 (48%) female  mean age 51.5 male, 53.8 female, overall 52.6 years  mean duration 10.6 years male, 11.6 years female, overall 11.6 years mean duration of IDDM, 13.5 years, NIDDM 4.3 years
<b>Other features</b>	Mydriasis 1% tropicamide drops and 10% phenylephrine drops stage of diabetic retinopathy in each eye assigned to one of six levels  Fundus diagnosis made to each eye, to allow grading of maculopathy to be made
<b>Exclusions</b>	Patients who wanted to drive home therefore mydriasis not possible, incomplete exams, those already in care of ophthalmologist and didn't want further diagnosis
<b>Patient details</b>	1000 eyes graded re visual acuity 985 eyes staged for diabetic retinopathy by ophthalmologist 975 maculae graded by ophthalmologist
<b>No of practitioners/details</b>	Two GPs examined 24 patients  25 junior medical staff examined 233 patients physician A examined 121 patients physician B examined 48 patients physician C examined 70 patients  =496 (no information on 4)
<b>Results</b>	Given in comparative percentage correlation between different professions

<b>Study</b>	<b>Moss 1985</b>
<b>Population</b>	Type 1 and Type 2 diabetics taking part in epidemiological study. actual population characteristics not reported
<b>Study Comparison(s)</b>	Direct ophthalmoscopy (and indirect where necessary) by ophthalmologist, optometrist and specially trained ophthalmic technician
<b>Reference standard</b>	Stereo fundus photographs in 7 fields
<b>Other features</b>	Patients had photographs taken in mobile van near their residences, visual acuity, slit lamp examination also taken ophthalmologist, optometrist (specially trained) and ophthalmological technician all had extensive training and were allowed to consult each other on examinations eyes classified as no retinopathy, non proliferative retinopathy, or proliferative retinopathy from Ophthalmoscopic examination Fundus photographs double graded by trained graders according to ETDRS adaptation of Modified Airlie House Classification Of Diabetic Retinopathy
<b>Location</b>	Wisconsin, USA
<b>Inclusion/Exclusion criteria</b>	Inclusion in analysis: those examined by 3 people only.  Excluded from analysis: 116 right eye, 120 left eye photographs ungradeable
<b>Blinding</b>	Yes
<b>Numbers in study</b>	2059 persons: 1949 right eyes 1939 left eyes right eye results presented
<b>Non participants</b>	649 people examined by other than 3 retina specialists other exclusions due to photographs not gradeable, no ophthalmoscopy performed
<b>Outcomes/endpoints</b>	Overall agreement between methods was 87.5% (Kappa 0.749) for all classifications of eyes as no retinopathy, non proliferative retinopathy and proliferative retinopathy no significant differences between the 3 performing ophthalmoscopy sensitivity and specificity of dilated direct/indirect ophthalmoscopy by ophthalmologist/trained assistant or optometrist for; i) non proliferative retinopathy; 82% (80-84); 95 % 93-96) ii) proliferative retinopathy; 79% (73-85); 99% (98-100) disagreement between diagnosis of proliferative retinopathy between ophthalmologists and standard were associated with current age (older $p < 0.01$ ) better visual acuity ( $p < 0.05$ ) examination in first year of study ( $p < 0.001$ ) for non proliferative retinopathy shorter duration of diabetes ( $p < 0.001$ ).

<b>Study</b>	<b>O'Hare et al 1996</b>
<b>Population</b>	General practice population
<b>Study Comparison(s)</b>	Volunteer GP and Opticians carried out ophthalmoscopy and analysed fundus photographs taken at practice by mobile retinal camera – dilated. Retinal camera with instantaneous picture development.
<b>Reference standard</b>	Ophthalmologists analysed same retinal pictures as the reference standard
<b>Other features</b>	Patients from 11 practices were screened by 31 general practitioners and patients from 12 practices were screened by 17 opticians
<b>Location</b>	General or optician practices
<b>Inclusion/Exclusion criteria</b>	Exclusion: Patients already blind, unable to climb steps of mobile retinal screening van, patients already attending hospital diabetic clinic or ophthalmologist clinic in last 12 months.
<b>Blinding</b>	Yes
<b>Numbers in study</b>	1010 patients (517 examined by general practitioners 493 by opticians)
<b>Non participants</b>	No reporting of numbers excluded or original sample frame Possible selection bias.
<b>Outcomes/endpoints</b>	GP's sensitivity (95% CI); specificity; PPV for detecting non-referable retinopathy Ophthalmoscopy alone 22% (12 to 31); 94%; 46% Ophthalmoscopy + photo: 39% (21-57); 92%; 51% for referable retinopathy Ophthalmoscopy alone 53% (26-81); 98%; 61% Ophthalmoscopy + photo: 64% (35-94) 98%; 48% Optician sensitivity (95% CI); specificity; PPV for detecting non-referable retinopathy Ophthalmoscopy alone 43% (24 to 62); 94%; 68% Ophthalmoscopy + photo: 56% (41-70) for referable retinopathy Ophthalmoscopy alone: 83% (66-109); 93%; 35% Ophthalmoscopy + photo: 83% (66-109); 98%; 40% addition of specialist review of photos to that of GP and optician in combination increased the sensitivity of detecting referable retinopathy from 73% to 84% (mean sensitivity 86%; 95% CI 74-97) Crude calculation: based on 80% of people receiving laser treatment having sight saved £1095 per patient saved from blindness

<b>Study</b>	<b>Penman et al 1998</b>
<b>Population</b>	Subjects of a population based survey in Egypt on diabetes mean age 53.7 years 347 had previously diagnosed diabetes (76%) for a mean duration of 11.2 years
<b>Study Comparison(s)</b>	Non mydriatic retinal photography (35mm) read by independent graders
<b>Reference standard</b>	Binocular indirect ophthalmoscopy
<b>Other features</b>	Ophthalmologists performed 45° non mydriatic retinal photography classification of DR was by modified Airlie House Classification Scheme
<b>Location</b>	Cairo, Egypt
<b>Inclusion/Exclusion criteria</b>	None stated
<b>Blinding</b>	Yes
<b>Numbers in study</b>	456 participants had eye examination. (109 newly diagnosed during study) Final sample 427 417 had ophthalmoscopy and retinal photography 10 had ophthalmoscopy only
<b>Non participants</b>	29 (6.4%) refused ophthalmology or retinal photograph or had incomplete examinations 62% of these were legally blind
<b>Outcomes/endpoints</b>	92 (22)% of photographs ungradeable - mainly due to cataract, 23 eyes ophthalmoscopy failed. sensitivity and specificity of ophthalmoscopy non mydriatic fundus photography: (all retinopathy) 85% and specificity 83% (STDR) 60% and specificity 96%  KAPPA = 0.51 (0.42-0.6) after sight threatening, removing ungradeable photographs.

<b>Study</b>	<b>Pugh et al 1993</b>
<b>Population</b>	Diabetes outpatients and patients from a medical centre (Type 1 and Type 2) mean duration of diabetes 9.8 years 76% male; 59.7% <65 years 52.1% non-Hispanic white, 10.3% Afro-American 37.6% Mexican-American
<b>Study Comparison(s)</b>	4 screening methods: direct and indirect ophthalmoscopy through dilated pupils by an ophthalmologist; physician assistant carrying out direct ophthalmoscopy through dilated pupils; single 45° retinal photograph non-dilated; 3 sets of 45° photos through dilated pupils
<b>Reference standard</b>	7 field 30° retinal photography
<b>Other features</b>	All photographs graded by University of Wisconsin Fundus photography reading centre 45° photographs assessed by 2 local internists
<b>Location</b>	Primary care setting, USA
<b>Inclusion/Exclusion criteria</b>	Exclusion: Already blind, previous laser treatment, under treatment for glaucoma, mentally incompetent.
<b>Blinding</b>	Yes for photograph readers, 10 ophthalmologists, with 4 doing 87.5% of examinations.
<b>Numbers in study</b>	553 eligible 352 participated, but 5 missed for ophthalmologists, 103 for physician assistants, rest refusals and 'no shows'. 106 some data missing (102 not examined by physicians assistant) (4 not by ophthalmologist) 5 Type 1 and rest were Type 2
<b>Non participants</b>	36% (no differences in participants/non participants in terms of age/sex/race and duration of diabetes) and 37.6% Mexican American
<b>Outcomes/endpoints</b>	Correctly grading worst eyes as none/mild non proliferative/moderate to severe non proliferative/proliferative against reference standard Indirect/direct ophthalmoscopy (sensitivity; specificity; Positive predictive value) Ophthalmologist: 33%; 99%; 72% Physician assistant: 14%; 99%; 12%; Undilated 45° photos read by reading centre 0.61; 0.85; 0.04; Dilated 45° photos read by reading centre 0.8; 0.96; 0.22 Undilated photographs read by internist 0.54; 0.87; 0.04 Dilated photographs read by internist 0.64; 0.90; 0.06 The dilated 45° photographs were significantly more sensitive than the other methods (Ophthalmologist p<0.0001, Undilated p<0.002 dilated photos read by internist p<0.01)

<b>Study</b>	<b>Reenders et al 1992</b>
<b>Population</b>	General practice population of people with Type 2 diabetes no reporting of patient characteristics
<b>Study Comparison(s)</b>	GP direct ophthalmoscopy through dilated eyes
<b>Reference standard</b>	Same method performed by hospital ophthalmologists
<b>Other features</b>	19 of 26 GP's in the region took part examining own patients after 2 training sessions were organised Retinopathy was classified into 4 stages of severity
<b>Location</b>	Hoogeveen, Holland, general practice
<b>Inclusion/Exclusion</b>	People with established retinopathy excluded
<b>Blinding</b>	Yes
<b>Numbers in study</b>	252 (from 507 eligible) 50%
<b>Non participants</b>	120 refused to participate 97 already with established eye pathology excluded 38 refused referral or GP unable to assess retina) no discussion of differences participants/non participants
<b>Outcomes/endpoints</b>	GP sensitivity (95% CI); specificity (95% CI) compared to reference standard any retinopathy: 52% (31-73); 84% (79-89) proliferative retinopathy (stages II, III, IV) 43% (1-91); 92% (88-95) Ophthalmologist detected 23 cases of retinopathy; GP found 12 (11 false negatives) 7 of 11 were stage I (background retinopathy) 2 were stage II retinopathy 2 were stage III (preproliferative retinopathy)

<b>Study</b>	<b>Ryder et al 1998b</b>
<b>Population</b>	Hospital diabetic clinic patients Mean age: Male 61 years (range 32-88) female 63 (range not reported)
<b>Study Comparison(s)</b>	Specialist optometrist examining mydriatic retinal Polaroid 45° photographs combined in all cases with ophthalmoscopy except if photos perfect and no retinopathy present – undilated/dilated
<b>Reference standard</b>	1 <sup>st</sup> audit, 2 diabetes physicians using ophthalmoscopy and analysing the retinal same photographs, and 2 <sup>nd</sup> audit discussing all cases with an ophthalmologist
<b>Other features</b>	Patients underwent optometrist screening as part of their annual review If photographs were less than perfect and there was any possibility of retinopathy, ophthalmoscopy (direct/indirect not stated) was also conducted. Cases of uncertainty could also be discussed by the optometrist with a Diabetologist
<b>Location</b>	City Hospital, Birmingham
<b>Inclusion/Exclusion</b>	People attending an ophthalmologist were excluded
<b>Blinding</b>	Yes
<b>Numbers in study</b>	145 consecutive hospital diabetic clinic patients (144 1 <sup>st</sup> audit, 145 repeat audit)
<b>Non participants</b>	None
<b>Outcomes/endpoints</b>	Sensitivity for the detection of any retinopathy: 97.2% Sensitivity for the detection of retinopathy requiring 6 month review: 100% Sensitivity for the detection of sight threatening retinopathy: 100%

<b>Study</b>	<b>Schachat et al 1993</b>
<b>Population</b>	Subset of population taking part in Barbados Eye Study (random sample of population aged 40-86 years) comprised people with and without diabetes
<b>Study Comparison(s)</b>	Indirect/direct, dilated ophthalmoscopy by ophthalmologist & slit lamp biomicroscopy
<b>Reference standard</b>	7 field 30 stereoscopic fundus photography, graded by 2 graders independently.
<b>Other features</b>	2643 participants received fundus photography - 1168 were referred for ophthalmic examination (visual acuity < 20/30, intraocular pressure > 21 mmHg, history of eye disease)
<b>Location</b>	Barbados, West Indies, hospital diabetes clinics.
<b>Inclusion/Exclusion criteria</b>	
<b>Blinding</b>	Yes
<b>Numbers in study</b>	1168 people who were referred for ophthalmic examination (9.5% definite diabetes), 13.3% probable) In terms of age, sex similar to original sample, although more had diabetes
<b>Non participants</b>	Of original sample of 2643, 341 did not have gradeable photographs
<b>Outcomes/endpoints</b>	Sensitivity and specificity of ophthalmological clinical examination compared with reference standard of 3 field 30? fundus photography read by 2 independent graders 76.47% (68-85) by CIA; 99% (98-100) frequency of diabetic retinopathy detection was 90/1168 (7.7%) by ophthalmic clinical examination and 102/1168 (8.7%) by photography

**Study** **Van der Kar et al 1990**

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<b>Population</b>	General practice population
<b>Study Comparison(s)</b>	Mydriatic 45° photos – Polaroid colour - read by 4 GPs and 1 hospital physician compared with the reference standard
<b>Reference standard</b>	2 ophthalmologists reading same photos 1 standard - when 1 ophthalmologist diagnoses retinopathy 2nd standard - when both ophthalmologists agreed on diagnosis of retinopathy
<b>Other features</b>	GP's/hospital physician received no special training. Reference charts of normal/abnormal fundus were available during assessment Analysis based on combined assessment of the two eyes of each patient.
<b>Location</b>	Breda, Holland
<b>Inclusion/Exclusion</b>	Not stated
<b>Blinding</b>	Yes
<b>Numbers in study</b>	62 patients (selected from 168 diagnosed with diabetes mellitus)
<b>Non participants</b>	Not stated
<b>Outcomes/endpoints</b>	Referable retinopathy: GPs + Physicians. Sensitivity 98 (96-100), specificity 48 (32-61) GP sensitivity 99, specificity 46%, physicians 96%, 52%. Any retinopathy diagnosing a) Standard: consensus between both ophthalmologists: sensitivity (95% CI); specificity (95% CI) b) GPs/hospital physicians: 99% (87-100); (95% CI): 55% (37-72) Standard: diagnosis by one or both ophthalmologists diagnosing any retinopathy: sensitivity (95% CI); specificity (95% CI) GPs/hospital physicians: 91% (88-94); 61% (37-76) a) For GPs (Average of 4) sensitivity 100% specificity, 53% (Average), for physicians sensitivity 96%, specificity 59% b) For GPs, sensitivity 91% (Average) specificity 57% (Average). For physicians sensitivity 89%, specificity 68%

<b>Study</b>	<b>Williams et al 1986</b>
<b>Population</b>	Random population attending general diabetes clinic and eye disease clinic
<b>Study Comparison(s)</b>	a) Non mydriatic retinal photography by routine doctor b) Polaroid colour print or ASA200 colour transparency read by 2 ophthalmologists
<b>Reference standard</b>	Ophthalmologists assessment by indirect and direct ophthalmology (dilated)
<b>Other features</b>	
<b>Location</b>	Hospital Clinics in London
<b>Inclusion/Exclusion</b>	Not stated
<b>Blinding</b>	Yes
<b>Numbers in study</b>	62 patients, 120 eyes (86 eyes Polaroid, 34 eyes transparencies)
<b>Non participants</b>	Yes
<b>Outcomes/endpoints</b>	Detection of any diabetic retinopathy Sensitivity of camera: 96% (95% CI: 88-99) specificity: 98%(95% CI: 87-100) Maculopathy: Sensitivity of camera: 100% specificity 96%  Doctor – detecting any retinopathy Sensitivity: 93% Specificity: 93% Doctor – detecting maculopathy Sensitivity 94% Specificity 95% Ophthalmologist (35mm or Polaroid) vs. clinical assessment by ophthalmologist AR sensitivity 96% Specificity 98%

# Selected cost-effectiveness studies

Study	James et al 2000																
<b>Study Comparisons:</b>	<p>systematic screening programme mobile screening unit that visits inner city GP practices plus a dedicated hospital assessment clinic.</p> <p>pre-existing opportunistic service.</p>																
<b>Screening methods</b>	<p>systematic screening programme 3 field non stereoscopic photography using mydriasis, 35mm transparencies and validated grading.</p> <p>pre-existing opportunistic service direct ophthalmoscopy performed by GPs, optometrists, diabetologists.</p>																
<b>Source data</b>	<p>for the analysis cross sectional observational study of 320 diabetic patients registered with 4 general practices, examined by ophthalmologist using slit lamp biomicroscopy. implementation of systematic screening in Liverpool – questionnaires to first 1363 diabetic patients recruited.</p>																
<b>Figure used</b>	<p>prevalence sight threatening eye disease, Liverpool 14.1% from cross sectional study.</p> <p>compliance systematic screening 80% (sensitivity 89% (80-98) opportunistic screening (overall sensitivity 63%, overall specificity 92%)</p>																
<b>Analysis approach for costing</b>	<p>ingredient approach (as costs as fixed or largely fixed)</p> <p>cost effectiveness = <math>\frac{\text{total cost}}{\text{no. of cases detected}}</math></p> <p>incremental cost effectiveness=extra cost needed to generate each additional true positive result after replacing opportunistic by systematic screening.</p> <p>sensitivity analysis to determine the effect on cost effectiveness of varying the key variables.</p>																
<b>Results</b>	<p>cost effectiveness of opportunistic and systematic screening programmes</p> <table border="1"> <thead> <tr> <th></th> <th>opportunistic screening</th> <th>systematic screening</th> <th>difference</th> </tr> </thead> <tbody> <tr> <td>cost of screening (£)</td> <td>99 981</td> <td>104 996</td> <td>5015</td> </tr> <tr> <td>no. of true cases detected</td> <td>346</td> <td>502</td> <td>156</td> </tr> <tr> <td>cost effectiveness (£)</td> <td>289</td> <td>209</td> <td>32 *</td> </tr> </tbody> </table> <p>* incremental cost effectiveness of systematic screening</p> <hr/> <p>a two way analysis of the effect on the systematic screening programme of varying sensitivity and specificity (within given confidence limits)</p> <p>low sensitivity (80%), low specificity (82%) = £237 high sensitivity (98%), high specificity (90%) = £186</p> <p>systematic screening is more cost effective than opportunistic screening within the 95% confidence range.</p> <p>systematic screening costs effectiveness at different compliance rates</p> <p>at 30% compliance = £487 at 100% compliance = £176</p> <p>At 54% compliance the cost effectiveness of systematic screening equals that of opportunistic at £289</p>		opportunistic screening	systematic screening	difference	cost of screening (£)	99 981	104 996	5015	no. of true cases detected	346	502	156	cost effectiveness (£)	289	209	32 *
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<b>Study</b>	<b>Lairson et al 1992 (same study as Pugh et al 1993)</b>																		
<b>Population</b>	Veterans receiving care at a hospital and retirees at a medical centre mean duration of diabetes 9.8 years 76% male; 59.7% >65 years 52.1% non Hispanic white, 10.3% Afro American and 37.6% Mexican American																		
<b>Study Comparison(s)</b>	Cost effectiveness of 45-degree fundus photographs versus indirect and direct ophthalmology by ophthalmologists, direct ophthalmology by technicians																		
<b>Reference standard</b>	Seven field stereoscopic fundus photography																		
<b>Other features</b>	45-degree photographs were taken by technicians and assessed by experts in dilated or undilated pupils. Technicians carrying out direct ophthalmology were physicians assistant or nurse practitioner assistant																		
<b>Location</b>	Veterans hospital and medical centre, Texas																		
<b>Inclusion/Exclusion criteria</b>	Already blind, previous laser treatment, under treatment for glaucoma																		
<b>Blinding</b>																			
<b>Numbers in study</b>	352																		
<b>Non participants</b>	36% non participation: no differences in participants/non participants in terms of age/sex/race and duration of diabetes																		
<b>Outcomes/endpoints</b>	Costs derived from medical system costs, such as personnel, time, equipment (specifically Canon CR camera), overheads etc patients costs include travel and opportunity costs cost effectiveness measure was ratio of total cost of screening compared to number of true positive tests <table border="0" style="margin-left: 20px;"> <tr> <td>Cost per true positive case: Technician</td> <td style="text-align: right;">\$794</td> </tr> <tr> <td>Ophthalmologist</td> <td style="text-align: right;">\$390</td> </tr> <tr> <td>45-degree (without dilation)</td> <td style="text-align: right;">\$378</td> </tr> <tr> <td>45-degree (with dilation)</td> <td style="text-align: right;">\$295</td> </tr> <tr> <td colspan="2">Patient costs per true positive case</td> </tr> <tr> <td>Technician</td> <td style="text-align: right;">\$1009</td> </tr> <tr> <td>Ophthalmologist</td> <td style="text-align: right;">\$306</td> </tr> <tr> <td>45-degree (without dilation)</td> <td style="text-align: right;">\$171</td> </tr> <tr> <td>45-degree (with dilation)</td> <td style="text-align: right;">\$139</td> </tr> </table>	Cost per true positive case: Technician	\$794	Ophthalmologist	\$390	45-degree (without dilation)	\$378	45-degree (with dilation)	\$295	Patient costs per true positive case		Technician	\$1009	Ophthalmologist	\$306	45-degree (without dilation)	\$171	45-degree (with dilation)	\$139
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<b>Study</b>	<b>Sculpher et al 1991 (same study as Buxton et al 1991)</b>
<b>Population</b>	Hospital and community diabetics Mean age range between groups 49 – 66 yrs; % Male Range 51 - 56%; Insulin treated range 5-75%; Mean duration of diabetes range 7-11 years
<b>Study Comparison(s)</b>	General practitioner or ophthalmic optician ophthalmoscopy plus non mydriatic retinal 45° photographs read by ophthalmologists.
<b>Reference standard</b>	Ophthalmoscopic examination by an ophthalmological clinical assistant
<b>Other features</b>	Patients recruited from 3 UK centres. One centre had screening by GPs, one centre had screening by GPs and ophthalmic opticians, and one centre had GP screening and hospital patients screened by hospital physician (Exeter)
<b>Location</b>	Exeter (GP), Oxford and Sheffield (Hospital)
<b>Inclusion/Exclusion</b>	Inclusion: Patients 16 years or older (3 centres); Patients under 16 but diabetes for greater than 5 years (1 centre) Exclusion: Blind, treated for diabetic retinopathy, under care of hospital ophthalmologist, other reasons (non attendance/GP records not up to date)
<b>Blinding</b>	Yes
<b>Numbers in study</b>	2891 in total. Hospital physician: 416 (Exeter) General practitioner: 2350 (Sheffield 641, Oxford 628, Exeter 1207) Ophthalmic optician: 415 (Oxford) Non-mydriatic retinal photographs: 2799 (all centres) plus 532 (Sheffield) no primary screener
<b>Non participants</b>	Hospital physician: 229 (34.9%) General practitioner: 2987 (54.7%; Range 35.8-72.4%) Optician: 680 (62.1%) overall 56% who had had ophthalmological examination in previous year
<b>Outcomes/endpoints</b>	Analysis of results according to 13 screen options. quality of photographs: 4.9% photographs unusable; 44.1% excellent (range 12-64%) referral of cases of sight threatening retinopathy: sensitivity, specificity and OR GP ophthalmoscopy + photography: 0.80; 0.86 Optician ophthalmoscopy + photography: 0.67;0.89

<b>Study</b>	<b>Sculpher et al 1992 (same study as Buxton et al 1991)</b>
<b>Population</b>	General practice and diabetes clinic population
<b>Study Comparison(s)</b>	Ophthalmoscopy by GP's and ophthalmic opticians Fundus photography (non mydriatic camera) hospital based: GP visiting GP and GP visiting camera combined Optician and GP visiting camera combined
<b>Reference standard</b>	Ophthalmoscopy by ophthalmological clinical assistant
<b>Other features</b>	Patients recruited from 3 UK centres. One centre had screening by GPs, one centre had screening by GPs and ophthalmic opticians, and one centre had GP screening and hospital patients screened by hospital physician
<b>Location</b>	General practices and hospital
<b>Inclusion/Exclusion criteria</b>	Patients 16 years or older (3 centres) Patients under 16 but diabetes for greater than 5 years (1 centre) Blind, treated for diabetic retinopathy, under care of hospital ophthalmologist, non attendance etc
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<b>Outcomes/endpoints</b>	Costs derived from staff involved, travel of staff where appropriate, consumable (drugs and film and location overheads) Fixed capital costs based on annual equivalent cost based on expected life of camera and discount rate of 6% Cost of ophthalmic screen based on 1989-90 rate of reimbursement of opticians by Family Practitioner committee for health services eye tests Patient costs included travel and opportunity costs of time away from work Expected cost per true positive case (£) Ophthalmoscopy: GPs £784 Ophthalmoscopy: opticians £784 Fundus photography (non mydriatic camera) hospital based £1178 GP visiting £497 Combined modality GP and GP visiting camera £734 Optician and GP visiting camera £968

Study	Vijan et al 2000																
	Sought to evaluate whether HbA <sub>1c</sub> level can be used to effectively stratify the frequency of diabetic retinal screening and improve the efficiency and cost effectiveness of screening																
<b>Methods</b>	nonstationary Markov model to simulate progression of diabetic retinopathy and macular oedema																
<b>Simulated patient characteristics</b>	stratified into no retinopathy non-proliferative retinopathy (based on Airlie House classification) proliferative retinopathy macular oedema blindness also classified further according to having diagnosis of retinopathy or macular oedema																
<b>Simulated population characteristics</b>	characteristics of diabetic population older than 40 years in ***** National Health and Nutrition Examination Survey (USA)																
<b>Assumption re HbA<sub>1c</sub> and eye disease</b>	based on UKPDS – decrease of 0.9% in HbA <sub>1c</sub> (from 7.9% to 7%) was related to 21% decrease in risk of retinopathy progression over 12 years progression beyond non-proliferative retinopathy to proliferative, macular oedema and blindness assumed to be independent of level of glycaemic control rates of progression taken from Diabetic Retinopathy Study (DRS) and Early Treatment of Diabetic Retinopathy Study (ETDRS) mortality rates based on USA fee tables modified to reflect increased rates of patients with diabetes in general. eye exams annual to 5 year intervals screening done by ophthalmologists																
<b>Outcome measures used</b>	QALYS discount 3%																
<b>Costs</b>	average Medicare reimbursement																
<b>Analysis</b>	one way sensitivity analyses conducted on individual estimates to assess their impact on the costs and effectiveness of screening range of possible effectiveness estimated – multivariate sensitivity analyses conducted using simulation approach to estimate the variance and distribution of the cost-effectiveness estimates – Monte Carlo Simulation																
<b>Selected outcomes of model</b>	Multivariate sensitivity analyses; estimated benefit across range of parameter estimates <sup>1</sup> range (encompassing 95%) of marginal value of screening <table border="1" data-bbox="485 1417 1342 1854"> <thead> <tr> <th data-bbox="485 1429 619 1473">group characteristics</th> <th data-bbox="740 1429 847 1473">ranges of outcomes</th> <th data-bbox="986 1429 1114 1473">every 2 vs every 3 yrs</th> <th data-bbox="1193 1429 1321 1473">annual vs every 2yrs</th> </tr> </thead> <tbody> <tr> <td data-bbox="485 1485 639 1563">high risk patients aged 45 yrs, HbA<sub>1c</sub> 11%</td> <td data-bbox="740 1485 954 1563">range of reduction in time spent blind cost-effectiveness range</td> <td data-bbox="986 1485 1129 1563">8.9 – 18.4 days \$10990 – 28850</td> <td data-bbox="1193 1485 1337 1563">7.9 – 15.5 days \$23210 - \$58920</td> </tr> <tr> <td data-bbox="485 1608 683 1709">moderate risk patients aged 65 yrs, HbA<sub>1c</sub> 11% \$205300</td> <td data-bbox="740 1608 954 1686">range of reduction in time spent blind cost-effectiveness range</td> <td data-bbox="986 1608 1129 1686">2.1 – 3.4 days \$41420 – 90030</td> <td data-bbox="1193 1608 1321 1686">1.8 – 3.2 days \$89740 -</td> </tr> <tr> <td data-bbox="485 1753 635 1854">low risk patients aged 75 yrs, HbA<sub>1c</sub> 7% \$366490</td> <td data-bbox="740 1753 954 1832">range of reduction in time spent blind cost-effectiveness range</td> <td data-bbox="986 1753 1153 1832">0.6 – 1.1 days \$82190 - \$193150</td> <td data-bbox="1193 1753 1321 1832">0.5 – 1.0 days \$169630 -</td> </tr> </tbody> </table>	group characteristics	ranges of outcomes	every 2 vs every 3 yrs	annual vs every 2yrs	high risk patients aged 45 yrs, HbA <sub>1c</sub> 11%	range of reduction in time spent blind cost-effectiveness range	8.9 – 18.4 days \$10990 – 28850	7.9 – 15.5 days \$23210 - \$58920	moderate risk patients aged 65 yrs, HbA <sub>1c</sub> 11% \$205300	range of reduction in time spent blind cost-effectiveness range	2.1 – 3.4 days \$41420 – 90030	1.8 – 3.2 days \$89740 -	low risk patients aged 75 yrs, HbA <sub>1c</sub> 7% \$366490	range of reduction in time spent blind cost-effectiveness range	0.6 – 1.1 days \$82190 - \$193150	0.5 – 1.0 days \$169630 -
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<b>Conclusions</b>	1. sensitivity analyses were conducted by repeated random sampling across the ranges of parameter estimates (e.g. annual disease progression rates, mortality multipliers, characteristics of screening test, costs) annual retinopathy screening for most patients with Type 2 diabetes produces little benefit that is not achieved with every second to third year screening																

# 7. Bibliography

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The Roman numerals indicate the evidence grading given to that particular paper. If no evidence grade is shown, it means that the paper was not of a type that could be graded according to the system used.

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# 8. Appendices

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# Appendix 1: Commentary on health economic issues

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# Screening and cost effectiveness

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This commentary was prepared by Dr James Mason, University of York.

Evidence presented in this guideline supports the general conclusion that organised (digital) camera screening using mydriasis and trained staff, or indirect ophthalmoscopy with mydriasis performed by optometrists, may perform better than other screening modalities. Variations between the studies in methodology, alternatives chosen, screening definitions and mode of assessment prevent more refined use of the evidence.

Important issues are raised when attempting to develop this evidence to address the cost-effectiveness of screening for diabetic retinopathy.

First, the incremental benefit of moving from informal to formal screening is uncertain and likely to be very variable. In stable diabetic populations with good patient registration, patient review with routine visual examination, uptake of free diabetic eye-care and liaison between primary and secondary care providers, it is likely that informal screening produces better outcomes than when some or all of these factors are not present.

Second, the additional cost of formal screening is uncertain. Opportunistic screening, when conducted, is one component of a (clinical) annual review or an (optometric) sight test for a range of possible diseases and conditions. These activities will have to continue regardless and it seems unreasonable to assert that any (realisable) savings will arise from redundant opportunistic screening if formal screening is introduced. The introduction of a mobile camera screening service at the Primary Care Trust level has very different service cost implications to the involvement of optometrists in formal screening.

Third, the appropriate interval for formal screening is unclear, but would have a major impact on the additional costs and benefits of formal screening since opportunistic case finding will occur regardless (Vijan et al, 2000).

Fourth, although there is some overlap, different people with diabetes are seen opportunistically by different healthcare providers. Even with formal screening, only those patients registered in local patient databases and responding to the request to attend will benefit from a formal screening programme. Although formal screening may prove desirable it is not a panacea, and vigilance on behalf of all healthcare providers should be valued rather than replaced.

Fifth, the value of screening rests upon the existence of effective treatment for those identified with sight threatening disease. Although not formally reviewed in this guideline, intervention during the progression of disease by laser photocoagulation was first shown to be effective during the 1970s. The Diabetic Retinopathy Study Research Group (DRS, 1976, 1981) and the British Multicentre Study Group (1984) demonstrated the effectiveness of photocoagulation treatment for proliferative retinopathy. Similarly, the British Multicentre Study Group (1983) and the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS, 1985) demonstrated the effectiveness of photocoagulation in preventing visual loss due to maculopathy. Valuation metrics vary between studies but estimates of reduction in impairment exceed 50% and depend on the stage at which disease is detected and the type of retinopathy.

A number of economic analyses have been conducted in British and American settings, which have explored various aspects of screening (UK: James et al, 2000; Sculpher et al 1991a,b; USA: Dasbach et al, 1991; Javitt et al, 1996; Lairson et al, 1992; Vijan et al, 2000). These reflect and

compound the weaknesses in the original clinical studies and serve simply to reinforce the need for definitive research.

It is beyond the scope of this guideline to resolve the issues raised here. However, the National Screening Committee is currently examining the resource implications of screening. Piloted implementation of any scheme should be considered to permit the added value of formal screening to be demonstrated by its impact upon diabetic retinopathy-related blindness registrations. This may circumvent many of the limitations found in existing studies in favour of an objective and patient-oriented outcome, and may permit adequate evaluation before a national screening programme is introduced.

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## Appendix 2: Recommendations panel: membership

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Professor Richard Baker	Director, Clinical Governance Research & Development Unit, University of Leicester
Professor Colin Bradshaw	General Practitioner, Marsden Road Health Centre, Tyne and Wear (until May 2000)
Ruth Davis	Senior Lecturer, School of Nursing & Midwifery, University of Glamorgan
Dr Anne Dawson	Senior Medical Officer Department of Health
Professor Martin Eccles	Professor of Clinical Effectiveness, Centre for Health Services Research, University of Newcastle
Professor Gene Feder	Professor of Primary Care Research and Development, Queen Mary and Westfield College, London
Professor John Forrester	Department of Ophthalmology, University of Aberdeen
Alethea Foster	Chief Podiatrist, Diabetic Foot Clinic, Kings College Hospital, London
Dr Gary Frost	Head of Service, Nutrition & Dietetics Department, Hammersmith Hospital, London
Professor Trisha Greenhalgh	Director Unit for Evidence Based Practice and Policy, Royal Free & University College Medical School, London
Dr Chris Griffiths	Reader, Department of General Practice, Queen Mary and Westfield College. London
Dr Margaret Guy	NHS Executive London Regional Office
Professor Philip Home	Professor of Diabetes Medicine, Department of Medicine, Medical School, University of Newcastle
Professor Allen Hutchinson (Chair)	Director, RCGP Effective Clinical Practice Programme, Professor of Clinical Public Health, Section of Public Health, ScHARR, University of Sheffield
Suzanne Lucas	Director of Care, Diabetes UK
Dr Sally Marshall	Reader in Diabetes Department of Medicine, Medical School, University of Newcastle

Paula-Jayne McDowell	Guidelines Initiative Officer, Royal College of General Practitioners
Aileen McIntosh	Senior Research Fellow, Section of Public Health, ScHARR, University of Sheffield & Programme Manager, RCGP Effective Clinical Practice Unit
Professor James Mason	Professor of Health Economics, Centre for Health Services Research, University of Newcastle
Professor Rhys Williams	Professor of Epidemiology & Public Health, Nuffield Institute for Health, Leeds
Dr Robert Young	Consultant Diabetologist, Salford Royal Hospital Trust, Hope Hospital, Manchester

## Appendix 3: Diabetic retinopathy working group

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The retinopathy management working group consisted of relevant health care professionals, and specialist resources (including reviewers and guideline methodologists).

### Membership of the eye care working group

Dr Bill Alexander	Consultant Physician, Western General Hospital, Edinburgh
Professor Richard Baker (chair)	Director, Clinical Governance Research & Development Unit, University of Leicester
Mrs Anne Eltringham-Cox	Diabetes Care Adviser, Diabetes UK
Professor John V Forrester	Head of Department of Ophthalmology, University of Aberdeen
Dr Richard Greenwood	Consultant in General Medicine, Department of Diabetes & Endocrinology, Norfolk and Norwich Hospital
Dr Gill Grimshaw	Senior Research Fellow, Centre for Health Services Studies, Warwick Business School
Dr Christine Hine	Consultant in Public Health, Avon Health Authority
Dr Kamlesh Khunti	Clinical Lecturer, Clinical Governance Research & Development Unit, University of Leicester
Aileen McIntosh	Senior Research Fellow and Programme Manager, RCGP Effective Clinical Practice Programme, University of Sheffield
Colin O'Keeffe (until August 1999)	Research Associate, ScHARR, University of Sheffield
Dr Jean Peters (from August 1999)	Senior Lecturer in Public Health, ScHARR, University of Sheffield
Dr Andrew Wilson	Senior Lecturer, Dept of General Practice & Primary Health Care, University of Leicester
Professor Geoff Woodward	Head of Department, Department of General Optometry and Visual Science, The City University