



Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts

Alan D Fleming, Keith A Goatman, Sam Philip, Gordon J Prescott, Peter F Sharp, John A Olson

► To cite this version:

Alan D Fleming, Keith A Goatman, Sam Philip, Gordon J Prescott, Peter F Sharp, et al.. Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts. British Journal of Ophthalmology, BMJ Publishing Group, 2010, 94 (12), pp.1606. 10.1136/bjo.2009.176784 . hal-00578459

HAL Id: hal-00578459

<https://hal.archives-ouvertes.fr/hal-00578459>

Submitted on 21 Mar 2011

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

TITLE

Automated grading for diabetic retinopathy: a large-scale audit using arbitration by clinical experts

AUTHORS

Alan D Fleming¹; Keith A Goatman¹; Sam Philip²; Gordon J Prescott³; Peter F Sharp¹; John A Olson²

ADDRESSES

1. Biomedical Physics, University of Aberdeen, Foresterhill, AB25 2ZD
2. Diabetes Retinal Screening Service, David Anderson Building, Foresterhill Road, Aberdeen AB25 2ZP
3. Section of Population Health, University of Aberdeen, Foresterhill, AB25 2ZD

CORRESPONDING AUTHOR

Dr John A Olson MD FRCPedin FRCOphth, Clinical Director, Diabetes Retinal Screening Service, NHS Grampian, David Anderson Building, Foresterhill Road, Aberdeen, AB25 2ZP. Telephone +44-845 330 2320. Fax +44-1224-550456. Email john.olson@nhs.net.

KEYWORDS

diabetic retinopathy, screening, computer-assisted image analysis, imaging, telemedicine

ACCEPTED FOR PUBLICATION IN BRITISH JOURNAL OF OPHTHALMOLOGY

31 January 2010

ABSTRACT

Background/aims: Automated grading software has the potential to reduce the manual grading workload within diabetic retinopathy screening programmes. This audit was undertaken at the request of Scotland's National Diabetic Retinopathy Screening Collaborative to assess whether the introduction of automated grading software into the national screening programme would be safe, robust and effective.

Methods: Automated grading, performed by software for image quality assessment and for microaneurysm/dot haemorrhage detection, was carried out on 78,601 images, obtained from 33,535 consecutive patients, which had been manually graded at one of two regional diabetic retinopathy screening programmes. Cases where the automated grading software assessment indicated gradable images with no disease but the screening programme indicated ungradable images or disease more severe than mild retinopathy were arbitrated by 7 senior ophthalmologists.

Results: 100% (180/180) of patients with proliferative retinopathy, 100% (324/324) with referable background retinopathy, 100% (193/193) with observable background retinopathy, 97.3% (1099/1130) with referable maculopathy, 99.2% (384/387) with observable maculopathy and 99.8% (1824/1827) with ungradable images were detected by the software.

Conclusion: The automated grading software operated to previously published results when applied to a large, unselected population attending two regional screening programmes. Manual grading workload reduction would be 36.3%.

INTRODUCTION

Systematic screening for diabetic retinopathy using retinal photography has been shown to reduce the incidence of blindness among people with diabetes.[1-4] Diabetic retinopathy screening programmes are challenged by the rising prevalence of diabetes,[5] the costs of implementation,[6,7] the maintenance of an effective quality assurance system,[8] and the repetitious nature of grading. As a result, means for improving the efficiency of screening are being sought such as optimisation of the screening interval,[9] reducing the number of photographic fields used,[10] and automation of image grading,[11] the topic of this paper.

The performance of automated grading software is often measured in terms of sensitivity and specificity for detecting retinopathy.[12,13] However, absolute values for these may not be immediately useful when deciding whether an automated grading system would be effective at improving screening programme efficiency. It is also important to know the relative sensitivities and costs between alternative grading systems, one of which is performed only by human graders while the other includes automated grading software. It is also important to know whether any missed cases have equivocal or unequivocal retinopathy.

In a previous study, involving 6,722 patients from Grampian, we compared automated and manual grading systems to a reference standard grading.[7,14] The automated grading software had a better detection rate, 90.5% (2283/2523), than manual grading, 86.5% (2182/2523), for any retinopathy (mild or more severe retinopathy) and there was no significant difference between the detection rates, 97.9% (323/330) by automated grading and 99.1% (327/330) by manual grading, for observable/referable retinopathy (more severe than mild retinopathy). With 45.7% of cases not requiring manual grading, an annual saving of £200,000 would be made for the 160,000 people with diabetes in Scotland, estimated for the financial year 2005/2006. However, before the software could be implemented into the Scottish national diabetic retinopathy screening programme, it was necessary to demonstrate that its performance was maintained when used in other Scottish screening centres.

Table 1: The Scottish grading scheme.[16] Inferior and superior hemi-fields are delineated by a line passing through the centres of the fovea and the optic disc. Designations in the Scottish grading scheme are given (R0...R6, M0...M2).

Grade	Features	Location	Outcome
Retinopathy			
No visible retinopathy (R0,M0)	No visible lesions of diabetic retinopathy		
Mild background retinopathy (R1)	Microaneurysms/dot haemorrhages Hard exudates Cotton wool spots Blot haemorrhages Superficial/flame shaped haemorrhages	Anywhere	Re-screen after 12 months
Observable background retinopathy (R2)	Four or more blot haemorrhages (\geq Airlie House standard photograph 2a)	In one hemi-field only	Re-screen after 6 months
Referable background retinopathy (R3)	Four or more blot haemorrhages (\geq Airlie House standard photograph 2a) Venous beading (\geq Airlie House standard photograph 6a) IRMA (Airlie House standard photograph 8a)	In both inferior and superior hemi-fields Anywhere	Refer to ophthalmology
Proliferative referable retinopathy (R4)	Active new vessels Vitreous haemorrhage	Anywhere	
Maculopathy			
Observable maculopathy (M1)	Hard exudates	>1 and ≤ 2 disc diameters from the centre of the fovea	Re-screen after 6 months
Referable maculopathy (M2)	Blot haemorrhages Hard exudates	≤ 1 disc diameter from the centre of the fovea	Refer to ophthalmology
Gradability			
Ungradable (R6)	Retina not sufficiently visible for assessment		Refer for slit-lamp examination

MATERIALS AND METHODS

The study outline is shown in figure 1. Images were obtained from two Scottish screening centres, Glasgow and Fife, working in accordance with the requirements of National Health Quality Improvement Scotland. Caldicott Guardian approval was obtained for the study.

Photography and grading were performed by graders employed within the Scottish screening programmes according to the recommendations of Scotland's National Diabetic Retinopathy Screening Collaborative.[15]

A single 45° macula-centred photograph was taken of each eye, with additional photographs obtained as required, for example, to obtain better image quality or a better view of pathology. Mydriasis was used where small pupils prevented the capture of adequate quality images; a process known as "staged mydriasis". Images were obtained with 7 fundus cameras in Glasgow (Canon EOS D30 and EOS 20D digital cameras with Canon CR6-45NM and CR-DGi non-mydratiac retinal cameras) and 3 in Fife (Canon EOS 20D digital cameras with Canon CR-DGi non-mydratiac retinal cameras). Image sizes were 2336x3504 (10,950 images), 1696x2544 (25,378 images) and 1440x2160 (42,273 images) pixels.

Manual grading was performed by the screening centres following the Scottish grading scheme illustrated in table 1. This table defines the lesions present at each grade of retinopathy, explains the terms observable and referable maculopathy/retinopathy and illustrates the associated patient outcomes. The outcome for the majority patients is 12-month recall. There are three more urgent possible outcomes; referral to ophthalmology, 6-month recall or referral for slit-lamp examination.

84,658 consecutive images and grading results from 34,785 anonymised patient screening episodes attending screening centres in Glasgow or Fife between 1st January 2007 and

SCREENING PROGRAMMES

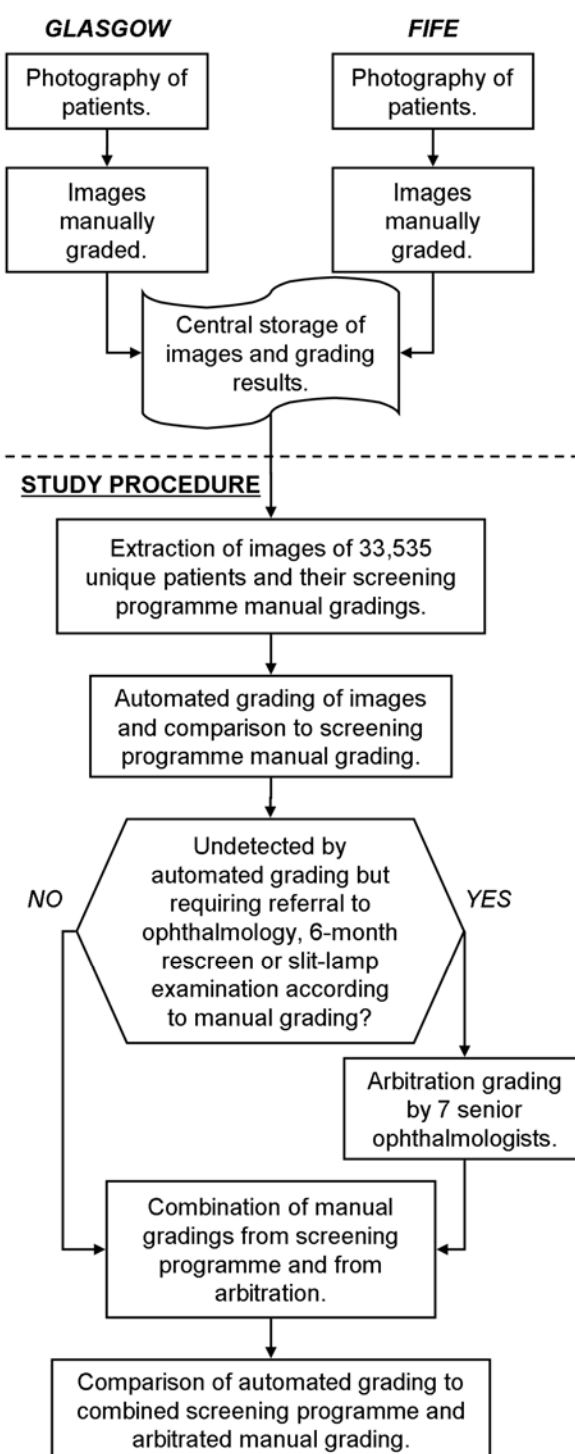


Figure 1: Diabetic retinopathy screening programme and study procedures.

31st January 2008. In the case of patients with repeat photographs, only the earliest screening episode was used. This set contained 78,601 images from 33,535 patients.

Automated grading software

All images were processed by the automated grading software which assessed image quality and disease using previously described algorithms [17,18], summarised here. The location of the optic disc and the fovea were determined to check that the image shows a macula-centred view and to determine whether the image is of a left or a right eye. Image clarity was assessed by checking that sufficient small vessels were visible in the macula region. If an adequate quality macula-centred image is present for each eye then disease is assessed in these images by performing microaneurysm/dot haemorrhage detection. The first stage in the detection of these was performed on the green plane of the image, after correction for uneven illumination, using a non-specific morphological filter that determines candidate lesions by separating dot-like dark objects from the linear vasculature [18]. The second stage performs more detailed analysis of the candidate lesions, measuring such features as their area, contrast and likelihood of lying on a vessel. An automated classifier, which had been previously trained using a set of 35 images containing 198 individually annotated microaneurysms/dot haemorrhages, separates true lesions from background objects based on the values of these features.

Artefacts caused by dirt on camera internal surfaces or by faulty photosensors can have a very similar appearance to microaneurysms/dot haemorrhages and hence cause frequent false positive detections. Therefore, an automated artefact masking algorithm was developed that noted the location of potential microaneurysms/dot haemorrhages in images taken with the same camera. Repeated detection of a potential microaneurysm/dot haemorrhage at the same location and in the same camera was judged to indicate the presence of an artefact.

The automated grading software produces a binary output: a patient is software positive if the software assessed quality to be inadequate or if it detected microaneurysms/dot haemorrhages. The automated grading software performance was evaluated by comparing this binary output against the screening programme manual grading results.

Arbitration

The most important discrepancies between the binary output of the automated grading software and the screening programme were those involving patients who were not detected by the automated grading software but who the screening programme referred to ophthalmology, recalled at 6 months or referred for slit-lamp examination. Arbitration grading was performed on these discrepancies.

The arbitration grading was performed by seven senior ophthalmologists working at screening centres in Scotland. The discrepancies were mixed with 40 control images and presented to each grader in random order. As the control images had been graded by the arbitrators at least 6 months earlier, during a quality assurance test, an intra-grader comparison was made.

If 5 or more arbitrators allocated a grade requiring referral to ophthalmology, recall at 6 months or slit-lamp examination, then this was defined as consensus for an outcome more urgent than the standard 12-month recall. In these cases, a consensus grade was allocated. This was necessary in order to evaluate the automated grading software performance for each grade. The grade assigned by the greatest number of arbitrators was used as the consensus grade. Where there was a choice between possible grades, due to more than one grade being associated with the same maximum number of arbitrators, the most severe of these grades was chosen as the consensus grade.

If 3 or 4 arbitrators allocated a grade which would imply that either referral to ophthalmology, recall at 6 months or slit-lamp examination was required, then this was defined as no consensus. The patient was deemed to be indeterminate regarding whether or not the outcome was more urgent than the standard 12-month recall. In this case the consensus grade was indeterminate.

If 2 or fewer arbitrators allocated a grade which would imply that referral to ophthalmology, recall at 6 months or slit-lamp examination was required, then this was defined as consensus that the patient required 12-month recall. The consensus grade was mild retinopathy or no retinopathy.

Statistical Methods

The intergrader agreement between the assigned grades of the 7 senior ophthalmologists were summarised using a Kappa statistic. A Kappa statistic was also used to assess intra-grader agreement, comparing the earlier and later gradings of the 40 control images. The detection rates within different ethnic groups were compared using Pearson chi-squared tests or Fisher's exact tests if required due to small numbers not being detected. This was done separately for those patients recalled at 12 months and those having a more urgent outcome. Stata version 10, StataCorp, Texas was used for these analyses.

RESULTS

The diabetic retinopathy screening centres referred 5.0% of patients to ophthalmology, recalled 1.8% at 6 months and referred 5.5% for slit-lamp examination.

Arbitration grading was performed on the images of 127 patients referred to ophthalmology, recalled at 6-months or referred for slit-lamp examination but who were not detected by the automated grading software. The Kappa statistic for inter-grader agreement was $\kappa=0.37$.

Table 2: Results of the arbitration grading. The second column groups the cases according to the definition used for consensus.

Number of arbitrators, out of 7, who assigned a grade implying referral to ophthalmology, 6-month recall or slit-lamp examination (number of cases)	Consensus grade (number of cases)
7 arbitrators (19)	Referable maculopathy (31) Observable maculopathy (3) Ungradable (3)
6 arbitrators (8)	
5 arbitrators (10)	
4 arbitrators (11)	Indeterminate (27)
3 arbitrators (16)	
2 arbitrators (13)	Mild retinopathy (17) No retinopathy (46)
1 arbitrator (22)	
0 arbitrators (28)	

Table 2 summarises the consensus grades resulting from the arbitration grading and shows the number of arbitrators who considered referral to ophthalmology, 6-month recall or slit-lamp examination was required for each case. In 63 cases the output of the automated grading software was appropriate and in 37 cases (31 with referable maculopathy, 3 with observable maculopathy and 3 ungradable) it was inappropriate according to the consensus of the arbitrators. 27 cases were indeterminate due to lack of consensus.

Considering the assigned grades, all 7 arbitrators gave identical grades in only 20 cases (5 cases of no retinopathy, 1 case of mild background retinopathy, 1 case of observable maculopathy, 12 cases of referable maculopathy, 1 case ungradable).

For the 40 control images, there was good intra-grader agreement with $\kappa=0.77$. 83% of the grades allocated to these images were identical to those allocated during a quality assurance test over 6 months earlier, 10.7% were higher than the previous ones and 6.3% were lower.

Table 3 displays the automated system results for each grade of retinopathy and for each possible patient outcome. The software was positive in 100% (193/193) of cases of proliferative retinopathy, 100% (324/324) of cases of referable background retinopathy and 100% (180/180) of cases of observable background retinopathy. Other software positive rates were, 97.3% (1099/1130) for referable maculopathy, 99.2% (384/387) for observable maculopathy and 99.8% (1824/1827) for patients classified as ungradable. The error rate for cases requiring referral to ophthalmology, 6-month recall or slit-lamp examination was 0.11% (37/33535).

Table 3. Proportions of patients, with confidence intervals (CI), for which the automated grading software output was positive. 27 cases have been omitted since they had indeterminate grade.		
Grade	Software positive %	95% CI
No visible retinopathy	49.6 (10668/21503)	48.9-50.3
Mild background retinopathy	83.9 (6678/7964)	83.0-84.6
Observable maculopathy	99.2 (384/387)	97.8-99.7
Observable background retinopathy	100 (180/180)	97.9-100
Referable maculopathy	97.3 (1099/1130)	96.1-98.1
Referable background retinopathy	100 (324/324)	98.8-100
Proliferative referable retinopathy	100 (193/193)	98.1-100
Ungradable	99.8 (1824/1827)	99.5-99.9
Outcome		
12-month recall	58.9 (17346/29467)	58.3-59.4
6-month recall	99.5 (564/567)	98.5-99.8
Slit-lamp examination	98.1 (1616/1647)	97.3-98.7
Refer to ophthalmology	99.8 (1824/1827)	99.5-99.9

51.7% (17346/33535) of all patients required 12-month recall but were software positive. Out of the 33,535 patients screened, 12,185 would not require manual grading since they were assessed by the automated grading software as having adequate quality and no microaneurysms. Automated grading would therefore reduce the number of patients requiring manual grading by 36.3%.

Ethnicity was recorded for 12,100 patients; 10,068 (83%) were Caucasian, 1,915 (16%) were Asian and 117 (1%) were Afro-Caribbean. Mean age of all patients was 62 years and 54.6% of all patients were male.

Table 4 displays the proportions which were software positive for the three ethnic categories for each patient outcome. No statistically significant differences were found between the ethnic groups in detection rates either for patients with non-referable retinopathy (Pearson chi-squared test $p=0.38$) or for patients requiring referral to ophthalmology, 6-month recall or slit-lamp examination (Fisher's exact test $p=0.82$).

Table 4: Proportions of patients, with confidence intervals (CI), for which the automated grading software gave a positive result for each possible patient outcome, split by ethnicity.

Outcome	Caucasian		Asian		Afro-Caribbean	
	Software positive %	95% CI	Software positive %	95% CI	Software positive %	95% CI
12-month recall	65.0 (5560/8555)	64.0-66.0	63.3 (989/1563)	60.9-65.6	66.3 (67/101)	56.7-74.8
6-month recall	99.6 (257/258)	97.8-99.9	100 (27/27)	87.5-100	100 (1/1)	20.7-100
Slit-lamp examination	100 (542/542)	99.3-100	99.3 (136/137)	96.0-99.9	100 (6/6)	61.0-100
Refer to ophthalmology	98.3 (695/707)	97.1-99.0	98.4 (183/186)	95.4-99.4	100 (9/9)	70.1-100

DISCUSSION

This audit assessed the performance of an automated system based on microaneurysm/dot haemorrhage detection and image quality assessment operating on a large, unselected population of people with diabetes participating in Scotland's systematic diabetic retinopathy screening programme. Out of 33,535 patients, all 697 patients with observable or referable retinopathy, other than maculopathy, were detected. In addition, the detection rates for observable and referable maculopathy and technical failures are compatible with published standards and quality assurance protocols and are very high compared to the sensitivity of retinal photography.[19-21] They are also higher than previously reported manual grading rates for detection of referable retinopathy which were 96% by Olson et al [23] and a maximum of 85% by Abramoff et al [24].

The scale of the audit means that there are sufficient arbitration results to warrant detailed consideration. It has been shown that for cases where the automated grading software and the diabetic retinopathy screening programme results are conflicting, the grading software result was correct more frequently than incorrect; only 29% of the 127 arbitrated discrepancies had 5 or more arbitrators (defined as consensus) assigning an outcome requiring more urgent action than the standard 12-month recall. There was much disagreement between the senior ophthalmologists; full agreement occurred in only 16% of arbitrated discrepancies. The good concordance in the grading of the control images suggest that there was no tendency by the arbitrators to give the images a less or more severe grade than they would have done outside this evaluation.

The automated system performed equally well for images from the three ethnic categories tested; Caucasian, Asian and Afro-Caribbean.

While the design of our earlier study made possible a direct comparison between manual and automated grading, this audit did not look for cases of referable retinopathy/maculopathy that were missed by manual grading. It is therefore not known if there were patients who were disadvantaged by manual grading.

All cases that required referral to an ophthalmologist but were not detected by the automated grading software were of referable maculopathy. This may be explained by

these cases having clear exudates but no obvious microaneurysms. However, in a study, also involving people attending the Scottish diabetic retinopathy screening programme, only 13.2% of patients with signs of referable maculopathy received laser treatment.[22] This implies that only a few of the cases of referable maculopathy not detected by the automated grading software would be considered for laser treatment and some of these may be detected on their next screening attendance.

It has been confirmed that the automated system achieves similar performance to that found in our previous study,[14] when applied to a larger multi-centre dataset. The current audit and our previous study achieved, respectively, detection rates of 87.0% and 87.9% for any retinopathy, 98.5% and 97.9% for observable/referable retinopathy/maculopathy and 99.8% and 99.5% for technical failures. While the earlier study indicated that 45.7% (3,070/6,722) of patients would be removed from the manual grading workload, in this audit 36.3% (12,185/33,535) would have been removed. This is may be due to the presence of artefacts, which affected 8 out of the 10 cameras used in the audit.

In this audit the automated grading software achieved 100% detection of proliferative, referable background and observable background retinopathy. It has been shown that the performance of an automated screening system for diabetic retinopathy is maintained at safe and effective levels over a large unselected set of images obtained from regional grading centres. Following this audit, Scotland's National Diabetic Retinopathy Screening Collaborative has concluded that automated grading should be introduced into Scotland's diabetic retinopathy screening programme.

ACKNOWLEDGMENTS

We thank Dr Alison Bow, Dr Brian Power, Dr Cynthia Santiago, Dr Anne Sinclair, Dr William Wykes, Dr Sonia Zachariah and Dr Usha Zamvar for voluntarily performing the arbitration grading. We thank staff of NHS Greater Glasgow & Clyde and NHS Fife retinal screening programmes, and their directors Dr William Wykes and Dr Caroline Styles, for their support. We thank Dr Nigel McLean of Scottish Health Innovations Limited and Scotland's National Caldicott Guardian, Dr Adam Bryson, for their support.

COMPETING INTERESTS

Implementation in Scotland and elsewhere is being considered. If this occurs it is likely that there will be some remuneration for the University of Aberdeen, NHS Grampian, Alan Fleming, John Olson and Peter Sharp. Authors Keith Goatman, Sam Philip and Gordon Prescott have no financial conflict of interest other than by association with the institutions mentioned above.

FUNDING

Funding for Alan Fleming was provided by Medalytix Ltd under an agreement with Scottish Health Innovations Limited.

LICENCE FOR PUBLICATION

The Corresponding Author has the right to grant on behalf of all authors and does grant on behalf of all authors, an exclusive licence (or non exclusive for government employees) on a worldwide basis to the BMJ Publishing Group Ltd to permit this article (if accepted) to be published in BJO and any other BMJ PGL products and sublicences such use and exploit all subsidiary rights, as set out in our licence (<http://bjo.bmj.com/ifora/licence.pdf>).

REFERENCES

1. Hutchinson A, McIntosh A, Peters J et al. Effectiveness of screening and monitoring tests for diabetic retinopathy - a systematic review. *Diabet Med* 2000;17:495-506

2. Arun CS, Al-Bermani A, Stannard K et al. Long-term impact of retinal screening on significant diabetes-related visual impairment in the working age population. *Diabet Med* 2009;26:489-492
3. Stefansson E, Bek T, Porta M et al. Screening and prevention of diabetic blindness, *Acta Ophthalmol* 2000;78:374-385
4. Zoega GM, Gunnarsdottir Þ, Bjornsdottir S et al. Screening compliance and visual outcome in diabetes. *Acta Ophthalmol* 2005;83:687-690
5. Wild S, Roglic G, Green A et al. Global prevalence of diabetes: estimates for the year 2000 and projections for 2030. *Diabetes Care* 2004;27:1047-53.
6. James M, Turner DA, Broadbent DM, Cost effectiveness analysis of screening for sight threatening diabetic eye disease. *Br Med J* 2000;320:1627-1631
7. Scotland GS, McNamee P, Philip S et al, Cost-effectiveness of implementing automated grading within the national screening programme for diabetic retinopathy in Scotland, *Br J Ophthalmol* 2007;91:1518-1523
8. Garvican L, Scanlon PH. A pilot quality assurance scheme for diabetic retinopathy risk reduction programmes. *Diabet Med* 21:1066-1074
9. Olafsdottir E, Stefansson E. Biennial eye screening in patients with diabetes without retinopathy: 10-year experience, *Br J Ophthalmol* 2007;91:1599-1601
10. Williams GA, Scott IU, Haller JA et al. Single-field fundus photography for diabetic retinopathy screening - A report by the American Academy of Ophthalmology, *Ophthalmology* 2004;111:1055-1062
11. Sharp PF, Olson JA, Strachan F et al. The value of digital imaging in diabetic retinopathy. *Health Technology Assessment* 2003;Vol 7:30
12. Larsen M, Godt J, Larsen N et al. Automated detection of fundus photographic red lesions in diabetic retinopathy. *Invest Ophthalmol Vis Sci* 2003;44:761-766
13. Usher D, Dumskyj M, Himaga M et al. Automated detection of diabetic retinopathy in digital retinal images: a tool for diabetic retinopathy screening. *Diabet Med* 2004;21:84-90.
14. Philip S, Fleming AD, Goatman KA et al. The efficacy of automated "disease/no disease" grading for diabetic retinopathy in a systematic screening programme, *Br J Ophthalmol* 2007;91:1512-1517
15. Leese GP, Morris AD, Olson JA. A national retinal screening programme for diabetes in Scotland. *Diabet Med* 2003;20:962-964.
16. Scottish Diabetic Retinopathy Screening Collaborative. Scottish Diabetic Retinopathy Grading Scheme 2007 v1.1 www.ndrs.scot.nhs.uk/ClinGrp/Docs/Grading%20Scheme%202007%20v1.1.pdf (accessed November 2009)
17. Fleming AD, Philip S, Goatman KA et al, Automated assessment of retinal image quality based on clarity and field definition. *Invest Ophthalmol Vis Sci* 2006;47:1120-1125
18. Fleming AD, Philip S, Goatman KA et al. Automated microaneurysm detection using local contrast normalization and local vessel detection, *IEEE T Med Imaging* 2006;25:1223-1232

19. British Diabetic Association. Retinal Photography Screening for Diabetic Eye Disease. London: British Diabetic Association 1997:1–19.
20. NHS Quality Improvement Scotland. Diabetic Retinopathy Screening. NHS Quality Improvement Scotland 2004:1-46.
21. Williams G A, Scott I U, Haller J A et al. Single-field fundus photography for diabetic retinopathy screening: a report by the American Academy of Ophthalmology. Ophthalmology 2004;111:1055-1062.
22. Schofield CJ, Ellis JD, Ellingford A et al. Macular oedema is not predicted by perifoveal single blot haemorrhages. Diabet Med. 2008 Feb;25(2):129-33. Epub 2008 Jan 4.133
23. Olson JA, Strachan FM, Hipwell JH et al. A comparative evaluation of digital imaging, retinal photography and optometrist examination in screening for diabetic retinopathy. Diabet Med. 2003 20(7):528-534
24. Abràmoff MD, Niemeijer M, Suttorp-Schulten MSA, et al. Evaluation of a System for Automatic Detection of Diabetic Retinopathy From Color Fundus Photographs in a Large Population of Patients With Diabetes. Diabetes Care 2008 31(2):193-198