Review of Diabetic Retinopathy Screening Methods and Programmes Adopted in Different Parts of the World

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Abstract

Introduction: One of most common diabetic complications is diabetic retinopathy (DR). Sight-threatening DR can be avoided when diagnosed early and treated in a timely fashion. The aim of this study is to review current worldwide DR screening programmes and studies. Methods: A PubMed platform search was performed to find clinical trials or studies of current DR screening methods. Results: Direct and indirect ophthalmoscopy is still used, but digital photography of the retina seems to be the most efficient, objective and cost-effective. Conclusions: DR screening programmes are developed all over the world. They help to detect early sight-threatening DR, treat it in a timely fashion and in this fashion help to avoid expensive, advanced treatment or even prevent to develop blindness among working age people.

Keywords

Diabetic retinopathy, screening methods, telemedicine

Disclosure: Janusz Pieczynski and Andrzej Grzybowski have no conflicts of interest to declare. No funding was received in the publication of this article.

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Compliance with Ethical Guidelines: This study involves a review of the literature and did not involve any studies with human or animal subjects. performed by any of the authors.

Received: 31 May 2015 Accepted: 10 July 2015 Citation: European Ophthalmic Review, 2015;9(1):49–55 DOI: 10.17925/EOR.2015.09.01.49 Correspondence: Janusz Pieczynski, Voivodal Specialistic Hospital, Zolnierska 18, 10-560 Olsztyn, Poland. E: janusz.pieczynski@op.pl

Diabetes mellitus (DM) is a growing socio-medical problem because of its increasing prevalence and diabetic complication rate. This is also the reason for the large amount of money spent on diabetes treatment and on diabetic complications despite continually improving diabetes care.^{1,2} The International Diabetes Federation's latest study has shown the number of people with diabetes rise from 382 million worldwide in 2013 to 592 million in 2035.³

One of most common microvascular diabetic complications is diabetic retinopathy (DR). It is a most common reason for blindness in developed countries. Sight-threatening DR can be avoided when identified early and cured in a timely fashion.⁴⁻⁷ This is the reason for diabetic screening implementation.

Rules of screening in medicine were established by Wilson and Jungner in 1968 and accepted by the World Health Organization (WHO).⁸ The basic principles for disease screening were as following:

- The condition sought should be an important health problem.
- There should be an accepted treatment for patients with recognised disease.
- Facilities for diagnosis and treatment should be available.
- There should be a recognisable latent or early symptomatic stage.
- There should be a suitable test or examination.
- The test should be acceptable to the population.
- The natural history of the condition, including development from latent to declared disease, should be adequately understood.

- There should be an agreed policy on whom to treat as patients.
- The cost of case finding (including diagnosis and treatment of patients diagnosed) should be economically balanced in relation to possible expenditure on medical care as a whole.
- Case finding should be a continuing process and not a 'once and for all' project.

These rules could be adapted for DR screening. The first attempts were made in 1989, when the St Vincent Declaration was made. According to this declaration, reduction of blindness due to DR by one-third in the following 5 years was planned.⁹ The next attempts on DR blindness reduction were established in 2005 in the Liverpool Declaration.¹⁰ The consensus was to reduce blindness due to DR by 2010, by DR systematic screening covering at least 80 % of the people with diabetes population with the use of trained personnel and access to the proper therapy.

Aim of Study

The aim of this study is to review current worldwide DR screening programmes and studies performed by technicians or primary care physicians (not ophthalmologists), quickly and simply.

Methods

This is a review study. A PubMed platform search was performed, using the following keywords: diabetic retinopathy screening programme, telemedicine and DR, prevented diabetic vision lost to find clinical trials or review studies of current DR screening programmes. We found 57 articles of which finally we analysed 45. English language was preferred, at least for abstracts.

Results UK

The UK comprises England, Wales, Scotland and Northern Ireland. Each of them started to screen DR and developed their own national DR screening programmes. These services are based on digital colour eye fundus photography and vary in details.^{11–15}

England

A national programme for retinopathy screening in England (English National Screening Programme for Diabetic Retinopathy [ENSPDR]) started in 2006 and in 2012 was relaunched as the NHS Diabetic Eye Screening Programme (NDESP). This service is designed to reduce loss of sight among people with diabetes by early detection and correct treatment of a sight-threatening DR. The programme covers all patients with diabetes 12 years old or over with light perception or more in at least one eye. Screening is performed annually. There are static and mobile screening locations with digital fundus cameras. The protocol consists of two-field colour eye fundus photographs: one in macula photographs are read in a few centralised grading centres.^{11,12,16}

Wales

The Diabetic Retinopathy Screening Service for Wales (DRSSW) was started in 2002 to detect any kind of DR, especially sight-threatening DR.^{17,18} The DRSSW is a mobile screening service with the following protocol of screening: visual acuity, two-field 45° digital photographs (one in macula centre; one nasal) after 1 % tropicamid mydriasis and graded by retinal professionals. Patients with diabetes aged 12 or more and not involved in other screening programmes are covered by this service. Patients with sight-threatening DR are referred to a hospital retinal service. Patients with mild states of DR are advised to improve metabolic control of diabetes. This programme consists of 30 photographic teams and 220 locations in Wales and uses Canon DGi digital cameras. Photographs are graded according to the DRSSW protocol based on the National Screening Committee¹⁹ and the European screening handbook.²⁰ Rate of patient cover is 80 %.¹⁴

Scotland

The Scottish National Diabetic Retinopathy Screening (DRS) service launched in 2006.²¹ Patients with diabetes 12 years and over are automatically identified according to the database of the Scottish Care Information-Diabetes Collaboration and due to this system patient coverage is above 99 %. Screening examination is based on a single, central 45° photograph with mydriasis if required. In case of complications with photographs, slit-lamp is performed. The grading system is centralised.²² Tests with good results with software for automated quality assessment and microaneurysm/dot haemorrhage have been carried out.^{13,23}

Northern Ireland

The Northern Ireland Diabetic Retinopathy Screening Programme (NIDRSP) started in 2002. Its methodology is similar to the DRSSW. It is based on digital eye fundus colour photography with selective pupil mydriasis in patients under 50 years of age. This programme covers all patients with diabetes 12 years of age or over, with patient identification sent to the programme by the GP. Trained readers grade photographs.¹⁵

US

Cuadros et al. presented a study on the EyePACS (picture archive and communication system) programme developed in California.²⁴ They used a licence-free system of taking pictures of the retina and sending them to a grading centre to assess retinopathy status. Pictures were taken by any kind of fundus cameras, but the non-mydriatic type was preferred, for instance, Canon CR-DGi or Canon CR-1. Certified EyePACS photographers took one picture of the external surface of the eye and three pictures of the retina, as follows: optic disc and macula, picture centred on optic disc and picture of the macula and temporal part of the retina. Retinopathy grading system reviewers performed grading of retinopathy. This programme was in operation in California in 2005 to 2006 and expanded to elsewhere in 2008.

We also found research on telemedicine reading of digital photographs of eye fundus of patients with diabetes.²⁵ Patients 18 years of age or over with DM type 1 or 2 were screened. Trained photographers took three photos of the fundus of each eye: one anterior segment and two of retina located nasally and temporally and subsequently read by trained readers using telemedicine. They graded photos according to the British National Health Service's DR grading classification system.²⁶

The American Diabetes Association suggests that seven-field stereo 30° is superior to non-mydriatic digital photography and the second method should only be used for situations where mydriasis does not allow it.²⁷

Analysis of the cost-effectiveness of screening DR in low socio-economic status areas has also been performed.²⁸ This research was carried out for 17 months with the use of digital photography of the retina and grading by a telemedicine centre. There are no data on the exact condition of patients' eye examinations.

Mansberger et al.²⁹ performed a study on checking the usefulness of long-term telemedicine DR screening compared with traditional eye examination. They screened patients with DM 18 years of age or older. One study group was examined traditionally and the second with the use of a non-mydriatic camera and six 45° photographies: stereo on macula and optic disc; non-stereo on peripheries. The researchers concluded that telemedicine increased the percentage of eye examinations and could be a useful method for DR screening.

France

The first telemedical screening for DR started in 2002 in the Paris region and was conducted by Massin et al.^{30,31} They used a non-mydriatic fundus camera by Topcon and performed five-colour photographs of 45° of the central (macula and optic disc) and peripheral retina without pupil dilatation taken by orthoptists. The photographs were compressed and sent via the Internet to the grading centre, where quality of pictures and DR status was assessed. They used Topcon software for that process. The study was active for 18 months.

The Ophthalmology Diabetes Telemedicine Network (Ophdiat), a programme for DR screening, (created 2004; covering the Paris region).³² They used non-mydriatic fundus cameras (Canon or Topcon) and took 45° two-fields colour photos of the retina (one centred in the macula; the second centred in the optic disc). The pictures were taking by orthoptists or nurses and compressed to JPEG format and sent via the Internet to the grading centre, where DR status was assessed. Patients with moderate or more advanced stages of DR, or with unclear pictures, were referred to an ophthalmologist. All other people were screened once a year.

Table 1: Diabetic Retinopathy Screening Studies – Europe

Authors	Country	Type of Study	Screening Method	Instant Grading/ Telemedicine	Covered Population	Population
NHS Diabetic Eye Screening Programme	England, UK	National programme	Digital fundus cameras/two-field 45° colour fundus photos/mobile/static camera/pupil dilatation	Telemedicine	Diabetics over 12 years old	Nationwide
Diabetic Retinopathy Screening Service for Wales	Wales, UK	National programme	Digital fundus cameras/two-field 45° colour fundus photos/mobile camera/ pupil dilatation	Direct grading from fundus camera	Diabetics over 12 years old	Nationwide
Scottish National Diabetic Retinopathy Screening service	Scotland, UK	National programme	Digital fundus cameras/one-field 45° colour fundus photos/mobile camera/ pupil dilatation if needed	Telemedicine	Diabetics over 12 years old	Nationwide
Northern Ireland DR Screening Programme	Northern Ireland	National programme	Digital fundus cameras/two-field 45° colour fundus photos/mobile camera/ pupil dilatation	Telemedicine	Diabetics over 12 years old, under 50 years old	Nationwide
Massin et al., 2004 ³⁰	France	18-month study	Digital fundus cameras/five-field 45° colour fundus photos/stationary camera/pupil dilatation if needed	Telemedicine	Patients who had no DR previews	Local
Ophthalmology Diabetes Telemedicine Network (Ophdiat) Schulze-Döbold, 2012 ³²	France	Programme in region of Paris	Digital fundus cameras/two-field 45° colour fundus photos/stationary camera/pupil dilatation	Telemedicine	Patients had either mild or no DR	Local
Deb-Joardar et al., 2007 ³³	France	Cross sectional study/1-year study	Digital fundus cameras/three-field 45° colour fundus photos/stationary camera/pupil dilatation	Telemedicine	All adult patients	Local
Creuzot-Garcher et al., 2010 ³⁴	France	Regional programme	Digital fundus cameras/three-field 45° colour fundus photos/mobile camera/ pupil dilatation	Telemedicine from USB drive	No data	Local
Andonegui et al., 2012³⁵	Spain	24-month study	Digital fundus cameras/five-field 45° colour fundus photos/stationary camera	Instant reading by GPs/possibly referral	Diabetic patients under care of GPs	Local
Gibelalde et al., 2010 ³⁶	Spain	Prospective study	Digital fundus cameras/one-field 45° colour fundus photos/stationary camera	Telemedicine	No previews DR	Local
Vleming et al., 2009 ³⁷	Spain	Prospective, observational study	Digital fundus cameras/four-field 45° colour fundus photos/stationary camera	Telemedicine	All patients sent by GPs and endocrinologist	Local
Gomez-Ulla et al., 2002 ³⁸	Spain	3-month study	Digital fundus cameras/four-field 45° colour fundus photos/stationary camera	Telemedicine	Patients of the endocrinology unit	Local
Lemmetty et al., 2009 ⁴³	Finland	Regional programme	Digital fundus cameras/colour fundus photos/mobile camera	First grading made by photographer (trained nurse); referral possible if needed	Patient with type 2 DM	Local
Kernt et al., 201246	Germany	Comparative study	Seven-field stereo ETDRS standard versus ultrawide field scanning laser ophthalmoscopy	Instant grading	DM duration over 3 years	Local
Liegl et al., 201447	Germany	Comparative study	Non-mydriatic ultrawide field versus mydriatic two-field 45° colour fundus photography	Instant grading	DM for at least 3 years	Local
Expert Advisory Group National Retinopathy Screening Committee, 2008	Ireland	National programme/ framework, did not start	Digital photography stationary and mobile	Telemedicine	Patient age 12 years old and over	Population based
McHugh et al., 2013 ⁵¹	Ireland	National programme	Digital fundus camera/two-fields photography	Telemedicine	Patient age 18 years old and over	Population based

Table 2: Countries Outside Europe

Authors	Country	Type of Study	Screening Method	Instant Grading/ Telemedicine	Covered Population	Population
Cuadros et al., 2009 ²⁴	California, US	Pilot programme	Digital retinal colour pictures, three-fields	Telemedicine	No data	No data
Owsley et al., 2015 ²⁵	US	Cross-sectional study	Digital retinal colour pictures, two-fields	Telemedicine	18 years old or over type 1 and 2 DM	Local
Mansberger et al., 2015 ²⁹	US	Randomised clinical trial	Digital retinal colour pictures, six 45° pictures of macula (stereo), optic disc (stereo) and peripheries (non-stereo)	Telemedicine	Patients with DM 18 years old or older	Local
Nathoo et al., 2010 ⁴²	Canada	Retrospective consecutive case series	Seven-field colour, stereoscopic, digital photography	Telemedicine	Patients with DM	Local
Khan et al., 2007 ³⁹	South Africa	Regional programme	Digital retinal colour pictures, mobile station	Instant grading	Uninsured and low socio-economic backgrounds patients	Local
Cook, 201341	South Africa	National Diabetic Retinopathy Screening Programme/ Ophthalmology Society of Southern Africa	Digital retinal colour pictures, single, central-field	Telemedicine	Population based	Internet DR data- based system
Levy et al., 201145	Israel	Pilot clinical trial	Digital retinal colour pictures, at least two-fields, 45° mobile station	Telemedicine	Diabetic members of Israel health fund – Clalit	Local/South Israel
Lau et al., 1995 ⁴⁷	Singapore	National programme	Retinal colour pictures, 45°	Instant grading	Government diabetic clinic patients	National
Lim et al., 200848	Singapore	National programme	Digital retinal colour pictures, one-field, 45°	Instant grading	Patients referred to evaluation from primary care clinics	National
Liu et al., 200349	Taiwan	Clinical trial	Ophthalmoscopy or fluorescein angiography	Instant grading	Patients of one Taipei clinic	Local
Mak et al., 2003⁵⁴ Murray et al., 2005⁵⁵	Australia	Local programmes	Retinal photography with Polaroid film	Instant grading or in grading centres	Patients of Western Australia	Local

DM = diabetes mellitus; DR = diabetic retinopathy; ETDRS = Early Treatment Diabetic Retinopathy Study.

Israel

Levy et al. described a study on DR screening in Southern Israel.⁴⁴ They described a service for DR screening with the use of the Topcon mobile non-mydriatic fundus camera. A trained photographer took at least two 45° images of retina-covering macula, optic disc and superior and temporal fields. The TIFF format pictures were sent to a grading server and within 2 weeks graded by the same doctor. They concluded that mobile digital photography increased the possibility of detecting sight-threatening DR.

Germany

Kernt et al. conducted a study on DR screening comparing ETDRS seven-field stereo standard versus one ultrawide field scanning laser ophthalmoscopy (Optomap).⁴⁵ They showed that the Optomap system did not need to dilate the pupil, the skills of the photographer may be not as good as the ETDRS standard and the efficiency of assessment DR is comparable. They concluded that ultrawide scanning laser ophthalmoscopy might be a promising alternative for DR screening.

The authors from the same university also compared ultrawide field scanning laser ophthalmoscopy with two-field fundus photography in DR screening.⁴⁶ They showed that ultrawide field ophthalmoscopy might be potentially better in DR screening, but it required further study.

Singapore

Mass screening for DR in Singapore started in 1991.⁴⁷ The founders of that programme chose Polaroid non-mydriatic 45° Topcon fundus photography because of an ophthalmologist was not required to take a picture. At that time the method was relatively cheap and suitable for mass screening. Pictures were taken by a trained photographer, usually after mydriasis and graded by hospital ophthalmologist. It was the first-in-the-world nationwide programme for DR screening.

Lim et al. showed in their study review of suspected DR patients sent to tertiary referral clinic from the Nationwide Screening Programme.⁴⁸ The programme is based on a one-field digital 45° image of central retina, performed annually in all patients with diabetes in Singapore.

They found that one of three patients have any kind of DR and only one of nine patients has sight-threatening DR. The screening programme used a Topcon fundus camera and the pictures were graded by trained family doctors.

Taiwan

Liu et al. presented a study on DR screening in an outpatient clinic performed between 1 January 1990 till 31 December 1992.⁴⁹ They used ophthalmoscopy or fluorescein angiography for DR evaluation. The authors suggested that DR screening is worthwhile.

Ireland

In 2007 in Ireland, the Diabetes Expert Advisory Group was established to develop a national, population-based DR screening programme.⁵⁰ The group created a framework for DR screening: it was never implemented.

When this screening programme did not begin, in 2003 McHugh et al. presented a study for DR screening in primary care in Ireland.⁵¹ They described Diabetes in General Practice (DiGP), a community-based initiative established in 2010, involving GPs, local optometrists and ophthalmologists. They screened patients with diabetes type 1 or 2, aged 18 or more with the use of digital fundus cameras. They took two-field pictures of the retina (macula and optic disc). The pictures were graded by MDTS software and the results in electronic records were sent to GPs, who were responsible for referring patients to the ophthalmic specialists. The study was conducted from 1 January until 30 June 2011 and found 26 % patients with DR. So they concluded the need for a national DR screening programme in Ireland.

Hungary

Szabó et al. presented a telemedical study on DR screening.⁵² They used three-field digital 45° retina photographs. Pictures were sent via Internet to the grading centre and an independent ophthalmologist assessed DR status. They used a non-mydriatic fundus camera, but also performed pupil dilatation and ophthalmoscopy if needed.

Czech Republic

The Czech National Diabetes Programme 2012–2022^{s3} also covers DR screening with the use of photography of retina. However, currently there is not enough information on this study.

Australia

It is a large country with many dispersed small towns and communities of people. This is why the DR screening is hard to carry out. Mak et al.⁵⁴ and Murray et al.⁵⁵ reported a DR-screening scheme in the Kimberly region of Western Australia. They described DR screening with the use of a non-mydriatic fundus camera 45°, but with Polaroid film. They did not use digital cameras because of difficulties with electricity in some places of examination. They used mobile cameras with instant grading of retinal pictures. Photographs were taken with mydriasis.

Portugal

One of the newest DR screening programmes study was reported by Dutra Medeiros et al.⁵⁶ They worked in the Study Group for Diabetic Retinopathy Screening (RETINODIAB) in Lisbon and Tagus Valley area from July 2009 till October 2014. The screening programme was held in several primary healthcare units with 45° non-mydriatic fundus cameras. They took two pictures of the retina: one of the macula centre; the second of the optic disc. When problems with good quality pictures were experienced, they performed pharmacological pupil dilatation. Photographs after compression in the DICOM format were sent to the grading centre, where they were assessed according to the International Clinical Diabetic Retinopathy Scale. The study group suggested that this screening method could be an effective technique for early DR detection.

Poland

There are standards for patients with diabetes care, prepared by the Polish Diabetologist Society.⁵⁷ The authors suggest that DR should be screened regularly, but there is no national programme for population-based DR screening.

The Polish National Health Fund (NFZ) recommend diabetic eye screening (with retina examination) performed by ophthalmologists in Complex Out-Patient Specialistic Care for Diabetes Mellitus (KAOS). This service does not include national population-based DR screening.⁵⁸

Discussion

There are different methods of DR screening in the world. Direct and indirect ophthalmoscopy is used, as well as different kinds of retinal photography.¹¹⁻⁵⁵ Conventional photography of the retina was used in early 1990 in Singapore.48 The digital photography of the eye fundus seems to be the most efficient and cost-effective. Retinal pictures are solid proof of the status of the retina and can be graded once again if needed. The gold standard for retinal diabetic photography is a seven-field stereo colour ETDRS standard,59 but this type of the fundus photography is time-consuming, expensive and requires an experienced photographer. The screening process should be: 'economically balanced in relation to possible expenditure on medical care as a whole's and this condition is made by digital, non-stereo retinal photography. There are also variations of this kind of photography, from seven-field colour retinal photography recommended by the American Diabetes Association (ADA)27 and trained in Canada,25 to five-field photography^{30,31,34} performed in France and Spain. There are also fourfield photographs of the retina^{37,38} taken in Spain and three-field retinal images^{24,33,34} (also in France and in the US). The most-often used method is two-field pictures of the retina: performed in the UK, USA, Israel and Ireland.^{11,12,16-18,25,44,51} Similarly, only one picture of the retina is used in Scotland,²¹ Spain,³⁶ South Africa⁴¹ and Singapore.⁴⁸ A special type of onefield retinal picture in the German project is the use of one, ultrawide picture taken by Optomap,45,46 which is a interesting alternative for two-field photography. The intervals between eye examinations in the above-mentioned studies are based on the severity of the retinal changes. There are recent studies and programmes that personalise intervals of screening timing not only on retinal status but also on DM control, e.g. blood glucose control (HbA1,), blood pressure, patient gender, type of DM and duration of DM.^{60,61} Mehlsen et al. in Denmark and Stefansson et al. in Iceland introduced this approach for screening intervals. It allows screening to be more cost-effective through extending the length between examinations to more than 1 year for mild stages of DR. It helps also to avoid excessive retinal treatment.

Mansberger et al.²⁹ compared telemedicine DR screening to traditional retina examination. They showed that telemedicine increased the percentage of DR screening examinations. They concluded that remote DR screening could be performed by primary care clinics.

One of the most important reasons for the use telemedicine in ophthalmology is the lack of retina specialists, even in developed countries. The use of remote assessment of retina pictures allows this problem to be managed (few doctors screen a large area). Dutra Medeiros et al. remarked on this problem in their study.56

In conclusion, it can be argued that DR screening programmes are developed all over the world, especially in developed countries. These programmes help to detect early sight-threatening DR, treat it in a timely fashion and in this way avoid expensive, advanced treatment or even prevent blindness developing among working age people. In summary, we can conclude that a good DR screening programme is simple, easy to perform, cheap, covering more than 80 % of patients, and protecting against serious complications. After a review of current DR studies, we recommend DR screening with the use of colour, two-field retina photography taken by technicians with the non-mydriatic fundus cameras, with telemedicine software and graded in centres by retina specialists.

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