Irish National Diabetic RetinaScreen Programme: report on five rounds of retinopathy screening and screen-positive referrals. (INDEAR study report no. 1)

Rajiv Pandey, Margaret M Morgan, Colette Murphy, Helen Kavanagh, Robert Acheson, Mark Cahill, Patricia McGettrick, Louise O’Toole, Fatima Hamroush, Therese Mooney, Helen Byrne, Patricia Fitzpatrick, David J Keegan

ABSTRACT

Objective To study the uptake of annual diabetic retinopathy screening and study the 5-year trends in the detection of screen-positive diabetic retinopathy and non-diabetes-related eye disease in a cohort of annually screened individuals.

Design Retrospective retinopathy screening attendance and retinopathy grading analysis.

Setting Community-based retinopathy screening centres for the Diabetic RetinaScreen Programme.

Participants 171,557 were identified by the screening programme to be eligible for annual diabetic retinopathy screening. 120,048 individuals over the age of 12 consented to and attended at least one screening appointment between February 2013 to December 2018.

Main Outcome Measures Detection rate per 100,000 of any retinopathy, screen-positive referable retinopathy and non-diabetic eye disease.

Results Uptake of screening had reached 67.2% in the fifth round of screening. Detection rate of screen-positive retinopathy reduced from 13,229 to 4,237 per 100,000 screened over five rounds. Detection of proliferative disease had reduced from 2,898 to 713 per 100,000 screened. Non-diabetic eye disease detection and referral to treatment centres increased almost eightfold from 393 in round 1 to 3,225 per 100,000 screened. The majority of individuals referred to treatment centres for ophthalmologist assessment are over the age of 50 years.

Conclusions Screening programme has seen a reduced detection rate both screen-positive retinopathy referral in Ireland over five rounds of screening. Management of non-diabetic eye diseases poses a significant challenge in improving visual outcomes of people living with diabetes in Ireland.

INTRODUCTION

Population-wide screening for diabetic retinopathy (DR) and provision of photocoagulation treatment have been shown to be effective in reducing the prevalence and incidence of blindness due to DR in a diabetic population. The 2005 Liverpool Declaration by European ophthalmologists made annual retinopathy screening a priority measure to reduce the rate of blindness caused due to DR. Today, DR is no longer the leading cause of blindness in the working-age population in England, Wales, and Iceland: nations where systematic population-wide DR screening programmes have been implemented. Several features make eliminating diabetes-related blindness achievable: DR progresses in a predictable pattern, a robust internationally accepted system of disease and risk stratification exists, digital photography as a method of screening has high sensitivity and specificity, and treatments administered promptly can reduce the risk of visual impairment by at least 90%.

Based on the recommendation of Health Service Executive, the healthcare regulatory body of Ireland, an annual DR screening programme was launched to offer free annual call/re-call-based diabetic retinopathy screening and treatment to people living with diabetes (PWD) aged 12 years or older. Diabetic RetinaScreen supervises annual eye screening and treatment by using a standardised retinopathy grading matrix, established urgent and routine pathways for screen-positive patients to access ophthalmological care, and provides evidence-based treatment for DR.

This study aims to report on the screening activity and referral of individuals screened for DR during the first five rounds of screening. These data will also highlight changes in the frequency of presentation of DR needing urgent or routine appointments since commencement of the Irish national retinal screening programme.

METHODS

Retinopathy screening protocol

Diabetic RetinaScreen was launched in February, 2013 to reduce the risk of vision loss by screening PWD at risk of visual impairment due to DR and providing treatments before individuals develop symptoms of visual loss. A register of PWD in Ireland was created using data from government-provided medical health schemes: Medical Card Scheme, Long Term Illness Scheme, and Drugs Payment Scheme. General practitioners (GP), ophthalmologists or endocrinologists could add patients to the screening register with the patient’s consent. Once registered, an invitation for screening was sent to individuals by post to confirm their identity and seek their consent to collect and analyse their data for screening. Guardians of children under the age of 16 had to provide consent and accompany their child to screening appointment.
Clinical science

At each screening visit, a screening technician measured individual's best corrected visual acuity with their usual distance correction and then used pinhole if the visual acuity was 6/9 or worse. Two 45° mydriatic digital photographs of the retina centred on the macula and the optic disc were used for DR grading.

The Diabetic RetinaScreen DR grading matrix is based on the English National Diabetic Eye Screening Programme (ENDESP) grading matrix. 9 Retinal images were given a retinopathy grade of R0, R1, R2 or R3 based on the number of signs and DR lesions. Images with surrogate markers of clinically significant macular oedema (CSMO) (dot/blot haemorrhages, hard exudates, retinal thickening within one disc diameter of the fovea) were given a maculopathy grade M1, while images with no surrogate markers of CSMO were assigned a maculopathy grade of M0 (for Diabetic RetinaScreen grading matrix see online supplemental table 1). If good-quality retinal images could not be obtained, then the images were given a U, ungradable, grade, and slit-lamp-based grading was conducted within 7 weeks. Individuals who were unable to complete digital screening because of immobility or other needs were screened using slit-lamp biomicroscope using the ungradable pathway, or in some instances were directly referred to a treatment centre.

Screen-negative individuals with no retinopathy (R0M0) or with only background retinopathy (R1M0) were returned to annual community-based retinal photographic screening. Screen-positive patients with background retinopathy (R1) and maculopathy (M1) were given a grade (R1M1), pre-proliferative retinopathy with or without maculopathy (R2M0/M1), and stable or active proliferative retinopathy with or without maculopathy (R3M0/M1) were referred through established pathways to treatment centres.

Urgent and routine screen-positive assessment pathways

Data regarding the number of times routine and urgent pathways were activated for individuals with screen-positive retinopathy have been reported to show the trends of screen-positive DR and nondiabetic eye diseases (NDED). The worse grade from the two eyes is used to make decisions and referrals to treatment centres. Individuals could have four possible outcomes: Urgent referral to treatment centre in 2 to 4 weeks, routine referral for assessment in 13 weeks to 18 weeks, U grade image for slit-lamp grading, or return to annual screening if patient is screen-negative. At each stage, individual’s nominated GP, ophthalmologist, and/or endocrinologist was sent a letter informing them of the retinopathy grade and screening outcome.

Individuals with R1M1, R2M0 and R2M1 screen-positive retinopathy and maculopathy were referred via routine pathway. Individuals with features of active or stable-treated proliferative disease graded R3 were referred via urgent access pathway to an ophthalmologist in 2 to 4 weeks. Individuals with stable-treated proliferative retinopathy were referred through the urgent pathway as there was initial concern regarding sub-optimal treatment in the diabetic population at the start of the programme.

Selected non-diabetic eye diseases (NDED) detected during annual DR screening were referred via routine referral pathway to the treatment centres (for a list of NDED referred for assessment please see online supplemental table 2). The diagnosis was confirmed by an ophthalmologist and onward referrals were made to appropriate ophthalmology clinics for follow-up and treatment. Urgent NDED related referrals were made for patients with suspected neovascular age-related macular degeneration.

Image acquisition and grading protocol

Retinopathy screening and grading of retinal screening images was done by two contracted companies Global Vision (Dublin, Ireland) and Northgate Public Services (NEC, Japan). Centralised electronic record keeping software, OptoMize (NEC, Japan) was used to store screening images and co-ordinate patient pathways through screening, slit-lamp examination and treatment. Colour retinal photographs were stored in a General Data Protection Regulation (GDPR) compliant manner in a central server from where they were viewed remotely by grading technicians, optometrists and ophthalmologists at grading centres; and, ophthalmologists at treatment centres.

Each screen-positive image went through two separate gradings by two graders to ensure grading accuracy. Every screen-positive image was reviewed by an ophthalmologist before patients were referred to treatment centres. If there was disagreement between graders then an arbitration level senior grader or ophthalmologist also graded the image before final grading. 10% of screen-negative images were automatically regraded as an internal quality assurance mechanism. Other internal quality assurance measures included continued screening technician and grading technician training involving multi-disciplinary team meetings (MDT), team training days, and internal audits, particularly regarding image quality. In addition, grading technicians were required to complete regular grading test sets from Gloucestershire Hospitals NHS Foundation Trust.

Setting

As of December 2018, Diabetic RetinaScreen provided fixed and mobile community-based screening service at 123 locations across Ireland. Each screening centre was equipped with a digital fundus camera and a 3 m Snellen chart. Images and demographic data were accessed at grading centre and treatment centres via Optomize.

Study population

Individuals with diabetes over the age of 12 years old, and with VA better than non-perception light (NPL) in the better seeing eye were eligible for screening. Individuals who attended at least one screening between February 2013 and 31 December 2018 were included in the present study. Written consents were sought at screening appointments to collect and store demographic data, fundal photographs, and treatment data for audit and quality evaluation of the programme. Individuals who did not have diabetes, unable to perceive light in both eyes, or did not consent for screening were not invited for screening. Patients already under the care of an ophthalmologist for DR management privately and patients referred to treatment centre by the Diabetic RetinaScreen programme were suspended from screening as long as their treatment continued.

Data source and ethical approval

As part of provision of screening, individuals living with diabetes are asked for a verbal consent for the use of demographic data and contact information for setting up a screening appointment. Once at the screening appointment, individuals are also asked for consent for the use of their anonymised demographics, screening images, grading data, and retinopathy treatment outcome data for the use of research, service provision studies, and screening service improvement projects. Individuals who attend retinopathy screening provide written consent for the use of their anonymised demographic, screening, grading and retinopathy treatment data to be used for the purpose of research, screening service evaluation, and quality improvement projects. Opinion from the Programme Evaluation


Unit was sought in the National Screening Service regarding the present study. This study was considered to be a screening and grading service evaluation, thus, did not require additional ethical approval.

Only individuals who have consented to the use of their retinopathy screening data to be used for research are included in this study. Only anonymised demographic data and screening outcome data were used for this study. Screening and attendance data were validated by the Programme Evaluation Unit. Data regarding screening grades and referral to treatment centres were extracted from Optomize software. Data were then anonymised using each participant’s unique Diabetic RetinaScreen ID. Results of screening outcomes and attendance were then validated by the Diabetic RetinaScreen Programme Evaluation Unit.

**Missing data**

Rounds one and two U grade and slit-lamp assessment screening outcome were not available for analysis. Demographic data of patients referred during the first round of screening was not available for analysis in the present study. Analysis of these variables was conducted only with available data. As there is no current integration of health records in Ireland, this study does not include analysis of referrals by type of diabetes, Hba1C concentration, body mass index, systolic or diastolic hypertension, or presence of dyslipidaemia.

**Uptake rate**

Uptake rate is reported for each round based on the number of patients under active management at treatment centre on 31st December of respective screening round. Patients who are discharged to routine digital screening were then annually invited to participate in DR screening, while the patients in treatment centre made up the in-care-of-opthalmology cohort (ICO).

Uptake rate = Number of PWD attending screening in each round/Number of PWD in the eligible cohort—Number of patients in-care-of-opthalmology in each round of screening.

This study assessed anonymised data of individuals who attended DR and had complete retinopathy screening grading. Data are presented regarding changes in the size of the total register number, eligible cohort, demographic data of the patients eligible and those attending screening appointments throughout the study period. Retinopathy/maculopathy grades and referral outcomes were analysed and reported for patients who had attended at least one screening appointment between 1 February 2013 to 31 December 2018.

**RESULTS**

Attributing the roll out years of 2013 and 2014 as round one of screening, Diabetic RetinaScreen had completed five rounds of annual screening from February 2013 to 31 December 2018. By the end of round 5, there were 171 557 PWD living in Ireland eligible for annual DR screening (for eligible population gender and age breakdown please see online supplemental table 3). Over five rounds, 455 172 screening events took place, with 30 369 screen-positive DR referred to be assessed by an ophthalmologist. Screening attendance and uptake data are presented in table 1. Uptake was noted to be low in the first two rounds of screening. Highest retinopathy screening uptake was noted in the fourth round where 67.5% of the eligible population were screened.

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Total number of patients in eligible cohort, patients attending screening, and patients in-care-of-opthalmology used in the current analysis</th>
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<tbody>
<tr>
<td>Screening round</td>
<td>Eligible population</td>
</tr>
<tr>
<td>1</td>
<td>143 376</td>
</tr>
<tr>
<td>2</td>
<td>149 498</td>
</tr>
<tr>
<td>3</td>
<td>156 855</td>
</tr>
<tr>
<td>4</td>
<td>164 569</td>
</tr>
<tr>
<td>5</td>
<td>171 557</td>
</tr>
</tbody>
</table>

Uptake rate: Numerator=patients attending screening appointment in respective round of screening Denominator=(Population eligible in each round of screening—patients in care of ophthalmology in treatment centre).

Any retinopathy, screen-positive retinopathy, and NDED detection rate

Five rounds of retinopathy and NDED detection rate data are presented in online supplemental table 4. Rate of screen-positive retinopathy per 100 000 screened was 13 229 in round one, which had reduced to 4237 in round five. Rate of any retinopathy detection per 100 000 screened was 41 840 in round one, which reduced to 28 269 in the last round of screening. Non-diabetic eye disease (NDED) detection rate per 100 000 increased from 393 to 3225 over five rounds of screening. Detection rate of NDED during national screening increased eight-fold from round one to round five.

**Routine and urgent screen-positive referrals**

Over five rounds of screening completed, mean (range) 88.2% (86.7–91.6%) of individuals screened were screen-negative and returned to annual retinal photographic screening (table 2). Figure 1 represents the proportion of the screen-positive individuals referred via urgent and routine diabetic and non-diabetic eye disease pathways over five rounds of screening. Cumulative screen-positive referrals to treatment centres showed a decreasing trend from 13.6 to 7.4% in rounds one to five, respectively. As the attendance for screening had increased, screen-positive maculopathy and retinopathy referrals had declined through five rounds of screening. In the first round, 6504 (10.3%) were referred with routine screen-positive pre-proliferative retinopathy.

<table>
<thead>
<tr>
<th>Table 2</th>
<th>Screening outcomes and referral pathways activated in each round of screening</th>
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</thead>
<tbody>
<tr>
<td>Screening round</td>
<td>Attended screening</td>
</tr>
<tr>
<td>1</td>
<td>62 951</td>
</tr>
<tr>
<td>2</td>
<td>79 184</td>
</tr>
<tr>
<td>3</td>
<td>95 040</td>
</tr>
<tr>
<td>4</td>
<td>102 522</td>
</tr>
<tr>
<td>5</td>
<td>105 475</td>
</tr>
</tbody>
</table>

DR, diabetic retinopathy; NDED, non-diabetic eye disease; (%), per cent of patients who attended screening in corresponding round.
with or without markers of treatable maculopathy. In the fifth round, screen-positive routine referrals had reduced to 3717 (3.5%) (table 2). Urgent PDR referrals were made for 1824 individuals (2.9%) in the first round, which had decreased to 752 (0.7%) in the fifth round (table 2).

Routine and urgent NDED referrals increased overall through five rounds of screening (table 2). Routine NDED referrals were made for 235 individuals (0.4%) to be assessed and referred for further care by an ophthalmologist. In the fifth round, routine NDED was detected in 3032 individuals (2.8%). Urgent NDED referral made for suspected neovascular AMD showed a small increase from 14 (0.02%) individuals in round one to 370 (0.35%) individuals in round five.

Slit-lamp grading and examination referrals provide a fail-safe for immobile patients and for patients with ungradable images. In round 3 to round 5 of screening, mean (range) 19.0% (16.8–23.3%) of all patients referred to treatment centres were referred after slit-lamp assessments. The majority of referrals made after slit-lamp assessment were for routine NDED (mean (range) 86.3% (84.9–88.1%)) assessment while mean (range) 2.0% (0.9–3.2%) were referred with suspected wet-AMD.

**Age-based breakdown of screen-positive routine and urgent referral**

72.2% (70.9–74.7%) of all patients eligible for screening were between the ages 50 and 79 years old. Figure 2A shows an age-based breakdown of all individuals referred via the urgent DED pathway with screen-positive PDR in rounds two to five. Analysis of the age of individuals with screen-positive PDR referred via urgent pathway from rounds 2 to 5 shows that the majority of individuals, mean (range) 64.3% (60.5–70%), were between the ages of 50 and 79 years old. This demographic trend is also observed in individuals who were referred for routine screen-positive DR (R1M1, R2M0, R2M1) assessment, where mean (range) 67.5% (66.6–68.2%) of the individuals referred for routine assessments were between 50 and 79 years old (figure 2B). Patients under the 30 years old made up a mean (range) 3.2% (3.1–3.4%) of the cohort screened yearly, and made up a mean (range) of 3.2% (2.3–4.5%) of the patients referred with screen-positive proliferative retinopathy in rounds 2 to 5 (figure 2A).

**Retinopathy levels detected**

In five rounds of screening, mean (range) 68.2% (62.4–70.6%) of all patients screened had no detectable retinopathy (table 2).

Screen-negative background retinopathy (R1M0) was detected in mean (range) 25.7% (22.8–28.9%) over five rounds of screening (see online supplemental table 5). The proportion of patients referred with PDR had reduced over the course of screening, from 1663 (2.6%) in round 1 to 785 (0.74%) individuals in round 5. Cumulative sight-threatening pre-proliferative (R2) and proliferative retinopathy (R3) referrals decreased from 4.3 to 1.5% from rounds 1 to 5 (figure 3).

**Figure 1** Percentage of patients referred via routine and urgent screen-positive pathways in each round of screening. Cumulative referrals for rounds one to five of screening were: 13.6, 10.4, 9.2, 7.4 and 7.4%, respectively. DED, diabetic eye disease; NDED, nondiabetic eye disease.

**Figure 2** (A) Proportion of individuals in 10 years age brackets referred via urgent pathway with screen-positive proliferative retinopathy in rounds two to five. (B) Proportion of individuals in 10 years age brackets referred via routine diabetic eye disease pathway with screen-positive maculopathy and/or pre-proliferative retinopathy in rounds two to five.

**Figure 3** Proportion of Proliferative R3/Pre-proliferative R3 retinopathy detected in each round of screening.
DISCUSSION

Diabetic RetinaScreen has identified 171 557 PWD eligible for annual retinopathy screening in Ireland. Over five rounds, 445 172 screenings and gradings were completed, and 41 227 individuals were referred to treatment centres for assessment and treatment. In the screening rounds completed in 2017 and 2018, more than 100 000 individuals were screened per annum. Attendance for screening had increased from 61 951 to 105 475 (+70.3%) over five rounds. Improved patient registration, educational materials provided to patients and screening promotional activities have prompted a steady increase in attendance.

The majority of patients being referred to treatment centres by the Diabetic RetinaScreen programme were above the age of 50. This is consistent with the increasing prevalence of diagnosed diabetes in Ireland from 2.2% (95% CI 1.7 to 2.7) in 1998 to 5.2% (95% CI 5.1 to 5.3) in 2013, with the largest increase noted in the men and women in the 40–69 age group.10 This demographic trend towards screen-positive retinopathy being detected in older adults is consistent with observed association of DR and duration of diabetes.11 12 The UK Clinical Practice Research Datalink data analysed by Mathur et al12 also demonstrated that incidence of DR increased in parallel with increasing prevalence of diabetes.

The proportion of screen-positive retinopathy detected through national retinal screening is comparable to a previous cross-sectional prevalence study of DR conducted in Ireland through a cohort of Irish patients screened in a primary care setting14, cross-sectional prevalence study of DR conducted in Ireland through national retinal screening is comparable to a previous prevalence of diabetes.

Cumulative screen-positive referrals to treatment centres in Ireland have not decreased significantly over the 5 rounds of screening this can be attributed to the steady rise in the detection rate of NDED cases (now nearly at parity with screen-positive DR referrals: 4237 DR vs 3225 NDED per 100 000 screened). Individuals referred with NDED just require one confirmatory visit and appropriate onward referral. High concordance rate between screen-positive NDED detected on screening images and ophthalmologists assessments in treatment centres highlight the opportunity presented by including selected ocular conditions where screening for those pathologies alone would not have been cost-effective. Through robust screening and grading protocols many nondiabetic ocular conditions are being detected earlier in Ireland. This, on one hand, reflects a significant achievement of the screening programme in identifying and promptly sending patients to treatment centres with sight-threatening NDED. However, the chronic shortage of capacity in the Irish Eye Service to manage and treat the wide range of ocular conditions has led to frustration for patients and their ophthalmologists. Initiatives such as the Primary Eye Care review17 and the National Eye Care Plan18 are helping by developing primary care ophthalmology centres to provide treatments for nondiabetic eye diseases in the community.

Currently, the large number of screen-positive NDED detected during screening represents a significant challenge to optimising visual outcomes for PWD in Ireland. In nations where ophthalmic care for common ocular conditions is not available DR screening will present an opportunity to provide individuals with sight-threatening nondiabetic ocular conditions access to care. These pathologies should be treated contemporaneously to prevent referrals of these individuals to treatment centres for reasons other than DR.

National data reveal that patients with no health insurance, living in deprived economic areas are at higher risk of having undiagnosed diabetes19 and have higher prevalence of diabetes.20 The Cycle of Care Programme21 has formalised diabetes care for patients in Ireland, as part of the programme GPs shall register all new diabetic patients with the annual screening programme and collate anonymised systemic data on a central database. This has already improved the number of individuals registered for screening by Diabetic RetinaScreen.
Strengths of the study are (a) the inclusion of data from a national retinopathy screening programme, (b) accurate retinopathy grading data, and (c) five rounds of national retinopathy screening outcome information. The national RetinaScreen cohort eligible for screening represents the biggest database of PWD in the country. This study did not include analysis of referral data based on the duration of disease, type of diabetes, medications used to control glycaemia, or medications used to control hypertension (as this data is not integrated into patients’ health record yet).

Now that more than 171,000 PWD have been identified to be eligible for screening, we expect that we will continue to increase access to screening for all people living with diabetes in Ireland. We have had a steady start to our national diabetic retinopathy screening and treatment programme. Attendance at screening has increased and retinopathy detection rates were at similar rates seen in other annual retinopathy screening programmes. Significant numbers of patients have received treatment for DR on the duration of disease, type of diabetes, medications used to control glycaemia, or medications used to control hypertension (as this data is not integrated into patients’ health record yet).

Author affiliations
1Diabetic RetinaScreen, National Screening Service, Health Service Executive, Dublin, Ireland
2Mater Retinal Research Group, Mater Misericordiae University Hospital, Dublin, Ireland
3Department of Ophthalmology, Letterkenny University Hospital, Letterkenny, Ireland
4Diabetic Retinal Screening Service, Northgate Information Solutions Ltd, Hemel Hempstead, UK
5Global Vision, Centric Health Ltd, Dublin, Ireland
6Programme Evaluation Unit, National Screening Service, Dublin, Ireland
7Department of Public Health, University College Dublin, Dublin, Ireland

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Contributors
The authors contributed to the data collection, analysis, interpretation, writing of the manuscript, and critical revision of the manuscript.

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Competing interests
MC is a beneficial owner of Global Vision (Dublin, Ireland).

Ethics approval
Only anonymised demographic data and screening outcome data were used for this study. Screening and attendance data was validated by the Programme Evaluation Unit.

Provenance and peer review
Not commissioned; externally peer reviewed.

Data availability statement
All data relevant to the study are included in the article or uploaded as supplemental information.

Supplemental material
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ORCID iD
Rajiv Pandey http://orcid.org/0000-0003-1061-2150

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