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Rates of referable eye disease in the Scottish National Diabetic Retinopathy Screening Programme

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ABSTRACT

Aims Diabetic retinopathy screening aims to detect people at risk of visual loss due to proliferative diabetic retinopathy, but also refers cases of suspected macular oedema (maculopathy). At the introduction of screening, ophthalmology was concerned that referral rates would be unmanageable. We report yield of referable disease by referral reason for the first 5 years of the programme.

Methods We extracted screening results from a nationwide clinical diabetes database to calculate annual referral rates to ophthalmic clinics. We used logistic regression to examine associations between clinical measures and referable disease.

Results 182 397 people underwent ≥1 successful retinal screening between 2006 and 2010. The yield of referable eye disease was highest in the first 2 years of screening (7.0% and 6.0%) before stabilising at ∼4.3%. The majority of referrals are due to maculopathy with 73% of referrals in 2010 based on a finding of maculopathy.

Conclusions The commonest cause for referral is for suspected macular oedema (maculopathy). Referral rates for retinopathy have stabilised, as predicted, at relatively low rates. However, ophthalmology workload continues to rise as new treatment options (ie, monthly intravascular injections) have unexpectedly increased the impact on ophthalmology. A review of the screening referral path for maculopathy may be timely.

INTRODUCTION

Diabetic retinopathy (DR) is one of the leading causes of visual impairment in the UK,1 and treatment to prevent vision loss requires early detection and careful monitoring to be most effective.2 Following a Health and Technology Board Assessment, Scotland launched a national Scottish DR Screening service (DRS) in 2006. The principal aim of screening was to prevent vision loss due to proliferative DR (PDR), with individuals identified as high risk being referred to eye clinics for assessment and further management. Maculopathy (MAC) did not meet the requirements to justify a screening programme, but as it can be detected on retinal photography, a MAC grading is included in the DRS protocols with referral based on MAC as well as DR grades. Based on pilot data from the Grampian region the expected long-term referral rate from the programme was expected to be 3–4%. This workload was thought to be manageable within existing ophthalmology provision.3 The aim of this study is to report the yield of referable disease over the first 5 years of the DRS (2006–2010), a measure important for health service planning, and to estimate the burden due to referable MAC.

METHODS

DRS protocols

The national roll out of the DRS began in 2006 to improve availability of high quality retinal screening in Scotland4 attaining nationwide coverage in 2007. Patients eligible for screening are identified via the national diabetes registry—the Scottish Care Information-Diabetes Collaboration (SCI-DC) database—which automatically captures data on people with a diagnosis code for diabetes and has an estimated current coverage of >99% of the Scottish population with diagnosed diabetes mellitus (DM). All new registrants on SCI-DC who are aged ≥12 years are automatically registered as new patients on the DRS database and this triggers their first appointment. Those who are already attending eye clinics for DM-related eye disease, and those who are too unfit or frail for screening, are suspended from the screening programme with suspensions reviewed at least every 3 years. The screening examination involves a single central 45° field digital photograph with mydriasis if required, and with centralised grading.5 When photographic images are ungradable, slit-lamp examination is undertaken within the screening programme. Slit-lamp examination gradings were not available for all health boards for the whole course of the study, but where slit-lamp data are available it is included in the results (within this study 4.2% of grades were from slit-lamp exams). The use of a single central field for detection of sight-threatening retinopathy has been validated.6,7 The programme includes internal and external quality control protocols to ensure the quality of the photographs and the grading.8

DRS grading

The grading system in Scotland provides a DR grade and a MAC grade (see online supplementary table S1). Action is determined by the most severe finding in the worst eye with grades of R3 (referable background retinopathy), R4 (proliferative retinopathy) or M2 (referable MAC) triggering referral to a specialist eye clinic. Previous analyses from the pilot phase of the DRS reported an overall referral rate for eye disease of ∼3%,9 10 DRS grading data is automatically uploaded into
the SCI-DC database. We use the results for the worst eye to determine grading in this study.

Data sources
We used an anonymised extract of SCI-DC data that includes data on all individuals alive and registered on SCI-DC as of 31 May 2008 (the most recent SCI-DC extract data available) which has updated DRS data up to 31 December 2010. Data was extracted from the SCI-DC audit server by an automated process and then cleaned and anonymised prior to use in this study.

Study population
All individuals age >12 years who were registered on SCI-DC with a diagnosis of diabetes before 31 May 2008 and had at least one successful DRS examination were included in this study.

Covariate data
Diabetes type was based on the type listed in SCI-DC by clinicians. Additionally, we employed an algorithm to identify individuals at high risk of being mislabelled, based on age of diagnosis and prescribed treatment. The date of diagnosis for DM was based on the diagnosis date entered into SCI-DC by clinicians, taking the earliest date where multiple dates were entered. This diagnosis date was checked against multiple data sources including prescription and hospital discharge records for any evidence of diabetes prior to the SCI-DC date of diagnosis. Where there is evidence of DM prior to the recorded date of diagnosis we used the earliest date available.

To determine the risk factor profile for cases of referable eye disease we considered risk factor data for those examined in 2008. Measures of Body Mass Index (BMI), HbA1c, serum total cholesterol, systolic and diastolic blood pressure and smoking status were selected from SCI-DC taking the measure made nearest to the screening exam. In order to limit missing risk factor data while retaining a temporal relationship between measure and screening we used a series of cut-points (HbA1c ±180 days, blood pressure ±90 days and BMI or smoking status ±1085 days). If no measure was available the data was considered to be missing. We used prescription data to determine diabetes treatment at the time of the screening examination.

Statistical methods
The proportion of screened individuals with referable eye disease was calculated by year. Where an individual had more than one screening examination in a year the worst result was used. We used univariate and multivariate logistic regression models to examine the role of DM type, age, sex and diabetes duration along with other covariates on risk for referable eye disease. All statistical analysis was undertaken using SAS v.9.2 (Cary, North Carolina, USA). We used a p value of <0.05 to indicate statistical significance.

RESULTS
There were 225 442 individuals eligible for inclusion in this study. During the course of the study 187 822 (83.3%) were screened at least once by the DRS, with 182 397 having at least one gradable result (figure 1). Demographics for the study population are shown in table 1.

Yield of referable eye disease
We included data on 560 362 screening episodes resulting in gradable images between 2006 and 2010. Slit-lamp examinations accounted for 23 311 (4.8%) of the data. Each individual had a median of three (IQR 2–4) successful screens during the study period and this did not differ by DM type (table 2). The yield of referable eye disease was greatest in the first 2 years of the programme where 7.0% and 6.0% of individuals successfully screened in the DRS had referable disease in 2006 and 2007, respectively. Over time, the proportion of people attending who had attended at least one previous screen by the DRS

<table>
<thead>
<tr>
<th>Table 1 Baseline demographics for population</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency/median</td>
</tr>
<tr>
<td>Male sex</td>
</tr>
<tr>
<td>Diabetes type (%)</td>
</tr>
<tr>
<td>Type 1 diabetes</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
</tr>
<tr>
<td>Other/unknown type</td>
</tr>
<tr>
<td>Year first screened (%)</td>
</tr>
<tr>
<td>2006</td>
</tr>
<tr>
<td>2007</td>
</tr>
<tr>
<td>2008</td>
</tr>
<tr>
<td>2009</td>
</tr>
<tr>
<td>2010</td>
</tr>
<tr>
<td>Age at first screen (years)</td>
</tr>
<tr>
<td>Diabetes duration at first screen (years)</td>
</tr>
</tbody>
</table>
increased from 23.5% of screens in 2007 to >90% of screens in 2009 and 2010. Referral rates were highest for first-time attendees with 6.9% of first screens finding referable eye disease compared to 3% for people attending their 4th or 5th screen.

For 2008 and onwards, the yield was stable at 4.3%. For all years, the yield for referable MAC was higher than that for referable DR accounting for between 60% of referrals in 2006 to 73% in 2010. Overall, the referral rates were higher for those screened by slit-lamp (7.2%) than those screened by retinal photography (5.1%).

Referable eye disease by type of diabetes
We excluded 741 individuals from this analysis as they had neither type 1 (T1DM) nor type 2 (T2DM) (eg, MODY, pancreatic causes, etc; table 3). There were 20 521 people with T1DM and 161 135 people with T2DM (table 2). The prevalence of referable eye disease was consistently higher among those with T1DM compared to those with T2DM (table 3). The proportion of referrals due to MAC alone were similar for both types of DM in 2006 (59.0% for T1DM and 60.3% for T2DM), but in subsequent years the proportion rose among the T2DM population to 76.1% in 2010 compared to 63.2% of the referrals among the T1DM population.

Risk factor profile for referable eye disease
Table 4 shows the risk factor profile by retinal screening grade. Regardless of diabetes type, compared to the no retinopathy group, those with referable disease were more often male, with longer DM duration, higher HbA1c, and higher systolic blood pressure. Additionally, for people with T1DM, referable disease was also associated with older age, higher BMI, higher diastolic blood pressure and higher prevalence of smoking. By contrast, in T2DM, referable disease was also associated with lower prevalence of smoking, lower BMI and greater use of insulin therapy.

Compared to people referred for DR, people referred with MAC had shorter DM duration and lower HbA1c values. Additionally, among people with T1DM, MAC referrals tended to be for older women with higher BMI than referrals for DR, whereas for people with T2DM, MAC referral was associated with lower BMI and lower systolic blood pressure.

In multivariate models restricted to those with no missing data (n=78 814) including all covariates and screening mode male sex, longer DM duration and higher HbA1c remained significantly associated with referable disease regardless of DM type. For T2DM, higher blood pressure, lower prevalence of smoking and higher prevalence of insulin use were also associated with referable disease.

In a univariate logistic regression model for the presence of any referable eye disease using data for 2008, the OR for T1DM compared to T2DM was 3.08 (95% CI 2.89 to 3.28, p<0.001), with risk seemingly mediated principally via DM duration (OR for referral due to T1DM 0.81 (95% CI 0.73 to 0.91) after adjustment for age, sex, DM duration and screening method), T1DM was a positive risk factor for referral due to PDR even after adjustment for age, sex and DM duration and screening method (OR=1.35, OR 1.06 to 1.73, p=0.017). However, due to the limited overlap between age and DM duration ranges for the DM types (table 4) these models may not fully account for the covariates.

DISCUSSION
The yield of referable eye disease within the DRS was at its highest during the first 2 years of the programme (2006–2007)

**Table 2** Yield of referable eye disease by year of screening

<table>
<thead>
<tr>
<th>Year (n=39 463)</th>
<th>2006 (n=32 685)</th>
<th>2007 (n=31 799)</th>
<th>2008 (n=31 064)</th>
<th>2009 (n=29 939)</th>
<th>2010 (n=28 569)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No eye disease</td>
<td>27 384 (69.1)</td>
<td>26 814 (69.6)</td>
<td>25 812 (82.8)</td>
<td>26 686 (89.2)</td>
<td>26 568 (93.5)</td>
</tr>
<tr>
<td>Non-referable DR</td>
<td>10 760 (27.2)</td>
<td>9 610 (23.7)</td>
<td>9 011 (29.2)</td>
<td>8 553 (28.5)</td>
<td>8 782 (30.5)</td>
</tr>
<tr>
<td>Referable eye disease</td>
<td>1 724 (4.5)</td>
<td>1 085 (2.8)</td>
<td>1 253 (4.1)</td>
<td>1 550 (5.2)</td>
<td>1 192 (4.2)</td>
</tr>
</tbody>
</table>

**Referable eye disease comprises referable maculopathy (M2 on the DRS grading scheme), preproliferative retinopathy (R3 on the DRS grading scheme) and proliferative retinopathy (R4 on the DRS grading scheme).**
Table 3

<table>
<thead>
<tr>
<th>Year</th>
<th>Type 1 diabetes</th>
<th>Type 2 diabetes</th>
</tr>
</thead>
<tbody>
<tr>
<td>2006</td>
<td>2007</td>
<td>2008</td>
</tr>
<tr>
<td>No eye disease</td>
<td>1886 (38.0)</td>
<td>5368 (41.3)</td>
</tr>
<tr>
<td>Non-referable eye disease</td>
<td>2346 (47.2)</td>
<td>5943 (45.8)</td>
</tr>
<tr>
<td>Referable eye disease</td>
<td>735 (14.8)</td>
<td>1676 (12.9)</td>
</tr>
<tr>
<td>Referable maculopathy alone</td>
<td>434 (8.7)</td>
<td>1023 (7.9)</td>
</tr>
<tr>
<td>Proliferative retinopathy±maculopathy</td>
<td>161 (3.2)</td>
<td>318 (2.4)</td>
</tr>
<tr>
<td>Total (100%)</td>
<td>4967</td>
<td>12 987</td>
</tr>
</tbody>
</table>

DRS, Diabetic Retinopathy Screening service.
people with DM of >20 years duration, the prevalence of any
dr among people with T1DM approaches 100%14 compared
with those diagnosed prior to 1980.25

While we may see reductions in the prevalence of referable
disease over time due to improvements in DM management,
the current referral rates indicate a steady rate of new referrals from
the national screening programme with the majority a result of
improvements in DM management, the
data were missing for 9946 people (7.7%) and BMI data was missing for 7025 people (5.5%).
Covariate data was complete for 78 814 (61.4%) of the individuals. Blood pressure data was missing for 31 767 (24.7%) Smoking data was missing for 15 101 (11.8%) HbA1c data
was missing for 9946 people (7.7%) and BMI data was missing for 7025 people (5.5%).

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Research Network (SDRN), the Diabetes Retinal Screening Collaborative and the
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contribute to the work of the Scottish Diabetic Retinopathy Screening collaborative
who have been vital to the success of this project.

Contributors HCL researched the data, contributed to the discussion, wrote and
evaluated the manuscript; SON researched the data and reviewed the manuscript; HMC
researched the data, contributed to the discussion and edited the manuscript. MBW,
DTC, JD, GPL, NL, SP, DWMP and JAO reviewed the manuscript. All authors
reviewed and approved the final version of the manuscript.

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and the Information Services Division of NHS Scotland.

Competing interests None.

Ethics approval Approval was obtained from the Scotland A Research Ethics
Committee, the Caldicott (data privacy) Guardian for the 14 Scottish Health Boards and
the ISD Privacy Advisory Committee.

Provenance and peer review Not commissioned; externally peer reviewed.

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Grampian Diabetes Research Unit, NHS Grampian, Aberdeen, UK

Acknowledgements

Table 4 Risk factors for referable eye disease for individuals with type 1 or type 2 diabetes in 2008

<table>
<thead>
<tr>
<th>Type 1 diabetes</th>
<th>No retinopathy or maculopathy</th>
<th>Non-referable retinopathy</th>
<th>Referable maculopathy only</th>
<th>Referable retinopathy or maculopathy</th>
<th>p Value No retinopathy vs Referable maculopathy</th>
<th>p Value Referable maculopathy vs Referable retinopathy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex*</td>
<td>5872</td>
<td>6146</td>
<td>856</td>
<td>521</td>
<td>0.006</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>3122 (53.2%)</td>
<td>3415 (55.6%)</td>
<td>498 (58.2%)</td>
<td>331 (63.5%)</td>
<td>&lt;0.001</td>
<td>0.049</td>
</tr>
<tr>
<td>Diabetes duration (years)†</td>
<td>35.1±16.9</td>
<td>42.6±14.5</td>
<td>43.8±13.8</td>
<td>41.8±12.3</td>
<td>&lt;0.001</td>
<td>0.046</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.7 (3.6–14.4)</td>
<td>19.6 (12.3–28.9)</td>
<td>20.7 (15.4–28.2)</td>
<td>23.1 (17.0–30.0)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>8.5±1.7</td>
<td>8.7±1.6</td>
<td>9.1±1.7</td>
<td>9.4±1.9</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>126.5±16.4</td>
<td>130.2±17.1</td>
<td>132.5±15.8</td>
<td>132.9±18.1</td>
<td>&lt;0.001</td>
<td>0.001</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>3.3±8.10</td>
<td>7.4±3.99</td>
<td>7.6±3.10</td>
<td>7.6±10.8</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Current smoking*</td>
<td>25.9±5.4</td>
<td>27.2±5.0</td>
<td>27.8±5.1</td>
<td>26.8±5.3</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
<tr>
<td>Type 2 diabetes</td>
<td>8096</td>
<td>29.95</td>
<td>2941</td>
<td>1187</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male sex*</td>
<td>44.65 (55.1%)</td>
<td>17.535 (58.6%)</td>
<td>1672 (56.9%)</td>
<td>708 (59.7%)</td>
<td>0.062</td>
<td>0.002</td>
</tr>
<tr>
<td>Age (years)</td>
<td>64.8±11.5</td>
<td>65.3±11.4</td>
<td>64.8±11.5</td>
<td>65.1±11.5</td>
<td>0.710</td>
<td>0.220</td>
</tr>
<tr>
<td>Diabetes duration (years)†</td>
<td>4.8 (2.4–8.1)</td>
<td>7.8 (4.1–12.8)</td>
<td>11.3 (6.2–16.2)</td>
<td>13.2 (7.4–18.1)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>7.3±1.4</td>
<td>7.6±1.6</td>
<td>8.1±1.8</td>
<td>8.4±1.8</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Systolic blood pressure (mm Hg)</td>
<td>134.3±15.9</td>
<td>136.3±17.1</td>
<td>138.4±18.0</td>
<td>139.9±20.6</td>
<td>&lt;0.001</td>
<td>0.003</td>
</tr>
<tr>
<td>Diastolic blood pressure (mm Hg)</td>
<td>75.7±10.2</td>
<td>75.3±10.2</td>
<td>75.8±10.4</td>
<td>75.7±10.4</td>
<td>0.886</td>
<td>0.818</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>31.6±6.3</td>
<td>31.4±6.3</td>
<td>31.2±6.3</td>
<td>31.9±6.5</td>
<td>0.001</td>
<td>0.037</td>
</tr>
<tr>
<td>Current smoking*</td>
<td>10 306 (14.5%)</td>
<td>3797 (14.6%)</td>
<td>310 (12.1%)</td>
<td>129 (12.1%)</td>
<td>&lt;0.001</td>
<td>0.015</td>
</tr>
<tr>
<td>Diabetes treatment*</td>
<td>25 464 (31.5%)</td>
<td>5729 (19.1%)</td>
<td>321 (10.9%)</td>
<td>111 (9.4%)</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>No medication</td>
<td>49 332 (60.9%)</td>
<td>18 593 (62.1%)</td>
<td>1652 (56.2%)</td>
<td>579 (48.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral agents only</td>
<td>6165 (7.6%)</td>
<td>5629 (18.8%)</td>
<td>968 (32.9%)</td>
<td>497 (41.9%)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Data are means with SDs except for * which are frequencies, and † which are medians with IQR.
Referable eye disease comprises referable maculopathy (M2 on the DRS grading scheme), preproliferative retinopathy (R3 on the DRS grading scheme) and proliferative retinopathy (R4 on the DRS grading scheme).

p Values are for multivariate logistic regression models including all covariates and screening modality (retinal photography or slit-lamp).
Covariate data was complete for 78 814 (61.4%) of the individuals. Blood pressure data was missing for 31 767 (24.7%) Smoking data was missing for 15 101 (11.8%) HbA1c data
was missing for 9946 people (7.7%) and BMI data was missing for 7025 people (5.5%).

BMD, Body Mass Index; DRS, Diabetic Retinopathy Screening service.
Clinical science

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REFERENCES
