Screening attendance, age group and diabetic retinopathy level at first screen
Scanlon, P. H.; Stratton, I. M.; Leese, G. P.; Bachmann, M. O.; Land, M.; Jones, C.; Ferguson, B.
Published in:
Diabetic Medicine

DOI:
10.1111/dme.12957

Publication date:
2016

Document Version
Publisher's PDF, also known as Version of record

Link to publication in Discovery Research Portal

Citation for published version (APA):
Scanlon, P. H., Stratton, I. M., Leese, G. P., Bachmann, M. O., Land, M., Jones, C., & Ferguson, B. (2016). Screening attendance, age group and diabetic retinopathy level at first screen. Diabetic Medicine, 33(7), 904-911. DOI: 10.1111/dme.12957

General rights
Copyright and moral rights for the publications made accessible in Discovery Research Portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from Discovery Research Portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain.

Take down policy
If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.
Research: Complications

Screening attendance, age group and diabetic retinopathy level at first screen

P. H. Scanlon¹, I. M. Stratton¹, G. P. Leese², M. O. Bachmann³, M. Land⁴, C. Jones⁵ and B Ferguson⁶ on behalf of the Four Nations Diabetic Retinopathy Screening Study Group

¹Gloucestershire Retinal Research Group, Gloucester, ²Ninewells Hospital and Medical School, Dundee, ³Norwich Medical School, Norwich, ⁴Landmark Health Consulting, York, ⁵Norfolk and Norwich University Hospital, Norwich and ⁶Public Health England, London, UK

Accepted 1 September 2015

Abstract

Aims To report on the relationships between age at diagnosis of diabetes, time from registration with the screening programme to first diabetic eye screening and severity of diabetic retinopathy.

Methods Data were extracted from four English screening programmes and from the Scottish, Welsh and Northern Irish programmes. Time from diagnosis of diabetes to first screening and age at diagnosis were calculated.

Results Time from registration with the screening programme to first screening episode is strongly related to age at registration. Within 18 months of registration 89% of 3958 young people under 18 years of age and 81% of 391 293 people over 35 years of age were seen. In 19 058 people between 18 and 34 years of age, 80% coverage was not reached until 2 years and 9 months. The time from diagnosis of diabetes to first screening is positively associated with severity of disease ($P < 0.0001$).

Conclusions This report is the first that to demonstrate that those in the 18–34 year age group are least likely to attend promptly for screening after registration with a higher risk of referable diabetic retinopathy being present at the time of first screen. Date of diagnosis should be recorded and prodigious efforts made to screen all people promptly after diagnosis. Screening programmes should collect data on those who have not attended within one year of registration.

Diabet. Med. 33, 904–911 (2016)

Introduction

Diabetic retinopathy is a microvascular consequence of diabetes, which in advanced stages leads to vision loss and blindness, with significant impact on health status and quality of life for people with diabetes.

Annual screening for diabetic retinopathy is recommended in England, Scotland, Wales and Northern Ireland (the Four Nations) for all those with diabetes aged 12 and above. The decision to screen annually was a pragmatic policy decision taken when national screening programmes were introduced in the Four Nations of the UK in 2002–2003. When the English screening programme was established in 2003 it was estimated that there were ~ 1.4 million people with diabetes in England. The number in 2013 is estimated to be 2.6 million, with the number in the UK as a whole having exceeded 3 million in 2013 [1], driven by lifestyle factors and the ageing population.

The Four Nations Diabetic Retinopathy Screening Intervals Project was established by the National Screening Committee in May 2012 to determine whether evidence supports the introduction of individualized screening intervals based on estimated risk of developing referable diabetic retinopathy (defined below) which is the threshold for referral to a hospital eye service. Data sets were obtained from Scotland, Wales, Northern Ireland and from four English screening programmes to examine the performance of an algorithm to estimate risk [2] and a recent report on this has been published [3].

A recent report in one English screening programme [4] highlighted the elevated rate of detection of referable diabetic retinopathy in those who were not screened promptly after diagnosis of Type 2 diabetes. The analyses reported here were designed to examine the relationship between time from diagnosis of diabetes and diabetic retinopathy level at first screening episode, and time from registration to screening by age group, in a very large data set.
We consider these programmes to encompass much of the Quality Assurance visit, had a population screening size of problems with their grading at their most recent External included programmes that were assessed as not having any from the Midlands and one from the South of England. We include programmes with sizeable ethnic minority populations. areas, high and low levels of socio-economic deprivation and to four English programmes were chosen to cover urban and rural data set have been reported in a previous publication [3]. The and Staffordshire). The inclusion criteria for this Four Nations programmes in Wales, Scotland and Northern Ireland and diabetic retinopathy screening programmes: whole nation were included from Scotland and three English programmes. included from the Scotland, Wales, Northern Ireland and levels vs. time from diagnosis to screening, data were analysed using Mantel–Haenszel chi-square tests. The retinopathy levels analysed are defined in the Scottish screening programme. Patients with unassessable images of either or both eyes were excluded from these analyses.

In the analysis of retinopathy levels vs. time from diagnosis to screening, data were analysed using Mantel–Haenszel chi-square tests. The retinopathy levels analysed are defined in Table 1 by the levels no diabetic retinopathy, mild non-proliferative diabetic retinopathy in one eye, mild non-proliferative diabetic retinopathy in both eyes, referable diabetic retinopathy (moderate non-proliferative diabetic retinopathy or M1 (maculopathy) in at least one eye and the equivalent levels were identified in the Scottish screening programme. Patients with unassessable images of either or both eyes were excluded from these analyses.

In the analysis of retinopathy levels vs. time from diagnosis to screening, data were analysed using Mantel–Haenszel chi-square tests. The retinopathy levels analysed are defined in Table 1 by the levels no diabetic retinopathy, mild non-proliferative diabetic retinopathy in one eye, mild non-proliferative diabetic retinopathy in both eyes, referable diabetic retinopathy (moderate non-proliferative diabetic retinopathy or maculopathy), fast track referable diabetic retinopathy (proliferative diabetic retinopathy) and the number and percentage of these grades and ungradable image sets is shown in Table 2. Logistic regression was used to analyse the effects of duration of diabetes and age at time of screening, type of diabetes and gender (Table 3).

Time from registration on the programme’s central collated list to date of screen was analysed using Kaplan–Meier estimates with follow-up censored on 1 January 2012 stratified by age at registration. Figure 1 shows the time to screening by age group overall, and Fig. 2 shows the time to screening by age group within each programme. Further analysis was carried out of time to screening using parametric survival models to look at the effects of age and gender.

Results

Over all seven programmes there were 689 025 people on the registers. Of these, 54.9% were men, 43.1% women and 2.0% had no gender recorded. Of these, 512 944 had a date of diagnosis of diabetes (74.4%); by programme the respective proportions were 0%, 8%, 58%, 77%, 79%, 99.6% and
Table 1 Comparison of English, Scottish and ETDRS grading classifications

| English grade and outcome | English screening programme levels | Scottish grade and outcome | Scottish screening programme levels | ETDRS final retinopathy severity scale | ETDRS (final) grade | Risk of progression to proliferative retinopathy in 1 year |
|--------------------------|-----------------------------------|---------------------------|------------------------------------|---------------------------------------|---------------------|--------------------------------------------------------|
| R0: rescreen in 12 months | R0 (No retinopathy)               | R0 (No visible retinopathy)| No apparent retinopathy            | 10                                    |                     |                                                         |
| R1: rescreen in 12 months | R1 (Background) Microaneurysm(s), retinal haemorrhage(s), any exudate, venous loop, cotton wool spot equivalent to Scottish | R1 (mild) Re-screen in 12 months | R1 (Background diabetic retinopathy – mild) | Mild non-proliferative retinopathy | 14, 15              | 6.2%                                                   |
| R2: routine referral     | R2 (Pre-proliferative) Venous beading, venous reduplication, intraretinal microvascular abnormality (IRMA), multiple blot haemorrhages | R2 (observable background) Re-screen in 6 months | R2 (Background diabetic retinopathy – observable) | Moderate non-proliferative retinopathy | 43                  | 11.3%                                                  |
|                          |                                   |                           | R3 (referable background) Refer to ophthalmology |                                       |                     |                                                         |
|                          |                                   |                           | R3 (Background diabetic retinopathy – referable) |                                       |                     |                                                         |
|                          |                                   |                           | Any of the following features: four or more blot haemorrhages (i.e. AH standard photograph 2a) in both inferior and superior hemi-fields; venous beading (AH standard photograph 6a); IRMA (AH standard photograph 8a) | Moderately severe non-proliferative retinopathy | 47                  | 20.7%                                                  |
| R3: urgent referral to ophthalmologist | R3 (Proliferative) New vessels on disc (NVD), new vessels elsewhere (NVE), pre-retinal or vitreous haemorrhage, pre-retinal fibrosis ± tractional retinal detachment | R4 (Proliferative diabetic retinopathy) | Active new vessels, vitreous haemorrhage | Proliferative retinopathy | ≥ 61                | Proliferative retinopathy has developed |
99.8%. Type of diabetes was recorded for 620 281, of these 9.4% had Type 1 diabetes and 90.6% had Type 2 diabetes. Median age of diagnosis of Type 1 diabetes was 22 years [interquartile range (IQR) 12–34], and for Type 2 diabetes was 59 years (IQR 50–68). Of those who were screened for the first time in 2011, date of diagnosis of diabetes was available for 38 710 people from five programmes (programmes 1, 3, 4, 5 and 6). Of those with a type of diabetes recorded, the proportion of people with any retinopathy and with referable and ‘fast track’ referable diabetic retinopathy (proliferative diabetic retinopathy) increased with time from diagnosis to screening. Between those diagnosed in 2010 or 2011 and those diagnosed before 1990 the proportion with any diabetic retinopathy increased from 18% to 67%, and the proportion with ‘fast track’ referable diabetic retinopathy increased from 0.1% to 8.7% (Table 2) (chi-squared for trend \( P < 0.0001 \)). Those diagnosed with diabetes before 1990 and first screened in 2010 or 2011 were 19 [95% confidence interval (CI) 16 to 21] times more likely to have referable diabetic retinopathy than those diagnosed in 2010 or 2011 and 69 (95% CI 47 to 101) times more likely to have ‘fast track’ referable diabetic retinopathy. Figure 3 shows the data for each of the five screening programmes.

Logistic regression analyses were carried out on 27 090 people, 1183 of whom had referable retinopathy, and of these 235 required urgent referral to ophthalmology. The explanatory variables were date of diagnosis, gender, date of registration, age at screening and type of diabetes. After adjustment for age at screening, type of diabetes and gender, the duration of diabetes and time from registration to screening were each highly significant predictors of both referable retinopathy and urgent referral (Table 3). For the analysis of ‘age vs. time from registration to date of first screening’, data were available for 3958 people aged 12–17 years, 19 058 aged 18–34 years, 15 5496 aged 35–59 years and 215 797 aged 60 years and above. Figure 1 demonstrates that the attendance soon after screening was good in the 12–17-year age group and in those aged 35 and above. Those least likely to attend for screening in the first 3 years after registration were those aged 18–34. In this age group it was not until 2 years and 9 months after registration that 80% of the people had been screened, this proportion having been reached in all other age groups 18 months after registration. At 2 years, one in seven of those aged below 18 or 35 or older have not attended for screening, but in the 18–34 year age group the proportion was one in four. There was heterogeneity between programmes in the time from registration to being screened for the first time as described in the methods section. For those programmes that were included, the proportions screened by 12 months ranged from 63% to 85% and at 36 months from 81% to 91%. In the 12–17-year age group, 9.3% (95% CI 8.4 to 10.2) failed to attend for screening over a 3-year period since diagnosis of diabetes, compared with 18.3% (95% CI 17.8 to 18.7) in the 18–34 age group, 10.2% (95% CI 10.0 to 10.3) in the 35–59 age
Using a Weibull model, age group and gender were significant because the hazards were not proportional. Figure 2 shows a comparison of uptake between screening programmes in different age groups.

The youngest age group (12–17 at registration) were slower to attend for screening in the first 6 months than those aged 35 and older, but the rate at which they attended for screening did not attenuate in the same way as older groups, so by 3 years this group were most likely to have been screened. Cox proportional hazards models were not appropriate because the hazards were not proportional. Using a Weibull model, age group and gender were significant associated with time to first screen ($P < 0.0001$ for both classification variables). Using age 60 and above as a reference group the parameter estimates for the 12–17, 18–34 and 35–59 age groups, respectively, were 0.24 (95% CI 0.18 to 0.30), 0.71 (0.67 to 0.75) and 0.20 (0.18 to 0.21).

After adjustment for age, men were more likely to be invited or may delay for two or more years before doing so. For people who have moved between screening programmes the date of diagnosis will not be the date when the patient is registered. However, as it is not currently possible to share data and images between screening programmes it is important that each programme has digital images soon after the patient is registered. However, as it is not currently possible to share data and images between screening programmes it is important that each programme has digital images soon after the patient is registered in order to have a "baseline" grading, whether or not they are newly diagnosed.

### Discussion

Previous evidence demonstrates a strong positive association between incidence of diabetic retinopathy and duration of diabetes [11,12]. People on the screening register are invited for screening within 3 months of registration and then annually. If they fail to attend they are given two further appointments and then recalled after 1 year in Scotland and in England. However, they may choose not to take up the invitation or may delay for two or more years before doing so. For people who have moved between screening programmes the date of diagnosis will not be the date when the patient is registered. However, as it is not currently possible to share data and images between screening programmes it is important that each programme has digital images soon after the patient is registered in order to have a "baseline" grading, whether or not they are newly diagnosed.

Factors that are known to affect attendance are:

- patient age – young adult people had a higher propensity for non-attendance at diabetic retinopathy screening [13,14];
- socio-economic deprivation [13,15];
- type of diabetes – attendance rates at diabetic retinopathy screening lower in people with Type 1 diabetes [14];
- poor glycaemic control, hypertension and smoking [13]; and
- primary care practice and screening-team-related factors [16].

### Table 2 Results of first screening by date of diagnosis of diabetes, at first screening in 2011, all programmes combined

| Year of diagnosis of diabetes | Total image sets | % of graded image sets | % of graded image sets | % of graded image sets | % of graded image sets | % of all image sets |
|------------------------------|------------------|------------------------|------------------------|------------------------|------------------------|---------------------|
| 1989 and earlier             | 1,462            | 443 (33.0)             | 176 (13.1)             | 362 (27.0)             | 244 (18.2)             | 116 (8.7)           |
| 1990–1999                    | 2,936            | 1,453 (52.6)           | 381 (13.8)             | 507 (18.4)             | 323 (11.7)             | 99 (3.6)            |
| 2000–2004                    | 3,923            | 2,574 (68.5)           | 527 (14.0)             | 389 (10.4)             | 210 (5.6)              | 56 (1.5)            |
| 2005–2009                    | 3,063            | 4,504 (76.7)           | 802 (13.7)             | 379 (6.5)              | 157 (2.7)              | 27 (0.5)            |
| 2010–2011                    | 27,326           | 21,508 (82.0)          | 3,244 (12.4)           | 1,108 (4.2)            | 344 (1.3)              | 33 (0.1)            |

*Chi-squared for trend in the level of referable retinopathy (both fast track and not fast track) $P < 0.0001$.

†Chi-squared for trend in the proportion of ungradable image sets $P < 0.0001$.

### Table 3 Patient characteristics associated with referable retinopathy and urgent referral: logistic regression models including 27 090 people with diabetes

| Referable retinopathy | Urgent referral to ophthalmology | Odds ratio and 95% CI | Odds ratio and 95% CI |
|-----------------------|---------------------------------|-----------------------|-----------------------|
| Duration of diabetes  |                                 |                       |                       |
| Up to 5 years (reference) | 1                              | 1                     |                       |
| 5–9 years             | 3.5 (2.8–4.5)                   | 4.5 (2.5–8.1)         |                       |
| 10–19 years           | 10.7 (8.6–13.2)                 | 17 (10–28)            |                       |
| 20 years or more      | 15.8 (12.3–20.4)                | 33 (20–54)            |                       |
| Time from registration to first screen |                       |                       |                       |
| Up to 2 months (reference) | 1                              | 1                     |                       |
| 2–11 months           | 1.2 (0.9–1.4)                   | 1.5 (0.9–2.6)         |                       |
| 12–35 months          | 1.9 (1.4–2.5)                   | 2.8 (1.4–5.4)         |                       |
| 36 months or more     | 2.9 (2.3–3.6)                   | 4.3 (2.6–7.1)         |                       |
| Diabetes type         |                                 |                       |                       |
| Type 1                | 1                               | 1                     |                       |
| Type 2                | 0.72 (0.58–0.90)                |                       |                       |
| Age group             |                                 |                       |                       |
| 18–34 years (reference) | 1                              | 1                     |                       |
| 35–59                 | 1.4 (1.1–1.9)                   | 1.1 (0.7–1.7)         |                       |
| 60 and above          | 1.1 (0.8–1.5)                   | 0.6 (0.4–1.0)         |                       |
| Gender                |                                 |                       |                       |
| Male                  | 1                               | 1                     |                       |
| Female                | 0.82 (0.72–0.93)                |                       |                       |
The major concern is that there is an association between non-attendance at screening, poor control of diabetes [17] and blindness registration [18]. One missed attendance at a retinal screening appointment is associated with a threefold increase in needing laser photocoagulation subsequently [13].

This report is the first that has demonstrated that those in the 18–34-year age group are more likely to have a longer time interval between registration and attendance for screening and a consequent greater risk of referable diabetic retinopathy being present at the time of first screen. This is most likely to be due to the known propensity of the 18–34-year age group for non-attendance [17] and the likelihood that younger people are more likely to have Type 1 diabetes. It is important that people in these groups are screened because, in addition to the significant quality of life implications, there are wider economic consequences such as lost productivity. This report also quantifies the increase in risk of referable and of proliferative retinopathy seen in those who are not screened promptly after registration, independently of the risk due to duration of diabetes. Risk of proliferative retinopathy is four times higher in those in whom screening is delayed 3 years or more, suggesting that this group are different from those who attend promptly. Further work could be undertaken with this

FIGURE 1 Kaplan–Meier curves of proportion screened since registration, by age at registration.

FIGURE 2 Comparison of uptake between screening programmes in different age groups.
group to understand reasons for delay and changes to screening programmes that might reduce this. This study from a large data set supports the suggestion that screening programmes should collect data on those who attend and on those who have not attended over a 1-, 2-, 3-, 4- and 5-year period. In addition to date of registration, the date of diagnosis of diabetes should be routinely recorded. Without these data it is impossible to identify the cohort of people at high risk who have never attended for diabetic retinopathy screening.

Screening programmes have different modalities of delivery and some differences of demographic characteristics of their population. Supplementary information from this data set (Fig. 2) demonstrates that some screening programmes are better than others at getting young people in to be screened. Protocols from screening programmes with higher attendance could be used to improve attendance in those with lower attendance.

The evidence from this study will also be helpful for those planning new screening programmes.

Funding sources
NHS Diabetic Eye Screening Programme, NIHR Health Technology Assessment Grant 10/66/01 & Scottish Diabetes Retinal Screening Programme.

Competing interests
None declared.

Acknowledgements
We are very grateful to individuals and Departments of Health in all Four Nations for working collaboratively on this project, in particular the screening programme staff from Wales, Scotland and Northern Ireland and four local English programmes (Brighton, Derbyshire, Leeds and Staffordshire).

Author contributions
PS wrote the first draft and IS conducted the analyses. GL, MB, ML, CJ and BF all commented on the drafts of the paper. Professor Peter Scanlon is the guarantor of this work and, as such, had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

References
1 Number of People Diagnosed with Diabetes Reaches Three Million. 2013. Available at https://www.diabetes.org.uk/About_us/News_Landing_Page/Number-of-people-diagnosed-with-diabetes-reaches-three-million/ Last accessed 23 May 2015.
2 Stratton IM, Adler AI, Aldington S, Histed M, Taylor DJ, Scanlon P. A simple algorithm to estimate the time to development of sight-threatening diabetic retinopathy. The Lancet 2012; 380: S69.
3 Leese GP, Stratton IM, Land M, Bachmann MO, Jones C, Scanlon P et al. Progression of diabetes retinal status within community screening programs and potential implications for screening intervals. Diabetes Care 2015; 38: 488–94.
4 Scanlon PH, Aldington SJ, Stratton IM. Delay in diabetic retinopathy screening increases the rate of detection of referable diabetic retinopathy. *Diabet Med* 2014; 31: 439–442.

5 National Institute for Health and Care Excellence. *Type 1 Diabetes: Diagnosis and Management of Type 1 Diabetes in Children, Young People and Adults*. Clinical guideline 15. Available at http://www.nice.org.uk/guidance/cg15/chapter/1-recommendations#identification-and-management-of-complications Last accessed 23 May 2015.

6 National Institute for Health and Care Excellence. *Type 2 Diabetes: The Management of Type 2 Diabetes*. Clinical guideline 87. Available at http://www.nice.org.uk/guidance/cg87/chapter/1-recommendations#eye-damage Last accessed 23 May 2015.

7 SIGN 116: *Management of Diabetes*. 2010. Available at http://www.sign.ac.uk/guidelines/fulltext/116/ Last accessed 23 May 2015.

8 Harding S, Greenwood R, Aldington S, Gibson J, Owens D, Taylor R et al. Grading and disease management in national screening for diabetic retinopathy in England and Wales. *Diabet Med* 2003; 20: 965–971.

9 Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs – an extension of the modified Airlie House classification. ETDRS report number 10. *Ophthalmology* 1991; 98: 786–806.

10 Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. *Ophthalmology* 1991; 98: 823–833.

11 Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. IX. Four-year incidence and progression of diabetic retinopathy when age at diagnosis is less than 30 years. *Arch Ophthalmol* 1989; 107: 237–243.

12 Klein R, Klein BE, Moss SE, Davis MD, DeMets DL. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. X. Four-year incidence and progression of diabetic retinopathy when age at diagnosis is 30 years or more. *Arch Ophthalmol* 1989; 107: 244–249.

13 Leese GP, Boyle P, Feng Z, Emslie-Smith A, Ellis JD. Screening uptake in a well-established diabetic retinopathy screening program: the role of geographical access and deprivation. *Diabetes Care* 2008; 31: 2131–2135.

14 Millett C, Dodhia H. Diabetes retinopathy screening: audit of equity in participation and selected outcomes in South East London. *J Med Screen* 2006; 13: 152–155.

15 Scanlon PH, Carter SC, Foy C, Husband RF, Abbas J, Bachmann MO. Diabetic retinopathy and socioeconomic deprivation in Gloucestershire. *J Med Screen* 2008; 15: 118–121.

16 Lindenmeyer A, Sturt JA, Hipwell A, Stratton IM, Al-Athamneh N, Gadsby R et al. Influence of primary care practices on patients’ uptake of diabetic retinopathy screening: a qualitative case study. *Br J Gen Pract* 2014; 64: e484–e492.

17 Sachdeva A, Stratton IM, Unwin J, Moreton R, Scanlon PH. Diabetic retinopathy screening: study to determine risk factors for non-attendance. *Diabetes & Primary Care* 2012; 14: 308–316.

18 Zoega GM, Gunnarsdottir T, Bjornsdottir S, Hreietharsson AB, Viggosson G, Stefansson E. Screening compliance and visual outcome in diabetes. *Acta Ophthalmol Scand* 2005; 83: 687–690.