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Research: Complications

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

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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.

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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.

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What's new?

- People in the 18–34 year age group are more likely to have a longer time interval between registration with the screening programme and attendance for screening.
- People with a longer time interval between registration and attendance for screening are at a greater risk of referable diabetic retinopathy being present at the time of first screen.

The current quality standard in the Four Nations programmes is the overall percentage uptake of the screening programme annually. There is no differentiation of those who have never been screened before or who have not attended for several years.

Patients and methods

Data for people referred to the eye screening programme and grading results at first screen were extracted from the screening programme databases. The retrospective analysis of anonymized data did not require ethical approval. Caldicott Guardian approval was given for use of the data in each of the screening programmes who contributed data.

Data for the Four Nations study were taken from seven diabetic retinopathy screening programmes: whole nation programmes in Wales, Scotland and Northern Ireland and four local English programmes (Brighton, Derbyshire, Leeds and Staffordshire). The inclusion criteria for this Four Nations data set have been reported in a previous publication [3]. The four English programmes were chosen to cover urban and rural areas, high and low levels of socio-economic deprivation and to include programmes with sizeable ethnic minority populations. One programme was from the North of England, two were from the Midlands and one from the South of England. We included programmes that were assessed as not having any problems with their grading at their most recent External Quality Assurance visit, had a population screening size of > 20 000 people with diabetes, and were willing to participate. We consider these programmes to encompass much of the heterogeneity seen in the English screening programme. For the present study, some programmes were excluded because of incomplete time data, as follows.

Recording the date of diagnosis of diabetes is not a mandated item in the English NHS diabetic eye screening programme data set. Hence, in the analysis of retinopathy levels vs. time from diagnosis to screening, data were included from the Scotland, Wales, Northern Ireland and two English programmes. One of the English programmes not included had no diagnosis date and the other had date of diagnosis for only 8% of the participants.

In the analysis, time to screening from registration, data were included from Scotland and three English programmes. Data were not included from Wales because they registered participants only when they were first screened, from the Northern Irish data set because it had had been running for a far shorter time than the other programmes, and from one English programme because the date when the patient was registered on the central collated list was not recorded in the database. National Institute for Health and Care Excellence (NICE) Type 1 and Type 2 guidelines [5,6] and the SIGN guideline [7] on diabetes both recommend that eye screening should be arranged at or around the time of diagnosis of diabetes from 12 years onwards.

In the English NHS Diabetic Eye Screening Programme all images are allocated a retinopathy (R) grade and a maculopathy (M) grade on the basis of the absence, presence and severity of features of diabetic retinopathy found during quality assured grading of the retinal images. The criteria used for grading and allocation of R and M levels are those required by the English NHS Diabetic Eye Screening Programme [8] and the relationship to the Early Treatment Diabetic Retinopathy Study (ETDRS) severity scale [9,10] are shown in Table 1. Referable diabetic retinopathy was defined in the English programmes by the presence of any of R2 (moderate to severe non-proliferative diabetic retinopathy), R3 (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 (R levels – R0, R1, R2 or R3) and Scottish retinopathy classification (R0, R1, R2 and R4)						
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 Rescreen in 12 months	R0 (No visible retinopathy)	No apparent retinopathy	10 14, 15	
R1: rescreen in 12 months	R1 (Background) Microaneurysm(s), retinal haemorrhage(s), any exudate, venous loop, cotton wool spot equivalent to Scottish	R1 (mild) Rescreen in 12 months	R1 (Background diabetic retinopathy – mild) Dot haemorrhages, microaneurysms, hard exudates, cotton wool spots, blot haemorrhages, superficial/ flame-shaped haemorrhages	Mild non-proliferative retinopathy	20–35	6.2%
R2: routine referral	R2 (Pre-proliferative) Venous beading, venous reduplication, intraretinal microvascular abnormality (IRMA), multiple blot haemorrhages	R2 (observable background) Rescreen in 6 months	R2 (Background diabetic retinopathy – observable) Four or more blot haemorrhages (i.e. AH standard photograph 2a) in one hemi-field only (inferior and superior hemi-fields delineated by a line passing through the centre of the fovea and optic disc)	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 Severe non-proliferative retinopathy	47 53	20.7% 44.2–54.8%
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 Refer to ophthalmology	R4 (Proliferative diabetic retinopathy) Active new vessels, vitreous haemorrhage	Proliferative retinopathy	≥ 61	Proliferative retinopathy has developed

Table 1 (*Continued*)

English maculopathy classification (M levels – M0, M1) and Scottish maculopathy classification (M levels – M0, M1, M2)			
English maculopathy grade and outcome	English screening programme maculopathy level	Scottish maculopathy grade and outcome	Scottish screening programme maculopathy levels
M0: rescreen in 12 months	M0 None of the features below	M0 Rescreen in 12 months	M0 (No maculopathy) No features 2 disc diameters from the centre of the fovea sufficient to qualify for M1 or M2 as defined below
M1: routine referral	M1 Circinate or group of exudates within the macula	M1 (Observable) Rescreen 6 months	M1 (Observable) Lesions as specified below within a radius of > 1 but < 2 disc diameters the centre of the fovea: any hard exudates
M1: routine referral	M1 Exudate within 1 disc diameter of the centre of the fovea	M2 (Referable) Refer ophthalmology	M2 (Referable) Lesions as specified below within a radius of 1 disc diameter of the centre of the fovea: • any blot haemorrhages • any hard exudates
M1: routine referral	M1 Any microaneurysm or haemorrhage within 1 disc diameter of the centre of the fovea only if associated with a best VA of ≤ 6/12 (if no stereo)		
M1: routine referral	M1 Retinal thickening within 1 disc diameter of the centre of the fovea (if stereo available)		

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

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	No retinopathy		Mild non-proliferative retinopathy in one eye		Mild non-proliferative retinopathy in both eyes		Referable retinopathy (not fast-track)*		Fast track referable retinopathy*		Ungradable†	
		n	% of graded image sets	*n*	% of graded image sets	*n*	% of graded image sets	*n*	% of graded image sets	*n*	% of graded image sets	*n*	% of all image sets
1989 and earlier	1,462	443	33.0	176	13.1	362	27.0	244	18.2	116	8.7	121	8.3
1990–1999	2,936	1,453	52.6	381	13.8	507	18.4	323	11.7	99	3.6	173	5.9
2000–2004	3,923	2,574	68.5	527	14.0	389	10.4	210	5.6	56	1.5	167	4.3
2005–2009	3,063	4,504	76.7	802	13.7	379	6.5	157	2.7	27	0.5	212	3.5
2010–2011	27,326	21,508	82.0	3,244	12.4	1,108	4.2	344	1.3	33	0.1	1,089	4.0

*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 $P < 0.0001$.

group and 11.6% (95% CI 11.5 to 11.8) in the 60 and above age group. 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 significantly 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 screened [parameter estimate –0.06 (–0.07 to –0.04)].

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

	Referable retinopathy Odds ratio and 95% CI	Urgent referral to ophthalmology 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	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	
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	
Female	0.82 (0.72–0.93)	

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].

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].

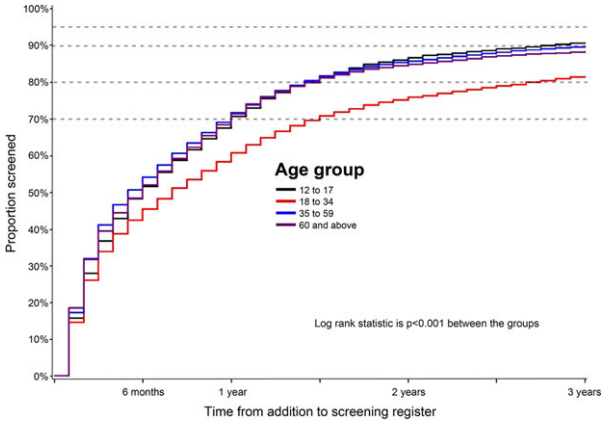

FIGURE 1 Kaplan–Meier curves of proportion screened since registration, by age at registration.

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

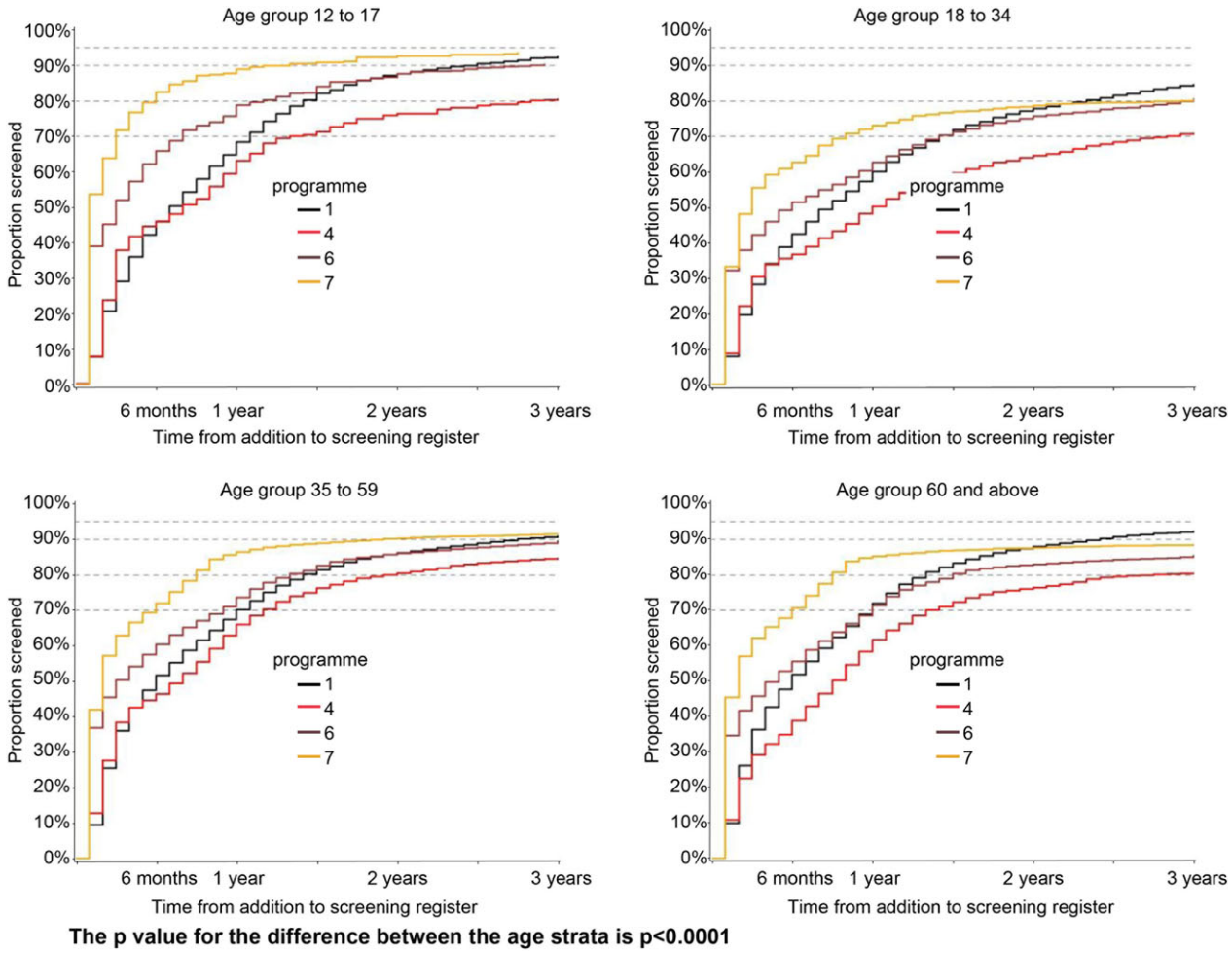

FIGURE 2 Comparison of uptake between screening programmes in different age groups.

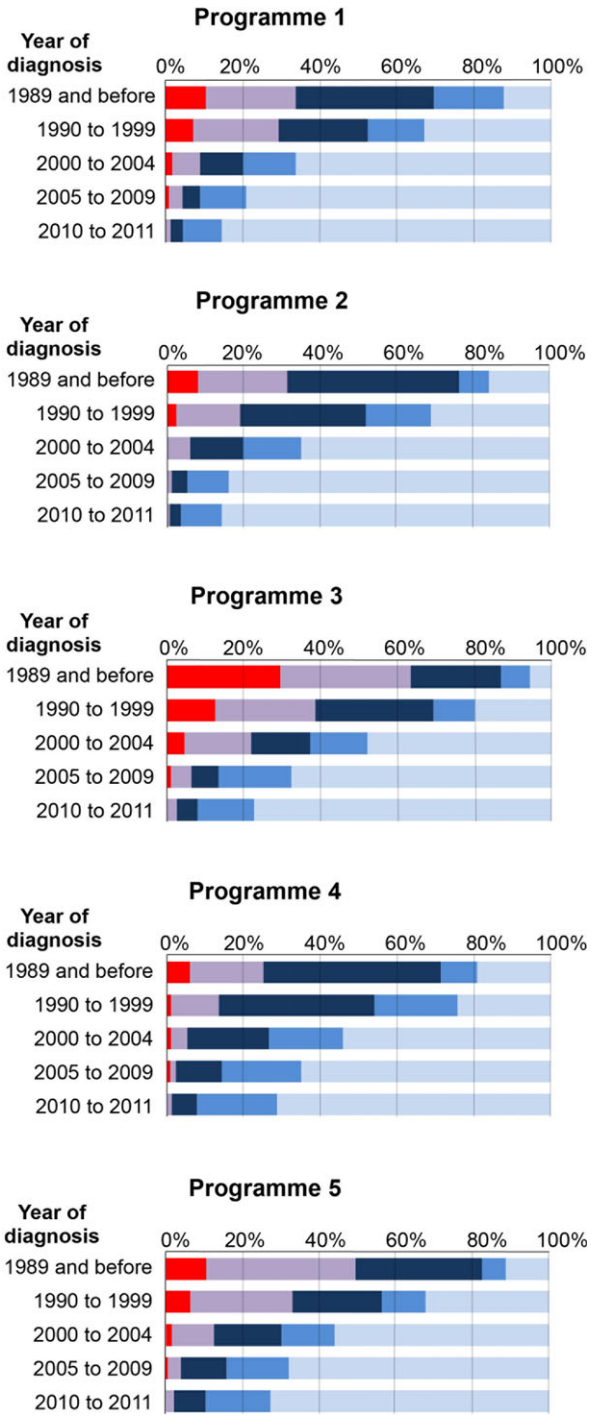

FIGURE 3 Results of first screening by date of diagnosis of diabetes, within each programme for those first screened in 2010 or 2011. DR, diabetic retinopathy; STDR, sight threatening diabetic retinopathy.

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.

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Competing interests

None declared.

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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.

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