Received: 28 November 2020 | Accepted: 22 March 2021

DOI: 10.1111/dme.14583

DIABETIC Medicine

RESEARCH: COMPLICATIONS

Incidence of sight-threatening diabetic retinopathy in an established urban screening programme: An 11-year cohort study

Christopher P. Cheyne[1] | **Philip I. Burgess**[2,3] | **Deborah M. Broadbent**[2,3] | **Marta García-Fiñana**[1] | **Irene M Stratton**[4] | **Ticiana Criddle**[2] | **Amu Wang**[2] | **Ayesh Alshukri**[2] | **Mehrdad M. Rahni**[2] | **Pilar Vazquez-Arango**[2] | **Jiten P. Vora**[5] | **Simon P. Harding**[2,3] | **ISDR Study Group**

[1]Department of Health Data Science, University of Liverpool, Member of Liverpool Health Partners, Liverpool, UK

[2]Department of Eye and Vision Science, Institute of Life Course and Medical Sciences, University of Liverpool, Member of Liverpool Health Partners, Liverpool, UK

[3]St Paul's Eye Unit, Liverpool University Hospitals NHS Foundation Trust, Member of Liverpool Health Partners, Liverpool, UK

[4]Gloucestershire Retinal Research Group, Cheltenham General Hospital, Cheltenham, UK

[5]Department of Diabetes and Endocrinology, Royal Liverpool University Hospital, Liverpool, UK

Correspondence
Philip I. Burgess, Department of Eye and Vision Science, William Henry Duncan Building, 6 West Derby St., Liverpool L69 3TX, UK.
Email: p.burgess@liverpool.ac.uk

Funding information
This study was funded by the UK National Institute for Health Research (NIHR) (Programme Grants for Applied Research [RP-PG-1210-12016]). The views expressed are those of the authors, not necessarily those of the NIHR or the Department of Health and Social Care. The funder had no role in study design, data collection, data analysis, data

Abstract

Aims: Systematic annual screening to detect sight-threatening diabetic retinopathy (STDR) is established in the United Kingdom. We designed an observational cohort study to provide up-to-date data for policy makers and clinical researchers on incidence of key screening endpoints in people with diabetes attending one screening programme running for over 30 years.

Methods: All people with diabetes aged ≥12 years registered with general practices in the Liverpool health district were offered inclusion. Data sources comprised: primary care (demographics, systemic risk factors), Liverpool Diabetes Eye Screening Programme (retinopathy grading), Hospital Eye Services (slit lamp biomicroscopy assessment of screen positives).

Results: 133,366 screening episodes occurred in 28,384 people over 11 years. Overall incidences were: screen positive 6.7% (95% CI 6.5–6.8), screen positive for retinopathy 3.1% (3.0–3.1), unassessable images 2.6% (2.5–2.7), other significant eye diseases 1.0% (1.0–1.1). 1.6% (1.6–1.7) had sight-threatening retinopathy confirmed by slit lamp biomicroscopy. The annual incidence of screen positive and screen positive for retinopathy showed consistent declines from 8.8%–10.6% and 4.4%–4.6% in 2007/09 to 4.4%–6.8% and 2.3%–2.9% in 2013/17, respectively. Rates of STDR (true positive) were consistently below 2% after 2008/09. Screen positive rates were higher in first time attenders (9.9% [9.4–10.2] vs. 6.1% [6.0–6.2]) in part due to ungradeable images (4.1% vs. 2.3%) and other eye disease (2.4% vs. 0.8%). 4.5% (3.9–5.2) of previous non-attenders had sight-threatening retinopathy. Compared with people with type 2 diabetes, those with type 1 disease demonstrated higher rates of screen positive (11.9% vs. 6.0%) and STDR (6.4% vs. 1.2%). Overall prevalence of any retinopathy was 27.2% (27.0–27.4).

Conclusions: In an established screening programme with a stable population screen, positive rates show a consistent fall over time to a low level. Of those who are screen

interpretation, or writing of the report. The corresponding author had full access to all data in the study and has final responsibility for the decision to submit.

positive, fewer than 50% are screen positive for diabetic retinopathy. Most are due to sight threatening maculopathy. The annual incidence of STDR is under 2% suggesting future work on redefining screen positive and supporting extended intervals for people at low risk. Higher rates of screen positive and STDR are seen in first time attenders. Those who have never attended for screening should be specifically targeted.

KEYWORDS

incidence, prevalence, screen positive, screening, sight-threatening diabetic retinopathy

1 | INTRODUCTION

By 2045, an estimated 693 million people (9.9% of the global adult population) will have diabetes[1] with around 10% having sight-threatening diabetic retinopathy (STDR, DR).[2] Early detection and treatment of STDR is key to avoiding visual impairment in people living with diabetes (PWD).[3-6] Laser photocoagulation remains the mainstay of treatment for proliferative disease, while intravitreal therapies are indicated in most patients requiring treatment for maculopathy. Systematic annual screening to detect STDR is established in several countries including the United Kingdom and has greatly improved the detection of treatable disease.

Landmark epidemiological studies on DR are around 30 years old,[7,8] and while providing important underpinning, data on incidence and progression are not directly applicable to screening programmes. As programmes become established, people with longstanding disease are detected reducing the prevlance in DR in the screening population. Data from screening programmes are limited and reporting is variable.[9-11] Screening populations are stable and provide large cohorts for longitudinal epidemiological studies and for interventional clinical studies of early disease, but their characteristics are changing as systematic screening becomes established and evolves. True positive cases are retained under hospital eye services (HES). Disease management has changed including improved glucose and blood pressure (BP) control, less smoking and longer life expectancy.

We conducted an observational cohort study of people attending during an 11-year period for DR screening in one established urban programme in England. Our study was conducted within the Individualised Screening for Diabetic Retinopathy (ISDR) programme of applied research in DR screening[12,13] (www.isdrproject.co.uk). Here, we present data on incidence of all key stages in the screening pathway, screen positive, screen positive due to DR and STDR. We aimed to provide up-to-date data to inform screening programmes, policy makers and clinical services and to support future clinical research in early retinopathy. We also investigated retrospective data collected since the beginning of screening in Liverpool to gain additional insights into long-term changes in incidence.

Novelty statement

- In an established urban diabetic retinopathy (DR) screening programme in England, screen positive rates show a consistent fall over time to a low level.
- The annual incidence of sight-threatening diabetic retinopathy (STDR) is low at under 2%. New proliferative disease is rare. The majority of referrals from screening programmes are not due to DR.
- Higher rates of screen positive and STDR occur in first time attenders, in particular previous non-attenders, and in type 1 disease who should be targeted.
- Once a steady state has been reached, screening programmes should consider revising referral thresholds and extending intervals for low-risk individuals.

Precis

- *What is already known about this topic?* Prevalence of diabetes is increasing worldwide against a background of inadequate and overstretched resources. Screening detects DR at a stage at which vision loss can be prevented; it is effective and cost-effective in high-income settings. Current programmes are designed to address incidence and prevalence based on 30-year-old data
- *What is the key question?* What is the incidence of DR, types of STDR and a screen positive result in an established screening programme? Can high risk groups be identified?
- *What are the new findings?* In an urban DR screening programme established for 30 years with a stable population, rates of screen positive and screen positive due to DR show a consistent fall over time to a low level. We report a consistently low annual incidence of STDR at under 2%. New proliferative disease is rare. Most referrals to the hospital eye service are for non-DR-related findings. Higher rates of screen positive and STDR are seen in first time attenders; previous non-attenders are at particular risk. Reporting of outcomes in the literature is highly variable.

- *How might this impact on clinical practice in the foreseeable future?* Low rates of STDR suggest that the purpose of screening should be reassessed once a steady state has been reached with changes in the referral threshold and extended intervals for people at low risk. People newly added to a programme, in particular those with a history of previous non-attendance, should be specifically targeted.

2 | MATERIALS AND METHODS

2.1 | Setting: Liverpool Diabetes Eye Screening Programme

The Liverpool Diabetes Eye Screening Programme (LDESP) was established in 1991, reaching full coverage by 2003 around the time of the introduction of the English National Diabetic Eye Screening Programme (NDESP). LDESP is one of 61 providers in the NDESP. The data domains held within the LDESP are shown in Figure 1 and apply to all English screening programmes. All PWD aged ≥12 years registered with a Liverpool general practice (GP; primary care) are considered eligible for routine screening apart from the following categories: moved out of area; seen by another programme; blind (no perception of light in both eyes). Of those individuals who are eligible, two groups are excluded: opted out of screening; medically unfit. Individuals are suspended from routine screening if they are attending the HES for any of the following: management of active diabetic eye disease; slit lamp biomicroscopy (SLB) due to ungradeable photographs; digital surveillance (monitoring of DR more frequently than annually by retinal photography in a dedicated surveillance clinic). The remaining people undergo active screening in the community by a qualified retinal screener at one of six primary care facilities across the city.

Screening in the NDESP involves technician-based digital photography through dilated pupils with at least two 45° colour photographs and manual grading using the grading schema shown in Table S1. Screen positive is defined as moderate pre-proliferative retinopathy (R2 in the NDESP scheme) and above; and/or maculopathy (grade M1); and/or other significant eye disease; or ungradeable images.[14] Screen positive individuals undergo clinical examination by an ophthalmologist trained in medical retina in dedicated HES-based clinics. For the purposes of our analysis, this examination defines 'true positive' for STDR defined as follows: moderate/severe pre-proliferative DR or proliferative DR (sight threatening retinopathy, STR) and/or sight threatening maculopathy (STM), i.e., any of the following features: multiple blot haemorrhages, venous beading, intraretinal microvascular abnormalities, new vessels, preretinal/vitreous haemorrhage, fibrovascular proliferation, exudates within 1 disc diameter (1500 μm) of the foveal centre, group of exudates within the macula more than 0.5 disc area in size, retinal thickening within 1 disc diameter of the foveal centre, haemorrhages/microaneurysms with reduced vision.

2.2 | ISDR cohort study participants

All PWD registered with the LDESP covering a single urban health district in the north west of England were offered

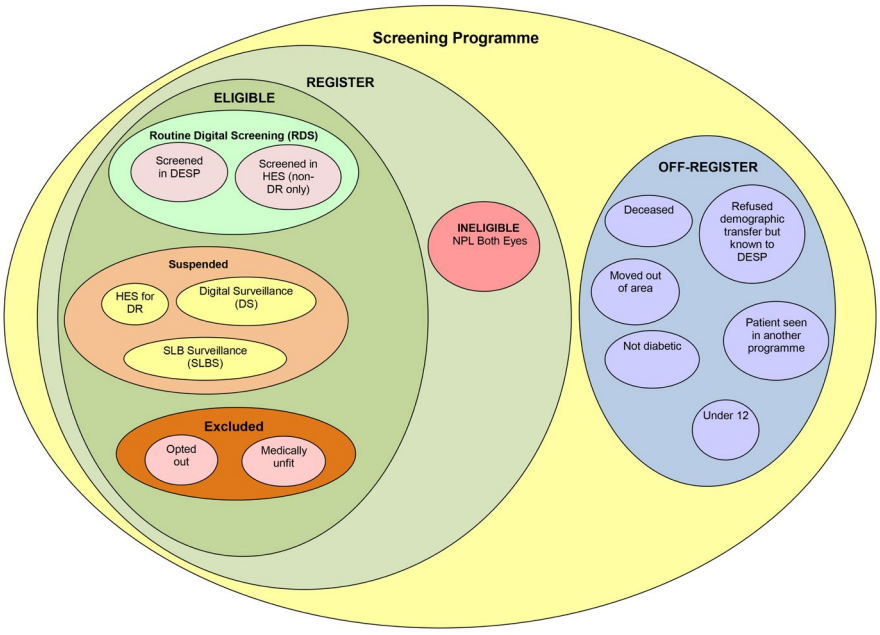

FIGURE 1 Diabetic eye screening cohort management in England and Wales. Source: https://www.gov.uk/government/publications/diabetic-eye-screening-cohort-management-overview/diabetic-eye-screening-cohort-management Accessed 27 January 2020

inclusion in the ISDR programme. The patient cohort was established in a recruitment process approved by the Preston North West NHS Ethics Committee (13/NW/0196) and the Royal Liverpool and Broadgreen University Hospitals NHS Trust (RLBUHT) governance teams. GPs in Liverpool were invited to participate commencing in June 2013 and continued until 2016 when all had agreed to participate. Recruitment occurred for all PWD in each practice. Newly diagnosed PWD and those PWD moving into area were added via the LDESP throughout the study. Consent was through an 'opt-out'. An invitation letter, information booklet and an opt-out form were sent to eligible participants. The dataset comprised data acquired both prospectively from June 2013 to September 2017 and retrospectively for PWD who did not opt out from April 2006 to 2013. This latter data exhibited a censoring effect: governance rules removed data from PWD who had died prior to a practice joining the study and who therefore had no opportunity to opt out.

2.3 | Data sources and analysis

Data on PWD in the UK NHS are collected in primary care, within screening programmes and in secondary care. A purpose-built real-time dynamic data warehouse was developed to store data from these three previously unlinked sources: (i) primary care electronic records (demographic and systemic variables; EMIS Web, EMIS Health, Leeds, UK), (ii) LDESP (DR photographic grading from both eyes; 'Orion' database (Digital HealthCare, Cambridge UK) before 2013 and 'OptoMize' database (Digital Health Care, then EMIS Health) from 2013), (iii) HES (SLB retinopathy grading at screen-positive assessment clinics at the RLBUHT; 'Diabolos' [a bespoke MS Access database] before 2016 and 'Patient Electronic Notes System' [a bespoke graphical user interface application] from 2016). Source data were validated against standard ranges.

This analysis incudes only individuals attending for DR screening in the community and their first follow-up in the HES. Collection of data on people attending the HES for management of active diabetic eye disease, SLB screening due to ungradeable photographs or hospital-based digital surveillance of DR was not possible; therefore, we are unable to report whole population data. For the purpose of analysis, the values of the time-dependent clinical variables closest to the time of the screen episodes (i.e., annual screening episodes) within a time window of 1 year prior to 1 week after the screening episode were used. For positive screen events, data from the first SLB recorded within 1 year of the positive screen event were used to provide the final outcome for that event. The first recorded screening attendance was defined as the first recorded screening attendance where there were no earlier recorded screening attendances or SLB records for that individual. Any other recorded attended screening appointment was defined as any screening appointment where there had been at least one earlier attended screening appointment or SLB.

Two thousand two hundred sixty-five participants from the cohort study were recruited to an RCT within the ISDR programme and allocated to individualised interval screening.[12] For those allocated to 24-month intervals (who under normal circumstances would have been screened annually) data on annual incidence were adjusted (with an assumed attendance proportion of 0.85): 2015/16 226 individuals (266 * 0.85), 2016/17 1232 individuals (1449*0.85). Of these, 2.7% were assumed to have type 1 diabetes and 89.9% type 2 diabetes. All were assumed to be screen negative at the first appointment (which under normal circumstances would have occurred 12 months before the allocated appointment at 24 months). Additionally, 96.2% were assumed to be R0R0 and 3.8% to be R1R0.

3 | RESULTS

3.1 | Dataset

The analysis dataset was extracted from the ISDR data warehouse on 25 September 2017. The size of the dataset varied throughout the 11 years studied with year-end effects and variation due to sampling time. Figure 2 shows the distribution of data in the ISDR cohort study. Of 30,771 invited to participate up to this time point, 2191 (7.1%) opted out and 196 had no LDES or HES data leaving data on 28,384 PWD available for analysis. Table S2 shows the numbers of people on the LDESP register categorised by inclusion in the ISDR study and attendance at 1 or more screening appointments in a screening year.

3.2 | Censoring effect

The number of individuals with at least one screening appointment recorded in our dataset increased each year between 2006/07 and 2014/15. Between 2006/07 and 2016/17, the median age increased from 60.3 to 64.5 years and the median disease duration from 2.3 to 7.0 years. In order to assess whether censoring altered our estimates of retinopathy, we examined rates of STDR during the time period with the most complete data: 2013/14 to 2016/2017. Of 28,580 individuals in the ISDR cohort, 2538 (8.9%) died. Rates of STDR were calculated from the last attended appointment. In individuals in whom STDR status was not missing, there was no significant difference in STDR rates between subjects who died and those who did not: 164/2311 (7.1%; 95% CI 6.1–8.2) vs. 1571/23,331 (6.7%; 6.3–7.0). We also performed exploratory modelling to investigate the effect of death in subjects pre-2013 (data not shown). Together, our analyses indicate that death appears to have had little or no confounding effect on estimated rates of STDR prior to 2013/2016.

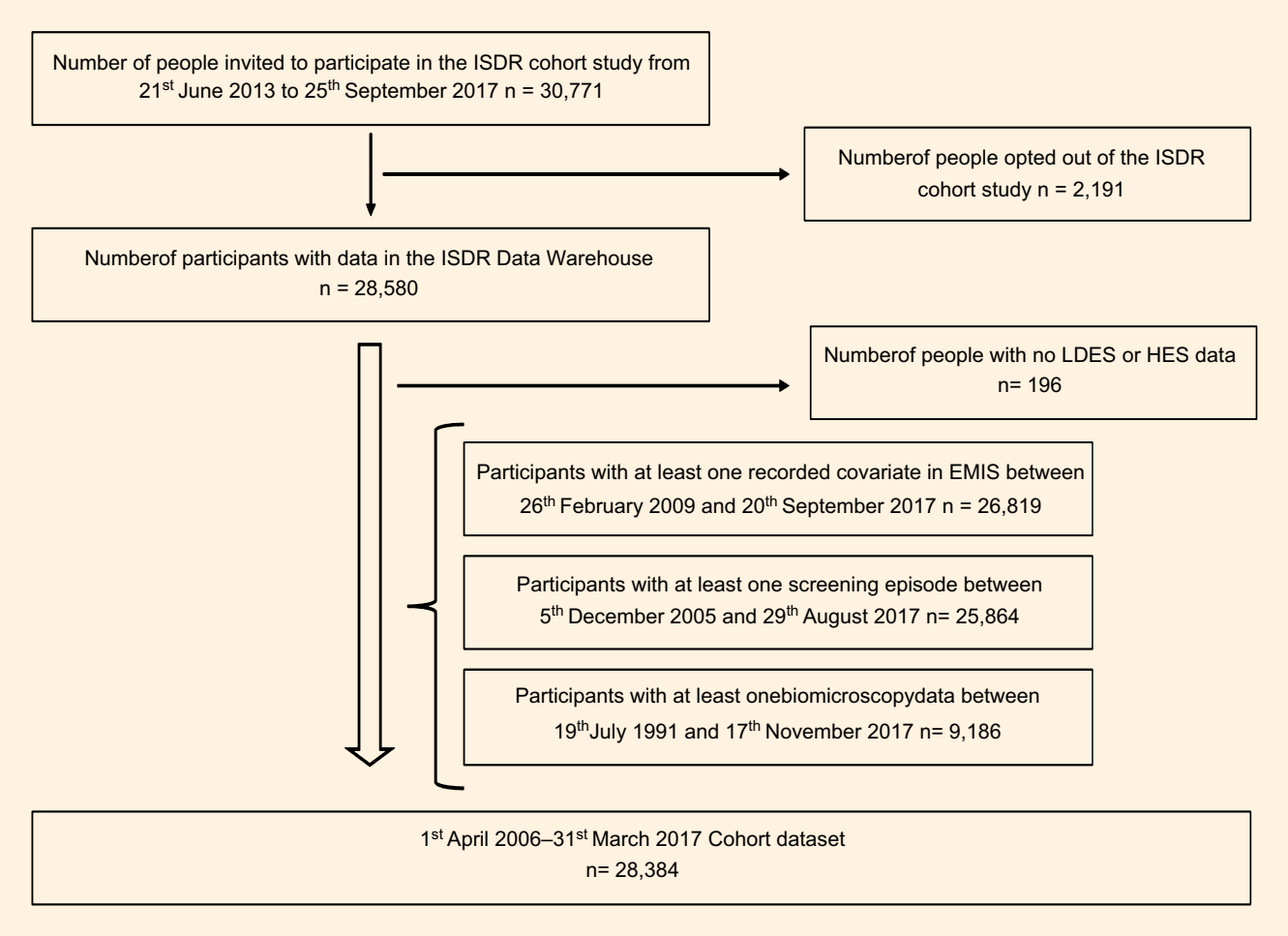

FIGURE 2 Data flows in the Individualised Screening for Diabetic Retinopathy cohort study with numbers from an illustrative time point of 25 September 2017

3.3 | Demographics

Overall demographics of the 11-year cohort are shown in Table 1. Gender proportions were relatively stable across all screening years (55%–58% male, 40%–43% female, 1%–3% unknown). The proportion of individuals with type 1 diabetes decreased over time from 6.7% to 4.7%, while the proportion with type 2 diabetes increased from 76.1% to 81.6%. The proportion with unknown diabetes type decreased proportionally from 17.2% to 13.7%. The median HbA1c was stable across all years (median: 50–52 mmol/mol; 6.7%–6.9%) although there was a high proportion of missing data prior to 2012/13.

3.4 | Incidence

Annual incidences of screen positive, STDR, STR and STM are shown in Table 2; 28,384 PWD attended at least one screening episode over the 11 years (total 133,366 screening episodes included). 6.7% (8906/133,366) were screen positive, 3.1% (4073/133366; 45.7% of screen positives) were screen positive for DR, 2.6% (3444/133,366; 38.7% of screen positives) due to ungradeable images and 1.0% (1389/133,366; 15.6% of screen positives) due to other significant eye disease. The proportion of subjects with no DR recorded (prevalence) was 72.8% (96,437/132,544 [excludes 822 unknown]) and with any DR in one or both eyes was 27.2% (36,107/132,544). Within the screen negative episodes retinopathy was identified in one eye only in 15.4% (19,726/128,471) and in both eyes in 9.6% (12,308/128,471).

In 7803 screen positive episodes, individuals attended the HES and were examined by a medical retina specialist. 28.2% (2193/7777 with known STDR status) had STDR (true positive) of whom 35.8% (781/2179 with known STR/STM status) had STR and 82.7% (1802/2179) had STM. STDR was detected in 1.6% (2193/133,366) of all screen episodes, STR in 0.6% (781/133,366) and STM in 1.4% (1802/133,366). Of the people referred as screen positive for DR, 53.8% (2193/4073) had STDR. The proportion of subjects who were screen positive but did not have a recorded SLB in the dataset was 0.8% (1103/133,366). Reasons for this include legitimate events (failure to attend two consecutive appointments;

TABLE 1 Demographics of people with diabetes attending at least one retinopathy screening episode in each screening year (1 April–31 March) in Liverpool between 2006 and 2017

	Screening year										
	2006/07	**2007/08**	**2008/09**	**2009/10**	**2010/11**	**2011/12**	**2012/13**	**2013/14**	**2014/15**	**2015/16**	**2016/17**
n	6637	8088	8664	10,266	11,214	13,124	13,518	15,115	15,518	14,995	14,769
Gender, *n* (%)											
Male	3647 (54.9)	4508 (55.7)	4804 (55.4)	5740 (55.9)	6367 (56.8)	7444 (56.7)	7713 (57.1)	8660 (57.3)	8932 (57.6)	8529 (56.9)	8174 (55.3)
Female	2823 (42.5)	3367 (41.6)	3670 (42.4)	4287 (41.8)	4603 (41.0)	5406 (41.2)	5533 (40.9)	6265 (41.4)	6469 (41.7)	6152 (41.0)	5973 (40.4)
Unknown	167 (2.5)	213 (2.6)	190 (2.2)	239 (2.3)	244 (2.2)	274 (2.1)	272 (2.0)	190 (1.3)	117 (0.8)	314 (2.1)	622 (4.2)
Diabetes type, *n* (%)											
Type 1	441 (6.7)	537 (6.6)	536 (6.2)	576 (5.6)	579 (5.2)	687 (5.2)	684 (5.1)	754 (5.0)	783 (5.0)	725 (4.8)	699 (4.7)
Type 2	5053 (76.1)	6241 (77.2)	6784 (78.3)	8194 (79.8)	9081 (81.0)	10,645 (81.1)	11,078 (81.9)	12,486 (82.6)	12,944 (83.4)	12,392 (82.6)	12,053 (81.6)
Unknown	1143 (17.2)	1310 (16.2)	1344 (15.5)	1496 (14.6)	1554 (13.9)	1792 (13.7)	1756 (13.0)	1875 (12.4)	1791 (11.5)	1878 (12.5)	2017 (13.7)
Ethnicity[a], *n* (%)											
White	5327 (80.3)	6456 (79.8)	6920 (79.9)	8094 (78.8)	8729 (77.8)	9940 (75.7)	10,156 (75.1)	11,258 (74.5)	11,457 (73.8)	10,770 (71.8)	10,180 (68.9)
Asian	158 (2.4)	183 (2.3)	224 (2.6)	256 (2.5)	271 (2.4)	353 (2.7)	369 (2.7)	428 (2.8)	460 (3.0)	436 (2.9)	452 (3.1)
Black	105 (1.6)	116 (1.4)	139 (1.6)	175 (1.7)	197 (1.8)	243 (1.9)	253 (1.9)	293 (1.9)	284 (1.8)	304 (2.0)	308 (2.1)
Chinese	57 (0.9)	75 (0.9)	85 (1.0)	79 (0.8)	85 (0.8)	108 (0.8)	121 (0.9)	125 (0.8)	144 (0.9)	149 (1.0)	159 (1.1)
Other	88 (1.3)	103 (1.3)	108 (1.2)	127 (1.2)	135 (1.2)	169 (1.3)	166 (1.2)	201 (1.3)	209 (1.3)	200 (1.3)	198 (1.3)
Unknown	902 (13.6)	1155 (14.3)	1188 (13.7)	1535 (15.0)	1797 (16.0)	2311 (17.6)	2453 (18.1)	2810 (18.6)	2964 (19.1)	3136 (20.9)	3472 (23.5)
Age (years)											
Observed, *n*	6470	7875	8474	10,027	10,970	12,850	13,246	14,925	15,401	14,681	14,147
Unknown, *n*	167	213	190	239	244	274	272	190	117	314	622
Median	60.3	61.0	61.5	62.3	62.6	62.9	63.3	63.9	64.2	64.5	64.5
IQR	51.2–68.7	51.9–69.4	52.4–70.1	53.1–70.6	53.4–71.1	53.6–71.5	54.0–72.1	54.4–72.6	54.6–73.0	55.0–73.1	55.1–73.4
Range	12.0–92.1	12.0–93.4	12.1–94.4	12.1–94.5	9.9–96.5	11.9–98.1	12.0–97.7	12.1–98.7	12.2–112.9	13.3–113.6	13.7–114.6
Disease duration (years)											
Observed, *n*	6637	8088	8664	10,266	11,214	13,124	13,518	15,115	15,518	14,995	14,769
Unknown, *n*	0	0	0	0	0	0	0	0	0	0	0
Median	2.3	2.6	2.9	3.5	4.2	4.9	5.5	6.1	6.4	6.7	7.0
IQR	0.2–5.6	1.1–6.1	1.7–6.5	2.1–6.9	2.1–7.2	2.2–7.7	2.6–8.2	3.1–8.9	3.3–9.4	3.4–9.9	3.1–10.5
Range	0.0–53.7	0.0–54.7	0.0–55.4	0.0–56.6	0.0–57.7	0.0–55.2	0.0–59.3	0.0–60.4	0.0–61.6	0.0–62.6	0.0–63.7

(Continues)

TABLE 1 (Continued)

	Screening year										
	2006/07	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17
HbA1c (mmol/mol)											
Observed, *n*	0	0	123	6216	8495	11,188	11,972	13,869	14,607	13,948	13,450
Unknown, *n*	6637	8088	8541	4050	2719	1936	1546	1246	911	1047	1319
Median	—	—	50	50	51	51	52	51	51	51	52
IQR	—	—	43–60	44–60	45–61	45–61	45–62	44–61	44–61	45–62	46–62
Range	—	—	33–117	23–157	21–160	24–172	22–168	22–166	22–174	20–156	22–140

[a]Recording of ethnicity is not mandatory in primary care in England and Wales. The method of recording ethnicity in primary care changed during the study with a revision to the categories and a more ethical approach to questioning. Our experience of the effect of this change is that fewer people were prepared to give their ethnicity.

death; moved out of area) as well as missing data which could not be recovered.

There was some variation across the years of rates of screen positive with an overall reduction over the 11 years from 8.8%–10.6% in 2007/09 to 4.4%–6.8% in 2013/17. The annual incidence of screen positive due to DR also decreased over the 11 years from 4.4%–4.6% in 2007/09 to 2.3%–2.9% in 2013/17. In contrast rates of screen positive for ungradeable images were stable, fluctuating around 2%–3%, similarly other eye disease was stable at around 1%. Rates of STDR (true positive; examined by a medical retina specialist using SLB) were relatively stable between 1.3% and 2.2%. STR at 0.4%–0.9% and STM at 1.1%–1.8% were also stable. Figure 3 illustrates these trends over time. Out of those with a known retinopathy level, the proportion of subjects with no DR rose steadily from 61.8% in 2006/07 to 79.4% in 2016/17.

3.5 | First time attenders

Tables 3 and 4 show the annual incidences of screen positive, STDR, STR and STM for individuals attending their first recorded screening appointment and for those attending a screening appointment which was not their first recorded screening episode, respectively. Data are displayed from screening year 2007/08 to allow for at least a full year of data collection prior to a first recorded screening event. Compared to people already attending screening, rates in first time attenders for screen positive were ×1.6 higher (9.9% vs. 6.1%) and for STDR ×1.4 higher (2.2 vs. 1.6). Much of this screen positive effect appears to be due to unassessable images (×1.8, 4.1% vs. 2.3%) and other eye disease (×3.0, 2.4% vs. 0.8%). Figures S1 and S2 show a graphical representation of the annual incidences of screen positive, screen positive for DR, STDR and STR in these two groups.

People living with diabetes attending for DR screening for the first time are a heterogeneous group comprising people newly diagnosed with diabetes and those with existing diabetes who were previous non-attenders. We investigated the annual incidences of screen positive, STDR, STR and STM for individuals attending their first recorded screening appointment where disease duration was ≤1 year (i.e., newly diagnosed) and where disease duration was greater than 1 year (Tables S3 and S4). The overall screen positive rate across all study years in the newly diagnosed group and those with diabetes >1 year was 8.4% (8.0–8.9, 95% CI) and 14.3% (13.2–15.4), respectively. Both figures are higher than the rate in people who had already attended at least one screening appointment: 6.1% (6.0–6.2). Similar but stronger effects were seen for rates of screen positive for DR (newly diagnosed diabetes 2.2% [2.0–2.5]; diabetes duration >1 year attending a first recorded screening event 7.1 [6.3–7.9]; at least one

TABLE 2 Annual incidences of screen positive, sight-threatening diabetic retinopathy (STDR), sight threatening retinopathy (STR) and sight threatening maculopathy (STM) for people with diabetes who attended at least one screening episode in each screening year (1 April–31 March) between 2006 and 2017

	Screening year				
	2006/07	**2007/08**	**2008/09**	**2009/10**	**2010/11**
Individuals who attended at least one screening appointment (*n* [%])	6637 [100.0]	8088 [100.0]	8664 [100.0]	10,266 [100.0]	11,214 [100.0]
Overall screen positive	527 [7.9]	714 [8.8]	922 [10.6]	854 [8.3]	695 [6.2]
Screen positive for DR	271 [4.1]	355 [4.4]	401 [4.6]	360 [3.5]	327 [2.9]
Screen positive for unassessable images	201 [3.0]	255 [3.2]	358 [4.1]	372 [3.6]	283 [2.5]
Screen positive for other eye disease	55 [0.8]	104 [1.3]	163 [1.9]	122 [1.2]	85 [0.8]
Biomicroscopy recorded[a]	446 [6.7]	618 [7.6]	794 [9.2]	712 [6.9]	612 [5.5]
STDR	116 [1.7]	145 [1.8]	192 [2.2]	178 [1.7]	160 [1.4]
STR	41 [0.6]	44 [0.5]	81 [0.9]	65 [0.6]	56 [0.5]
STM	91 [1.4]	119 [1.5]	157 [1.8]	135 [1.3]	130 [1.2]
STR & STM unknown	0 [0.0]	0 [0.0]	2 [<0.1]	2 [<0.1]	4 [<0.1]
Not STDR	330 [5.0]	473 [5.8]	602 [6.9]	534 [5.2]	452 [4.0]
Unknown STDR status	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
No biomicroscopy recorded[a]	81 [1.2]	96 [1.2]	128 [1.5]	142 [1.4]	83 [0.7]
Screen negative	6110 [92.1]	7374 [91.2]	7742 [89.4]	9412 [91.7]	10519 [93.8]
Retinopathy level					
Screen negative DR					
R0R0	3978 [59.9]	4901 [60.6]	5440 [62.8]	6536 [63.7]	7805 [69.6]
R1R0	1205 [18.2]	1536 [19.0]	1545 [17.8]	1906 [18.6]	1646 [14.7]
R1R1	947 [14.3]	994 [12.3]	879 [10.1]	1065 [10.4]	1124 [10.0]
One assessable eye (R0)	166 [2.5]	168 [2.1]	186 [2.1]	167 [1.6]	143 [1.3]
One assessable eye (R1)	54 [0.8]	52 [0.6]	57 [0.7]	64 [0.6]	64 [0.6]
Unknown	6 [0.2]	82 [1.0]	156 [1.8]	168 [1.6]	105 [0.9]
Screen positive DR					
R2 or M1	256 [3.9]	344 [4.3]	375 [4.3]	339 [3.3]	309 [2.8]
R3	15 [0.2]	11 [0.1]	26 [0.3]	21 [0.2]	18 [0.2]

Note: Denominator for a given year is the total number of individuals who attended at least one screening appointment during that year. For example, for screening year 2012–13, the denominator is 13,518, and the annual incidence of overall screen positive is 5.7% (774/13,518). STM and STR are not mutually exclusive categories. 95% CI are based on the Wilson score method.

Abbreviation: DR, diabetic retinopathy.

[a]Biomicroscopy recorded within 1 year of screening appointment when positive screen result occurred.

[b]Adjusted for subjects recruited to the ISDR RCT and assigned to 24-month screening intervals.

previous screening event 2.9% [2.8–3.0]) and true positive STDR (1.4% [1.2–1.6], 4.5% [3.9–5.2], 1.6% [1.5–1.6]).

3.6 | Type 1 and type 2 diabetes

Tables S5 and S6 show the annual incidences by diabetes type of screen positive, STDR, STR and STM for individuals with known type of diabetes. Rates of both screen positive (11.9% vs. 6.0%) and screen positive due to DR (10.7% vs. 2.3%) were higher in people with type 1 diabetes. Rates of STDR were much higher (6.4% vs. 1.2%) in type 1 diabetes; a higher proportion of STDR was due to STR (47% vs. 33%) in these individuals. Both unassessable images (0.8% vs. 2.7%) and other eye disease (0.4% vs. 1.1%) were lower in type 1 diabetes. Across the 11 years of the study, there was a fall in screen positive, screen positive for DR and STDR in both type 1 and type 2 diabetes consistent with overall rates.

4 | DISCUSSION

In this observational cohort study of people with diabetes attending an established retinopathy screening programme, we

2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	Overall *n* [%; 95% CI]
13,124 [100.0]	13,518 [100.0]	15,115 [100.0]	15,518 [100.0]	15,221[b] [100.0]	16,001[b] [100.0]	133,366 [100.0]
921 [7.0]	774 [5.7]	669 [4.4]	805 [5.2]	1031 [6.8]	994 [6.2]	8906 [6.7; 6.5–6.8]
419 [3.2]	330 [2.4]	345 [2.3]	387 [2.5]	441 [2.9]	437 [2.7]	4073 [3.1; 3.0–3.1]
425 [3.2]	322 [2.4]	179 [1.2]	258 [1.7]	408 [2.7]	383 [2.4]	3444 [2.6; 2.5–2.7]
77 [0.6]	122 [0.9]	145 [1.0]	160 [1.0]	182 [1.2]	174 [1.1]	1389 [1.0; 1.0–1.1]
774 [5.9]	650 [4.8]	621 [4.1]	742 [4.8]	965 [6.3]	869 [5.4]	7803 [5.9; 5.7–6.0]
223 [1.7]	179 [1.3]	212 [1.4]	246 [1.6]	251 [1.6]	291 [1.8]	2193 [1.6; 1.6–1.7]
75 [0.6]	57 [0.4]	69 [0.5]	98 [0.6]	85 [0.6]	110 [0.7]	781 [0.6; 0.5–0.6]
197 [1.5]	149 [1.1]	79 [1.2]	191 [1.2]	216 [1.4]	238 [1.5]	1802 [1.4; 1.3–1.4]
0 [0.0]	4 [<0.1]	1 [<0.1]	1 [<0.1]	0 [0.0]	0 [0.0]	14 [<0.1; 0.0–0.0]
551 [4.2]	471 [3.5]	406 [2.7]	496 [3.2]	714 [4.7]	555 [3.5]	5584 [4.2; 4.1–4.3]
0 [0.0]	0 [0.0]	3 [<0.1]	0 [0.0]	0 [0.0]	23 [0.1]	26 [<0.1; 0.0–0.0]
147 [1.1]	124 [0.9]	48 [0.3]	63 [0.4]	66 [0.4]	125 [0.8]	1103 [0.8; 0.8–0.9]
12203 [93.0]	12744 [94.3]	14446 [95.6]	14713 [94.8]	14190 [93.2]	15007 [93.8]	124460 [93.3; 93.2–93.5]
9093 [69.3]	9547 [70.6]	11,030 [73.0]	11,658 [75.1]	11,506 [75.6][b]	12,407 [77.5][b]	93901 [70.4; 70.2–70.7]
1938 [14.8]	2032 [15.0]	1971 [13.0]	1845 [11.9]	1799 [11.8][b]	1631 [10.2][b]	19,054 [14.3; 14.1–14.5]
1205 [9.2]	1239 [9.2]	1509 [10.0]	1289 [8.3]	993 [6.5]	1064 [6.6]	12,308 [9.2; 9.1–9.4]
228 [1.7]	210 [1.6]	211 [1.4]	277 [1.8]	392 [2.6]	388 [2.4]	2536 [1.9; 1.8–2.0]
65 [0.5]	61 [0.5]	47 [0.3]	57 [0.4]	85 [0.6]	66 [0.4]	672 [0.5; 0.5–0.5]
176 [1.3]	99 [0.7]	2 [<0.1]	5 [<0.1]	5 [<0.1]	8 [<0.1]	822 [0.6; 0.6–0.7]
398 [3.0]	314 [2.3]	331 [2.2]	387 [2.5]	441 [2.9]	437 [2.7]	3931 [2.9; 2.9–3.0]
21 [0.2]	16 [0.1]	14 [0.1]	0 [0.0]	0 [0.0]	0 [0.0]	142 [0.1; 0.1–0.1]

report estimates of incidence of key stages in the diabetes eye care pathway. Average annual incidences across the 11 years studied were 6.7% for screen positive, 3.1% screen positive due to DR, 1.0% other significant eye disease and 2.6% ungradeable images. 1.6% had STDR confirmed by a medical retina specialist. The prevalence of any DR was 27.2%. Our latest estimates of the incidence of STDR should be seen in the context of STDR rates recorded since 1991/92 in the LDESP. From an initial 6.9%, a steady fall was observed during the phased roll-out of screening over 16 years to 1.8% in 2007/08 (screening programme data; available on request from authors). These long-term observed data are likely to represent a 'first pass effect' where existing disease is detected in a population screened for the first time.

Other factors may have influenced the observed decline in STDR rates from the early years of screening in Liverpool. Medical care for PWD has improved over this time. Diagnostic criteria for diabetes have changed in recent years,[15] and there have been concerted efforts to detect diabetes early. A similar reduction in more advanced stages of disease was identified in a systematic literature review by Liew et al.,[16] who reported a two to threefold reduction in PDR and DMO over the last 30 years. Over the 11 years, there was a gradual fall in the prevalence of DR in the screened population from 38%

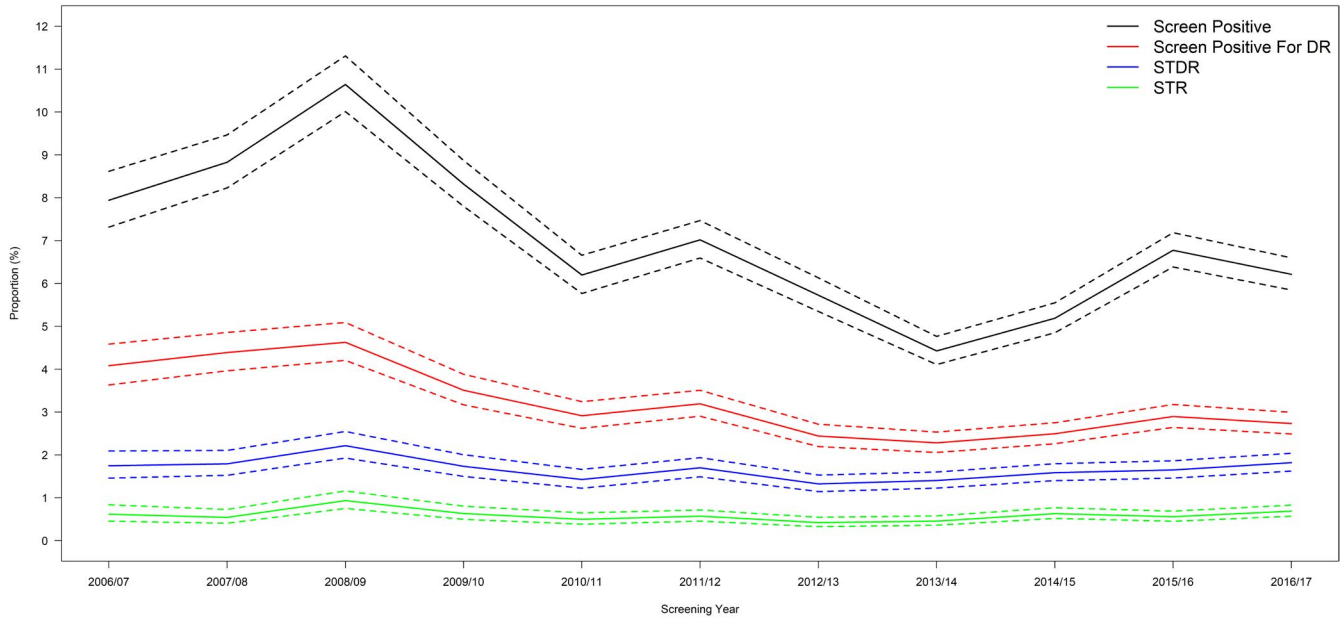

FIGURE 3 Graphical illustration of the annual incidences of screen positive, screen positive for diabetic retinopathy (DR), sight-threatening diabetic retinopathy (STDR) and sight threatening retinopathy (STR) for people living with diabetes categorised by screening year (1 April–31 March) between 2006 and 2017. Solid lines represent proportions, and the corresponding 95% confidence intervals based on the Wilson score method are represented by dashed lines

to 21% with equivalent falls in annual rates of screen positive and screen positive for DR. In contrast STDR, rates remained relatively stable at under 2.0%. This steady decline in diagnostic categories prior to the STDR stage requires further research. They may represent improvements in grading. A lowering of the threshold for the diagnosis of diabetes [15] may have increased the proportions with no retinopathy.

The strengths of our study include the size of the dataset and the duration of data collection.

$HbA1_c$ levels were generally well controlled in our population. This may reflect current standards of medical care but better compliance with medical care amongst those attending screening cannot be excluded. The current prevalence of diabetes in adults aged 17+ in Liverpool is 6.6% (29,993 people), slightly lower than the 7.1% in England as a whole.[17] DR screening coverage in Liverpool is low compared to other programmes: 80.4% in year April 2016 to March 2017.[18] The main limitation of our study is the mixed prospective and retrospective dataset reflecting changes in governance regulations and data collection platforms, a common issue in long-term, observational studies of real-world collected data. Around 5% of the population died or moved away each year and without consent, we were unable to access their historical data. This censoring could have affected our findings between 2006/7 and 2012/13 and is seen in the change in median age and disease duration. Subjects with worse retinopathy would be expected to have higher mortality, so our numerators may be underestimates. However, our exploratory analyses suggested that taking this effect into account would have a negligible effect on STDR rates. The ISDR RCT commenced in 2014 resulting in a proportion of patients moving to 2-yearly screening. We corrected for this effect in the last 2 years of our analysis.

In this study, we report results from PWD attending screening. Collection of data on people attending the HES with other eye disease (who undergo screening in the HES) was not possible; therefore, we cannot report whole population data. In Liverpool in 2017/18, 9.4% (2054/21,853) of PWD were attending the HES for management of DR or slit lamp-based screening. Nonetheless, it is possible to estimate a rate of STDR in people attending screening of 164/10,000 PWD/annum (2193/133,366 * 10,000). Comparison of our data with other studies is limited by the inconsistent and incomplete reporting of different screening outcomes. Longitudinal cohort studies from our group,[19,20] and from Norwich [21] and Wales,[22] have estimated annual incidences of preproliferative retinopathy and maculopathy. Looker et al. [9] reported data from the first 5 years of the DR Screening in Scotland. Rates of referable eye disease equivalent to our screen positive due to DR were highest in the first 2 years of screening (7.0% 2006, 6.0% 2007) before stabilising at 4.3%, slightly higher than our 3.1%.

Misra et al.[10] reported data from 20,788 PWD undergoing annual retinal photography between 1990 and 2006 in one English region. Rates of referable retinopathy (NDESP grades R2 or R3 or M1) increased from 2.0% in 1990 to 6.7% in 2001, then decreased to 4.7% by 2006. Scanlon et al.[11] reported a rate of referable retinopathy/STDR of 2.3% in a

TABLE 3 Annual incidences of screen positive, sight-threatening diabetic retinopathy (STDR), sight-threatening retinopathy (STR) and sight-threatening maculopathy (STM) for individuals attending their first recorded screening episode in each screening year (1 April–31 March) between 2007 and 2017

	Screening year										
	2007/08	2008/09	2009/10	2010/11	2011/12	2012/13	2013/14	2014/15	2015/16	2016/17	Overall *N* *n* [%; 95% CI]
Individuals attending first recorded screening *n* [%]	1883 [100.0]	1542 [100.0]	1566 [100.0]	1665 [100.0]	1941 [100.0]	1503 [100.0]	1588 [100.0]	1631 [100.0]	1629 [100.0]	1876 [100.0]	16,824 [100.0]
Overall screen positive	230 [12.2]	226 [14.7]	169 [10.8]	148 [8.9]	197 [10.1]	131 [8.7]	112 [7.1]	129 [7.9]	157 [9.6]	160 [8.5]	1659 [9.9; 9.4–10.3]
Screen positive for DR	98 [5.2]	67 [4.3]	48 [3.1]	52 [3.1]	64 [3.3]	42 [2.8]	40 [2.5]	49 [3.0]	55 [3.4]	56 [3.0]	571 [3.4; 3.1–3.7]
Screen positive for unassessable images	3 [4.4]	88 [5.7]	87 [5.6]	72 [4.3]	103 [5.3]	57 [3.8]	33 [2.1]	43 [2.6]	55 [3.4]	62 [3.3]	683 [4.1; 3.8–4.4]
Screen positive for other eye disease	49 [2.6]	71 [4.6]	34 [2.2]	24 [1.4]	30 [1.5]	32 [2.1]	39 [2.5]	37 [2.3]	47 [2.9]	42 [2.2]	405 [2.4; 2.2–2.6]
Biomicroscopy recorded[a]	186 [9.9]	197 [12.8]	135 [8.6]	127 [7.6]	169 [8.7]	114 [7.6]	106 [6.7]	119 [7.3]	145 [8.9]	144 [7.7]	1442 [8.6; 8.2–9.0]
STDR	39 [2.1]	37 [2.4]	31 [2.0]	31 [1.9]	42 [2.2]	30 [2.0]	33 [2.1]	36 [2.2]	40 [2.5]	45 [2.4]	364 [2.2; 2.0–2.4]
STR	15 [0.8]	26 [1.7]	18 [1.1]	14 [0.8]	20 [1.0]	13 [0.9]	14 [0.9]	23 [1.4]	14 [0.9]	23 [1.2]	180 [1.1; 0.9–1.2]
STM	35 [1.9]	29 [1.9]	21 [1.3]	25 [1.5]	39 [2.0]	26 [1.7]	28 [1.8]	23 [1.4]	35 [2.1]	38 [2.0]	299 [1.8; 1.6–2.0]
Unknown STR & Unknown STM	0 [0.0]	0 [0.0]	1 [0.1]	1 [0.1]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	2 [<0.1; 0.0–0.0]
Not STDR	147 [7.8]	160 [10.4]	104 [6.6]	96 [5.8]	127 [6.5]	84 [5.6]	73 [4.6]	83 [5.1]	105 [6.4]	96 [5.1]	1075 [6.4; 6.0–6.8]
Unknown STDR status	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	3 [0.2]	3 [<0.1; 0.0–0.1]
No biomicroscopy recorded[a]	44 [2.3]	29 [1.9]	34 [2.2]	21 [1.3]	28 [1.4]	17 [1.1]	6 [0.4]	10 [0.6]	12 [0.7]	16 [0.9]	217 [1.3; 1.1–1.5]
Screen negative	1653 [87.8]	1316 [85.3]	1397 [89.2]	1517 [91.1]	1744 [89.9]	1372 [91.3]	1476 [92.9]	1502 [92.1]	1472 [90.4]	1716 [91.5]	15165 [90.1; 89.7–90.6]
Retinopathy level											
Screen negative DR											
R0R0	1162 [61.7]	1066 [69.1]	1082 [69.1]	1249 [75.0]	1439 [74.1]	1121 [74.6]	1271 [80.0]	1298 [79.6]	1343 [82.4]	1565 [83.4]	12,596 [74.9; 74.2–75.5]
R1R0	342 [18.2]	227 [14.7]	259 [16.5]	184 [11.1]	226 [11.6]	202 [13.4]	161 [10.1]	155 [9.5]	133 [8.2]	144 [7.7]	2033 [12.1; 11.6–2.6]
R1R1	189 [10.0]	85 [5.5]	84 [5.4]	101 [6.1]	103 [5.3]	73 [4.9]	76 [4.8]	79 [4.8]	35 [2.1]	42 [2.2]	867 [5.2; 4.8–5.5]
One assessable eye (R0)	52 [2.8]	55 [3.6]	43 [2.7]	35 [2.1]	57 [2.9]	28 [1.9]	37 [2.3]	47 [2.9]	53 [3.3]	57 [3.0]	464 [2.8; 2.5–3.0]
One assessable eye (R1)	17 [0.9]	9 [0.6]	8 [0.5]	7 [0.4]	10 [0.5]	10 [0.7]	3 [0.2]	3 [0.2]	9 [0.6]	12 [0.6]	88 [0.5; 0.4–0.6]
Unknown	23 [1.2]	33 [2.1]	42 [2.7]	37 [2.2]	42 [2.2]	27 [1.8]	0 [0.0]	0 [0.0]	1 [0.1]	0 [0.0]	205 [1.2; 1.1–1.4]
Screen positive DR											
R2 or M1	92 [4.9]	58 [3.8]	39 [2.5]	48 [2.9]	54 [2.8]	36 [2.4]	39 [2.5]	49 [3.0]	55 [3.4]	56 [3.0]	526 [3.1; 2.9–3.4]
R3	6 [0.3]	9 [0.6]	9 [0.6]	4 [0.2]	10 [0.5]	6 [0.4]	1 [0.1]	0 [0.0]	0 [0.0]	0 [0.0]	45 [0.3; 0.2–0.4]

Note: STM and STR are not mutually exclusive categories. 95% CI are based on the Wilson score method.

Abbreviation: DR, diabetic retinopathy.

[a]Biomicroscopy must be recorded within 1 year of screening appointment when positive screen result occurred.

TABLE 4 Annual incidences of screen positive, sight-threatening diabetic retinopathy (STDR), sight threatening retinopathy (STR) and sight threatening maculopathy (STM) for individuals attending a screening appointment in each screening year (1 April–31 March) which was not their first recorded screening episode between 2007 and 2017

	Screening year				
	2007/08	**2008/09**	**2009/10**	**2010/11**	**2011/12**
Individuals attended screening appointment (excluding first recorded events) *n* [%]	6349 [100.0]	7155 [100.0]	8769 [100.0]	9585 [100.0]	11,248 [100.0]
Overall screen positive	486 [7.7]	698 [9.8]	686 [7.8]	549 [5.7]	724 [6.4]
Screen positive for DR	258 [4.1]	334 [4.7]	13 [3.6]	276 [2.9]	355 [3.2]
Screen positive for unassessable images	173 [2.7]	271 [3.8]	285 [3.3]	212 [2.2]	322 [2.9]
Screen positive for other eye disease	55 [0.9]	93 [1.3]	88 [1.0]	61 [0.6]	47 [0.4]
Biomicroscopy recorded[a]	432 [6.8]	598 [8.4]	578 [6.6]	485 [5.1]	605 [5.4]
STDR	106 [1.7]	155 [2.2]	148 [1.7]	129 [1.3]	181 [1.6]
STR	29 [0.5]	55 [0.8]	47 [0.5]	42 [0.4]	55 [0.5]
STM	84 [1.3]	128 [1.8]	115 [1.3]	105 [1.1]	158 [1.4]
Unknown STR & Unknown STM	0 [0.0]	2 [<0.1]	1 [<0.1]	3 [<0.1]	0 [0.0]
Not STDR	326 [5.1]	443 [6.2]	430 [4.9]	356 [3.7]	424 [3.8]
Unknown STDR status	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]	0 [0.0]
No biomicroscopy recorded[a]	54 [0.9]	100 [1.4]	108 [1.2]	64 [0.7]	119 [1.1]
Screen negative	5863 [92.3]	6457 [90.2]	8083 [92.2]	9036 [94.3]	10524 [93.6]
Retinopathy level					
Screen negative DR					
R0R0	3816 [60.1]	4390 [61.4]	5476 [62.4]	6570 [68.5]	7682 [68.3]
R1R0	1234 [19.4]	1327 [18.5]	1673 [19.1]	1475 [15.4]	1727 [15.4]
R1R1	830 [13.1]	800 [11.2]	1000 [11.4]	1030 [10.7]	1124 [10.0]
One assessable eye (R0)	117 [1.8]	132 [1.8]	125 [1.4]	109 [1.1]	171 [1.5]
One assessable eye (R1)	5 [0.6]	48 [0.7]	56 [0.6]	57 [0.6]	5 [0.5]
Unknown	59 [0.9]	124 [1.7]	126 [1.4]	68 [0.7]	134 [1.2]
Screen positive DR					
R2 or M1	253 [4.0]	317 [4.4]	301 [3.4]	262 [2.7]	344 [3.1]
R3	5 [0.1]	17 [0.2]	12 [0.1]	14 [0.1]	11 [0.1]

Note: STM and STR are not mutually exclusive categories. 95% CI are based on the Wilson score method.

Abbreviation: DR, diabetic retinopathy.

[a]Biomicroscopy must be recorded within 1 year of screening appointment when positive screen result occurred.

[b]Adjusted for subjects recruited to the ISDR RCT and assigned to 24-month screening intervals.

screening cohort from Gloucestershire used for a cost effectiveness modelling study. None of these studies appear to have reported true positive STDR after confirmation by a medical retina specialist, considered as the clinical standard for treatment decision making. Authors should report screen positive due to DR, other eye disease and ungradeable images in addition to true STDR (confirmed by a medical retina specialist). Standardisation of outcomes reporting across regions and countries would aid comparison.

In our study, around half (53.8%) of subjects who were screen positive for DR had STDR. Of these people with true STDR, 82.7% had STM and 35.5% had STR. The proportion was similar when comparing new and previously acquired screened patients and similar to reports from Scotland in 2010 where 73% of referrals for DR were due to maculopathy.[9] We report very low rates of R3 with none in the last 3 years. Compared to STR, STM is more expensive to treat and monitor. Our results are of interest to health service providers and to researchers developing new therapies who require candidates for clinical trials.

Current UK screening definitions and pathways were established over 15 years ago to support the introduction of screening and were consensus based.[23] Now that the rates of STDR are low, it may be appropriate to revisit the definition of screen positive in order to ensure optimum resource allocation. Extended screening intervals should be considered by programme managers; data on the proportions of patients with R1/R0 and R1/R1 will inform risk stratification.[13,24] The

2012/13	2013/14	2014/15	2015/16	2016/17	Overall *n* [%; 95% CI]
12,037 [100.0]	13,561 [100.0]	13,904 [100.0]	13,597[b] [100.0]	14,135[b] [100.0]	11,0340 [100.0]
644 [5.4]	557 [4.1]	676 [4.9]	875 [6.4]	835 [5.9]	6730 [6.1; 6.0–6.2]
289 [2.4]	305 [2.2]	338 [2.4]	387 [2.8]	382 [2.7]	3237 [2.9; 2.8–3.0]
265 [2.2]	146 [1.1]	215 [1.5]	353 [2.6]	321 [2.3]	2563 [2.3; 2.2–2.4]
90 [0.7]	106 [0.8]	123 [0.9]	135 [1.0]	132 [0.9]	930 [0.8; 0.8–0.9]
537 [4.5]	515 [3.8]	623 [4.5]	820 [6.0]	725 [5.1]	5918 [5.4; 5.2–5.5]
149 [1.2]	179 [1.3]	210 [1.5]	211 [1.6]	246 [1.7]	1714 [1.6; 1.5–1.6]
44 [0.4]	55 [0.4]	75 [0.5]	71 [0.5]	87 [0.6]	560 [0.5; 0.5–0.6]
123 [1.0]	151 [1.1]	168 [1.2]	181 [1.3]	200 [1.4]	1413 [1.3; 1.2–1.3]
4 [<0.1]	1 [<0.1]	1 [<0.1]	0 [0.0]	0 [0.0]	12 [<0.1; 0.0–0.0]
388 [3.2]	333 [2.5]	413 [3.0]	609 [4.5]	459 [3.2]	4181 [3.8; 3.7–3.9]
0 [0.0]	3 [<0.1]	0 [0.0]	0 [0.0]	20 [0.1]	23 [<0.1; 0.0–0.0]
107 [0.9]	42 [0.3]	53 [0.4]	55 [0.4]	110 [0.8]	812 [0.7; 0.7–0.8]
11393 [94.6]	13004 [95.9]	13228 [95.1]	12722 [93.6]	13300 [94.1]	103,610 [93.9; 93.8–94.0]
8432 [70.1]	791 [72.2]	10370 [74.6]	10166 [74.8][b]	10850 [76.8][b]	77,543 [70.3; 70.0–70.5]
1838 [15.3]	1812 [13.4]	1694 [12.2]	1666 [12.3][b]	1488 [10.5][b]	15,934 [14.4; 14.2–14.6]
1172 [9.7]	1433 [10.6]	1213 [8.7]	959 [7.1]	1022 [7.2]	10,583 [9.6; 9.4–9.8]
182 [1.5]	174 [1.3]	230 [1.7]	339 [2.5]	331 [2.3]	1910 [1.7; 1.7–1.8]
52 [0.4]	44 [0.3]	54 [0.4]	76 [0.6]	54 [0.4]	531 [0.5; 0.4–0.5]
72 [0.6]	2 [<0.1]	5 [<0.1]	4 [<0.1]	8 [0.1]	602 [0.5; 0.5–0.6]
279 [2.3]	292 [2.2]	338 [2.4]	387 [2.8]	382 [2.7]	3155 [2.9; 2.8–3.0]
10 [0.1]	13 [0.1]	0 [0.0]	0 [0.0]	0 [0.0]	82 [0.1; 0.1–0.1]

low rates also support moves to introduce personalised risk-based variable-interval screening using clinical risk factor data.[12,25] Of those identified as screen positive in our study, only 28.1% had true positive disease. A high proportion of screen positive cases were due to ungradeable images (most likely due to cataract) and other significant eye disease, identification of which is not an objective of screening. New technologies may overcome ungradeable images (38.7% in our study); agreement is needed on approaches to managing screen positive due to other eye disease (15.7% in our study).

Despite high rates of ungradeable images, newly screened PWD in our study demonstrated rates of STDR 1.4× higher than existing screening participants (2.2% vs. 1.6%). This effect appears to be driven by previous non-attenders and is consistently seen in other epidemiological studies. In the United Kingdom Prospective Diabetes Study (type 2 disease), 4.5% of female and 7.9% of male participants had STDR at diagnosis of diabetes,[26] while the LDES reported 6.6% (9.8% for Type 1) having STDR at first screen.[19,20] In the Scottish programme, 6.9% of first-time attenders had referable disease compared to 3% for people attending their fourth or fifth screen.[9] New systematic DR screening programmes in Asia report similar findings. In Hong Kong, where screening following the English NDESP protocol was introduced for the first time in 2014, STDR was detected in 9.8% of 174,532 new screened patients in 12 months.[27] A phased introduction of screening into populations may reduce the service delivery pressures on HES. We report higher rates of screen positive

and STDR in people with type 1 diabetes. Lower rates of assessable images and other eye disease in these individuals compared to those with type 2 diabetes are likely to reflect younger age. Interestingly, type of diabetes was not identified as being predictive for referable DR by the Liverpool Risk Calculation Engine.[14] However, this may reflect a low number of events in the dataset used.

We have shown that in an established screening programme with a stable population, rates of screen positive DR show a consistent fall over time to a low level. The annual incidence of STDR is under 2% highlighting the need for future work defining screen positive and supporting extended intervals for people at low risk. Higher rates of disease are seen in new screened patients and previous non-attenders who should be specifically targeted, and in people with type 1 diabetes. Our results should be generalised with caution, particularly in populations with higher rates of STDR, higher proportions of ethnic minorities and programmes in set-up. Our data represent a benchmark against which other screening programmes can be measured and will inform both redesign of screening services and future intervention studies.

ACKNOWLEDGEMENTS

The authors are grateful to the ISDR Patient and Public Involvement Group for essential input into design and review and enthusiastic support for the study, to the Liverpool Care Commissioning Group for data extraction and transfer, and to the Liverpool Local Medical Committee and local general practitioners for support with establishing patient lists and consent.

ISDR Study Group Authors: Christopher P. Cheyne, Philip Burgess, Deborah M. Broadbent, Marta García-Fiñana, Irene M. Stratton, Ticiana Criddle, Amu Wang, Ayesh Alshukri, Mehrdad M. Rahni, Pilar Vazquez-Arango, Jiten P. Vora, Simon P. Harding (Study Group Chair). Collaborators: ISDR investigators: Paula Byrne, Anthony C. Fisher, Mark Gabbay, Marilyn James, Tracy Moitt, John R. Roberts, Daniel Seddon, Paula Williamson; ISDR Research staff: Duncan Appelbe, Antonio Eleuteri, Christopher Grierson, Lola Howard, Susan U. Howlin, James G. Lathe, Andy Ovens, Christopher J. Sampson, Kate Silvera, David Szmyt, Clare Thetford, Abigail E. Williams; Patient and Public Involvement Group: John Collins, Emily Doncaster John Kelly, Peter Lees, Sandra Lees, Betty Williams; Programme and Independent Data Safety Committees: Helen Cooper, Gideon Smith, Vineeth Kumar, Chris Rogers, Alison Rowlands, Julia West, Naveed Younis, Nathalie Massat, Catey Bunce; Liverpool Diabetic Eye Screening Programme: Stephanie Perrett: Liverpool Clinical Commissioning Group: Lisa Jones.

CONFLICT OF INTEREST

None.

ROLE OF THE STUDY SPONSOR

The study was sponsored by The Royal Liverpool and Broadgreen University Hospitals NHS Trust who approved the study design and protocol and provided membership of the Project Steering Committee.

AUTHORS' RELATIONSHIPS AND ACTIVITIES

All authors declare grant support from the National Institute for Health Research (NIHR) UK for the submitted work and no other relationships or activities that could appear to have influenced the submitted work. Professor Mark Gabbay is part-funded by the NIHR Collaboration for Leadership in Applied Health Research and Care North West Coast.

AUTHOR CONTRIBUTION

Simon Harding (programme CI), Deborah Broadbent, Irene Stratton, Jiten Vora and Marta Garcia Finanaobtained funding (with other members of the ISDR Study Group) and designed the study. Amu Wang led recruitment and managed all aspects of the study, supported by Pilar Vazquez-Arango, Marta Garcia Finana, Ticiana Criddle, Simon Harding and Jiten Vora. Mehrdad Rahni and Ayesh Alshukri designed and built the data warehouse. Marta Garcia Finana led the statistical team. Christopher Cheyne conducted statistical analysis and produced the tables supported by Marta Garcia Finana and Irene Stratton. Jiten Vora led the involvement of the PPI group. Philip Burgess drafted the manuscript with revisions from Christopher Cheyne, Deborah Broadbent and Simon Harding. All members of the writing committee read and approved the final manuscript. Philip Burgess is guarantor for the submission.

DATA AVAILABILITY STATEMENT

A dataset with supporting data dictionary will be available from the corresponding author to recognised research institutions subject to approval by the ISDR Data Governance Committee of an analysis plan, a data access agreement, appropriate acknowledgment, and funding for additional costs.

ORCID

Philip I. Burgess https://orcid.org/0000-0002-3959-2299
Irene M Stratton https://orcid.org/0000-0003-1172-7865

REFERENCES

1. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: global estimates of diabetes prevalence for 2017 and projections for 2045. *Diabetes Res Clin Pract*. 2018;138:271-281.
2. Yau JWY, Rogers SL, Kawasaki R, et al. Global prevalence and major risk factors of diabetic retinopathy. *Diabetes Care*. 2012;35:556-564.
3. Wong TY, Mwamburi M, Klein R, et al. Rates of progression in diabetic retinopathy during different time periods: a systematic review and meta-analysis. *Diabet Care*. 2009;32:2307-2313.

4. Scanlon PH. The English national screening programme for sight-threatening diabetic retinopathy. *J Med Screen*. 2008;15:1-4.
5. Klein R, Knudtson MD, Lee KE, Gangnon R, Klein BE. The Wisconsin Epidemiologic Study of Diabetic Retinopathy: XXII the twenty-five-year progression of retinopathy in persons with type 1 diabetes. *Ophthalmology*. 2008;115:1859-1868.
6. Javitt JC, Aiello LP. Cost-effectiveness of detecting and treating diabetic retinopathy. *Ann Intern Med*. 1996;124:164-169.
7. Klein R, Klein BE, Moss SE, Cruickshanks KJ. The Wisconsin Epidemiologic Study of Diabetic Retinopathy. XIV. Ten-year incidence and progression of diabetic retinopathy. *Arch Ophthalmol*. 1994;112(9):1217-1228.
8. Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report 12. *Ophthalmology*. 1991;98:823-833.
9. Looker HC, Nyangoma SO, Cromie DT, et al. Predicted impact of extending the screening interval for diabetic retinopathy: the Scottish Diabetic Retinopathy Screening programme. *Diabetologia*. 2013;56:1716-1725.
10. Misra A, Bachmann MO, Greenwood RH, et al. Trends in yield and effects of screening intervals during 17 years of a large UK community-based diabetic retinopathy screening programme. *Diabet Med*. 2009;26:1040-1047.
11. Scanlon PH, Aldington SJ, Leal J, et al. Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. *Health Technol Assess*. 2015;19:1-116.
12. Broadbent DM, Wang A, Cheyne CP, et al. Safety and cost-effectiveness of individualised screening for diabetic retinopathy: the ISDR open-label, equivalence RCT. *Diabetologia*. 2021;64:56-69.
13. Eleuteri A, Fisher AC, Broadbent DM, et al. Individualised variable-interval risk-based screening for sight-threatening diabetic retinopathy: the Liverpool Risk Calculation Engine. *Diabetologia*. 2017;60:2174-2182.
14. Harding S, Greenwood R, Aldington S, et al. Grading and disease management in national screening for diabetic retinopathy in England and Wales. *Diabet Med*. 2003;20:965.
15. Wareham NJ, O'Rahilly S. The changing classification and diagnosis of diabetes. *Br Med J*. 1998;317:359-360.
16. Liew G, Wong VW, Ho I-V. Mini review: changes in the incidence of and progression to proliferative and sight-threatening diabetic retinopathy over the last 30 years. *Ophthamol Epidemiol*. 2017;24:73-80.
17. Public Health England. Prevalence of Diabetes by NHS region. https://fingertips.phe.org.uk/profile/diabetes-ft/data#page/4/gid/1938133138/pat/44/par/E40000010/ati/154/are/E38000101/iid/241/age/187/sex/4/cid/4/tbm/1/page-options/ovw-do-0. Accessed 7 February 2021.
18. NHS DESP. Data tables. https://www.gov.uk/government/publications/diabetic-eye-screening-2016-to-2017-data. Accessed 2 June 2020.
19. Younis N, Broadbent DM, Harding SP, Vora JP. Incidence of sight threatening retinopathy in type 1 diabetes in a systematic screening programme. *Diabet Med*. 2003;20:758-765.
20. Younis N, Broadbent DM, Vora JP, Harding SP. Incidence of sight threatening retinopathy in patients with type 2 diabetes in the Liverpool Diabetic Eye Study: a cohort study. *Lancet*. 2003;361(9353):195-200.
21. Jones CD, Greenwood RH, Misra A, Bachmann MO. Incidence and progression of diabetic retinopathy during 17 years of a population-based screening program in England. *Diabetes Care*. 2012;35(3):592-596.
22. Thomas RL, Dunstan F, Luzio SD, et al. Incidence of diabetic retinopathy in people with type 2 diabetes mellitus attending the diabetic retinopathy screening service for Wales: retrospective analysis. *Br Med J*. 2012;344:e874.
23. English National Diabetic Eye Screening Programme. Retinal Image Grading Criteria. https://www.gov.uk/government/publications/diabetic-eye-screening-retinal-image-grading-criteria. Accessed 4 May 2020
24. Scanlon PH, Stratton IM, Histed M, Chave SJ, Aldington SJ. The influence of background diabetic retinopathy in the second eye on rates of progression of diabetic retinopathy between 2005 and 2010. *Acta Ophthalmol*. 2013;91(5):e335-e339.
25. Aspelund T, Þórisdóttir Ó, Ólafsdottir E, et al. Individual risk assessment and information technology to optimise screening frequency for diabetic retinopathy. *Diabetologia*. 2011;54:2525-2532.
26. Kohner EM, Aldington SJ, Stratton IM, et al. United Kingdom Prospective Diabetes Study, 30: diabetic retinopathy at diagnosis of non-insulin-dependent diabetes mellitus and associated risk factors. *Arch Ophthalmol*. 1998;116(3):297-303.
27. Lian JX, Gangwani RA, McGhee SM, Chan CKW, Lam CLK, Wong DSH. Systematic screening for diabetic retinopathy (DR) in Hong Kong: prevalence of DR and visual impairment among diabetic population. *Br J Ophthalmol*. 2016;100(2):151-155.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

How to cite this article: Cheyne CP, Burgess PI, Broadbent DM, et al. Incidence of sight-threatening diabetic retinopathy in an established urban screening programme: An 11-year cohort study. *Diabet Med*. 2021;00:e14583. https://doi.org/10.1111/dme.14583