Short Report: Care Delivery

Risk of diabetic retinopathy at first screen in children at 12 and 13 years of age

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Abstract

Aims   To investigate the relationships between age at diagnosis of diabetes, age at diabetic eye screening and severity of diabetic retinopathy at first and subsequent screenings in children aged 12 or 13 years.

Methods   Data were extracted from four English screening programmes and from the Scottish, Welsh and Northern Irish programmes on all children with diabetes invited for their first and subsequent screening episodes from the age of 12 years. Retinopathy levels at first and subsequent screens, time from diagnosis of diabetes to first screening and age at diagnosis in years were calculated.

Results   Data were available for 2125 children with diabetes screened for the first time at age 12 or 13 years. In those diagnosed with diabetes at 2 years of age or less, the proportion with retinopathy in one or both eyes was 20% and 11%, respectively, decreasing to 8% and 2% in those diagnosed between 2 and 12 years ($P < 0.0001$). Only three children (aged 8, 10 and 11 years at diagnosis of diabetes) had images graded with referable retinopathy and, of these, two had non-referable diabetic retinopathy at all subsequent screenings. Of 1703 children with subsequent images, 25 were graded with referable diabetic retinopathy over a mean follow-up of 3.1 years, an incidence rate of 4.7 (95% confidence interval, 3.1–7.0) per 1000 per year.

Conclusions   In this large cohort of children, the low prevalence and incidence rates of referable diabetic retinopathy suggest that screening earlier than age 12 is not necessary.

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Introduction

Screening for diabetic retinopathy is a highly cost-effective health initiative and blindness caused by diabetes is lower in populations where a diabetic eye screening programme is established [1–3].

There is a global increase in the incidence of Type 1 diabetes mellitus in children [4], particularly in those aged under 5 years [5]. Young children face long pre-pubertal years of hyperglycaemia, with pre-pubertal, pubertal and post-pubertal years contributing [6,7] to an increased risk of development of microvascular complications of diabetic retinopathy. In 2013–2014, it was reported [8] that there were 26 687 young persons under 25 with diabetes in England and Wales.

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Annual screening for diabetic retinopathy is recommended in England, Scotland, Wales and Northern Ireland for all those with diabetes aged 12 and above. This was a pragmatic policy decision taken in 2002–2003 because the youngest person reported with sight-threatening diabetic retinopathy in the literature at that time was aged 11.3 years [9].

We report on the relationships between age at diagnosis of diabetes, diabetic retinopathy levels at first screen at either 12 or 13 years of age, and time to development of sight-threatening diabetic retinopathy after first screen.

Methods

We recruited data for the Four Nations study [10] from seven diabetic retinopathy screening programmes: the whole-nation programmes in Wales, Scotland and Northern Ireland and four local English programmes (Brighton, Derbyshire, Leeds and Staffordshire). For the present study, one English programme

> **What's new?**
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> • This is the largest reported study in the literature of baseline levels of diabetic retinopathy in the age group 12 or 13 years.
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> • This is the largest reported study showing the rate of progression of diabetic retinopathy in adolescents.
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> • Of 2125 children with diabetes screened for the first time at age 12 or 13 years, three were found to have referable disease.
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> • The absence of referable disease in subsequent screens in two of the children and of pre-proliferative changes in the third child suggest that it is unlikely that any treatment is required.

was excluded because no data were available for age at diagnosis of diabetes. Data for all children referred to the eye screening programme, grading results at first screen, and age in years at diagnosis of diabetes were extracted from the screening programme databases. The inclusion criteria were all children aged 12 and 13 years, who attended their first annual digital photographic screening in the UK. There are very few exclusion criteria, such as when a child is terminally ill.

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. A mapping exercise was undertaken between the English, Scottish and ETDRS Grading Criteria [10–12]. Referable or sight-threatening diabetic retinopathy was identified by the presence of features of moderate to severe non-proliferative, proliferative diabetic retinopathy or maculopathy in at least one eye. Children with images of either or both eyes that could not be assessed were excluded from these analyses.

Time from diagnosis of diabetes to first screening and age at diagnosis were calculated. Screening data from both eyes were combined to provide four possible categories of children:

• no diabetic retinopathy (R1M0) in both eyes;
• mild non-proliferative diabetic retinopathy (R1M0) in one eye;
• mild non-proliferative diabetic retinopathy (R1M0) in both eyes;
• referable diabetic retinopathy (R2 or M1) or fast-track proliferative diabetic retinopathy (R3) – the referable diabetic retinopathy group including the fast-track proliferative diabetic retinopathy is referred to as sight-threatening diabetic retinopathy in this article.

For survival analyses of time to diabetic retinopathy in children who had at least two retinal screenings, follow-up was censored at the time of second screening. We estimated

binomial confidence intervals for diabetic retinopathy incidence rates. Kaplan–Meier survival curves of time to diabetic retinopathy were plotted, stratified by duration of diabetic retinopathy at first screening. Cox proportional hazards models estimated the hazard ratio for diabetic retinopathy in children by duration of diabetes at first screening.

Results

In total, 2125 children received their first screening at the age of 12 or 13 years. The results of the baseline screen of 2125 children at the age of 12 or 13 years are shown in Table 1. This has been categorized according to the age of diagnosis of diabetes. O the children diagnosed under the age of 2 years, 20.1% had signs of any retinopathy compared with 6.3% of those diagnosed at the age of 10 years.

Three children were reported as having referable retinopathy at first screening.

1. The first was diagnosed with diabetes at the age of 8 years in 2000, first screened in November 2005 at age 13 years, and approximately annually thereafter until 2012. Referable diabetic retinopathy was recorded at the first screening, followed by referable diabetic retinopathy in 2007, 2009, 2011 and 2012 with possible pre-proliferative changes (R2), but mild non-proliferative diabetic retinopathy (NPDR) in both eyes in 2008.

2. The second was diagnosed with diabetes at the age of 10 years in 2004, and first screened in November 2007 and again in 2012. Referable retinopathy (maculopathy – a blot haemorrhage or exudate < 1 disc diameter from the foveal centre) was reported in 2007, but only mild NPDR in one eye was found in 2012.

3. The third was diagnosed with diabetes at the age of 11 years in 2005, and screened in 2006, 2009, 2010 and 2011. The screening result in 2006 reported 'proliferative retinopathy' but subsequent screening reported no diabetic retinopathy in 2009 and mild NPDR in one eye in 2010 and 2011.

Follow-up data were available for 1703 children who had baseline gradable images and at least one subsequent set of images. Of these 1703 children, the median age at diagnosis of diabetes was 8 years with an interquartile range (IQR) of 5–11 years; 52% of these children were male. At baseline, 1531 (89.9%) children were graded as having no retinopathy, 129 (7.6%) were graded as having mild NPDR in one eye and 43 (2.5%) were graded as having mild NPDR in both eyes.

Of the 1703 children with subsequent images, 16 had a valid screening result at first screen that was not gradable at the second screen but had at least one subsequent gradable image. Of the 129 children with mild NPDR in one eye at first screen, 88 (68.2%) were graded as no diabetic retinopathy, 26 (20.2%) as mild NPDR in one eye and 15 (11.6%) as mild NPDR in both eyes at the second screen. Of the 43 children with mild NPDR in both eyes at first screen, 18 (41.9%) were

Table 1 Results of the baseline screen at the age of 12 years or 13 years

Age at diagnosis of diabetes	Number (total = 2125)	Number and proportion with any diabetic retinopathy N/total (%)	Number and proportion with mild non-proliferative diabetic retinopathy in one eye N/total (%)	Number and proportion with mild non-proliferative diabetic retinopathy in both eyes N/total (%)	Number and proportion with fast track or referable diabetic retinopathy N/total (%)
2 or under	164	33/164 (20.1)	15/164 (9.1)	18/164 (11.0)	0/164 (0.0)
3	118	22/118 (18.6)	18/118 (15.3)	4/118 (3.4)	0/118 (0.0)
4	141	21/141 (14.9)	19/141 (13.5)	2/141 (1.4)	0/141 (0.0)
5	130	15/130 (11.5)	10/130 (7.7)	5/130 (3.8)	0 /130 (0.0)
6	149	15/149 (10.1)	10 /149 (6.7)	5 /149 (3.4)	0/149 (0.0)
7	181	21/181 (11.6)	17 /181 (9.4)	4/181 (2.2)	0 /181 (0.0)
8	193	13/193 (6.7)	9/193 (4.7)	3/193 (1.6)	1/193* (0.5)
9	224	21/224 (9.4)	15 /224 (6.7)	6/224 (2.7)	0 /224 (0.0)
10	271	17/271 (6.3)	14/271 (5.2)	2/271 (0.7)	1/271* (0.4)
11	290	20/290 (6.9)	12 /290 (4.1)	7 /290 (2.4)	1/290* (0.3)
12	264	22/264 (8.3)	17/264 (6.4)	5/264 (1.9)	0/264 (0.0)

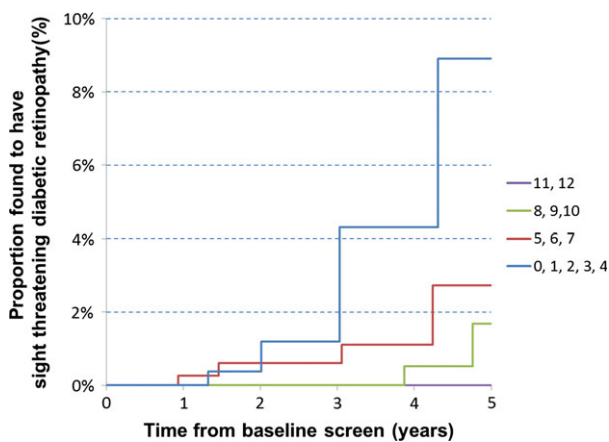*Three children were reported as having referable retinopathy at first screening.

FIGURE 1 Time to sight-threatening diabetic retinopathy from baseline screen at 12 or 13 years by age of diagnosis of diabetes. The lines represent the age at which a child was diagnosed with diabetes. The blue line represents children diagnosed with diabetes at 0,1,2,3 or 4 years. The red line represents children diagnosed with diabetes at 5, 6 or 7 years. The green line represents children diagnosed with diabetes at 8, 9 or 10 years. The purple line represents children diagnosed with diabetes at 11 or 12 years.

graded as no diabetic retinopathy, 12 (27.9%) as mild NPDR in one eye and 13(30.3%) as mild NPDR both eyes at the second screen (chi-squared for trend = 146, $P < 0.0001$).

During subsequent follow-up visits, 25 children were graded as having sight-threatening or referable diabetic retinopathy, three of whom were graded as having proliferative diabetic retinopathy. Figure 1 shows the time to sight-threatening diabetic retinopathy from baseline screen at 12 or 13 years by age of diagnosis of diabetes in these 25 children. The median time from baseline to sight-threatening diabetic retinopathy was 3.1 years with an IQR of 1.7–4.1 years.

The results of the Cox proportional hazards model analysis show that those with longer duration of diabetes at baseline screening episode at age 12 or 13 years were at higher risk of progression to referable diabetic retinopathy with a hazard

ratio of 1.36 per year [95% CI (95% CI), 1.20 to 1.53). Figure S1 shows the time to referable retinopathy from diagnosis of diabetes.

Conclusion

Since 2002, the UK National Screening Committee, the SIGN Guideline [13] and the NICE guidelines [14,15] have recommended annual digital photographic screening for all children over the age of 12 years and adults with diabetes, with evidence from studies [16,17] demonstrating that one- and two-field digital photographic screening could show sensitivities of > 85% against a reference standard of an ophthalmologists examination or seven-field stereo-photography. Specificities of 85–95% were also achieved for mydriatic photography [16,17] and for staged mydriasis [18].

The American Academy of Ophthalmology [19] recommends annual ophthalmic examinations beginning 3–5 years after the diagnosis of Type 1 diabetes mellitus. The International Diabetes Federation/International Society for Pediatric and Adolescent Diabetes guideline [20] recommends examination for diabetic retinopathy in Type 1 diabetes from age 11 years and after two years' diabetes duration, and from diagnosis in Type 2 diabetes.

This study provides original evidence supporting the UK recommendations. It found that, although 10% of children have some retinopathy at baseline screening at the age of 12–13 years, only three children (0.17%) were graded as having sight-threatening diabetic retinopathy. Of the three we identified, it seems likely that none required treatment because only one case was consistently diagnosed as sight-threatening and this was pre-proliferative diabetic retinopathy which does not normally require laser treatment. In those diagnosed with diabetes in early childhood, the rate of retinopathy was significantly higher than for those diagnosed later on. The low prevalence and incidence rates in this large cohort of children suggest that earlier screening for sight-

threatening diabetic retinopathy is not necessary in this age group. There may be value in detecting diabetic retinopathy at a mild stage, but only if it could be shown that closer follow-up in this at-risk group could reduce the progression rate and the development of complications in these children.

Competing interests

None declared.

Author contributors

PS wrote the first draft and IS conducted the analyses. GL, MB, ML, CJ and BF all commented on the drafts of the paper. Prof. 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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Supporting Information

Additional Supporting Information may be found in the online version of this article:

Figure S1. Time to referable retinopathy from diagnosis of diabetes. DR, diabetic retinopathy.