Prevalence of Diabetic Retinopathy within a National Diabetic Retinopathy Screening Service

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ABSTRACT

Aims: Determine the prevalence and severity of diabetic retinopathy and risk factors in a large community based screening programme, in order to accurately estimate the future burden of this specific and debilitating complication of diabetes.

Methods: A cross-sectional analysis of 91,393 persons with diabetes, 5,003 type 1 diabetes and 86,390 type 2 diabetes, at their first screening by the community based National Diabetic Retinopathy Screening Service for Wales from 2005 to 2009. Image capture utilised 2x45° digital images per eye following mydriasis, classified by qualified retinal graders with final grading based on the worst eye.

Results: The prevalence of any diabetic retinopathy and sight-threatening diabetic retinopathy in those with type 1 diabetes was 56.0% and 11.2% respectively and in type 2 diabetes was 30.3% and 2.9% respectively. The presence of diabetic retinopathy both non-sight-threatening and sight-threatening was strongly associated with increasing duration of diabetes for either type 1 and type 2 diabetes and also associated with insulin therapy in those with type 2 diabetes.

Conclusions: Prevalence of diabetic retinopathy within the largest reported community-based, quality assured, diabetic retinopathy screening programme, was higher in persons with type 1 diabetes however, the major burden is represented by type 2 diabetes being 94% of the screened population.

INTRODUCTION

Diabetic retinopathy (DR) continues to be an important microvascular complication in both type 1 and type 2 diabetes. Previous evidence suggests that DR is evident in approximately 50% of persons with type 1 diabetes for 28 years and advanced DR after 39 years. (1) In contrast about 12-19%%,(2, 3) of persons with type 2 diabetes have some DR already at the time of diagnosis,(4) with 4% of developing proliferative DR after 20 years or more of diabetes.(2) In both the UK and USA, DR unfortunately remains among the leading causes of blindness and low vision, along with age related macular degeneration and glaucoma.(5-8)

The St Vincent Declaration (1989) recommended that new onset blindness arising from DR should be reduced by one third within five years.(9) However, it is only in the last decade that significant progress has been made in implementing screening programmes to detect and monitor DR. To date many different DR screening models have been introduced worldwide.(10-19) In the UK the National Screening Committee (NSC) for England and Wales (1999) produced guidelines for DR screening programmes to ensure standardisation and quality assurance. The recommended screening procedure includes assessment of visual acuity and obtaining digital fundal photographs following mydriasis,(20) in persons aged 12 years and older.(21) The recommendation of screening beginning from the age of 12 years reflects the low incidence of DR, and especially proliferative DR, in younger children.(22) In Scotland a three tiered screening approach has been implemented which involves obtaining only one macular centred digital fundal photograph per eye without mydriasis (tier 1) and if unsuccessful then mydriasis is used (tier 2) and finally biomicroscopy with a slit lamp if photography remains unsuccessful (tier 3).(23)

Wales currently has a population of 3.06 million is predominantly Caucasian, with the majority situated in the industrial south (~60%) with the remainder of the country generally regarded as rural.(24) The prevalence of diabetes in Wales is currently estimated at approximately 5%, 160,000 people affected.(25) Following a pilot regional programme,(26) a national DR screening programme, the Diabetic Retinopathy Screening Service for Wales (DRSSW) was commissioned in 2002. The aim of the service was initially to identify all undiagnosed sight-threatening DR and facilitate timely onwards referral to hospital eye services (HES). The secondary aim was to identify the presence of any DR so that improvements in glycaemic control, hypertension and dyslipidaemia could be implemented where necessary.(20)

The prevalence of DR has previously been described for several populations,(8, 27) using different methods for the detection and classification of DR which accounts in part for the broad variations observed. A recent systematic review,(27) conducted an individual participant analysis to estimate the global prevalence of DR and also to determine the major risk factors by pooling a total 35 studies (22,896 people) conducted between 1980 and 2008 in the USA, Australia, Europe and Asia. The studies obtained retinal photographs using a mixture of 35mm film and digital images, through dilated and undilated pupils capturing between one and nine fields per eye with a minority photographing one eye only. There were also several different grading protocols used to ascertain the prevalence and severity of DR.

The objective of our study was to accurately determine the prevalence of DR at entry into a National screening programme utilising standardised protocols and quality assured methodology for both photography and grading and also to explore the relationship between

certain putative risk factors with the presence of any lesions of DR and also the presence of sight-threatening DR in persons with type 1diabetes and type 2 diabetes.

MATERIALS AND METHODS

The Diabetic Retinopathy Screening Service for Wales (DRSSW) is a community based mobile screening service. Visual acuity is recorded (achieved with or without glasses or with pinhole) using a 3m illuminated Snellen chart and two 45° fields (one macula centred and one nasal) digital fundal photographs are captured following mydriasis (1% tropicamide) followed by grading by accredited retinal graders. Images are stored on laptop computers and then downloaded daily onto a central server, either directly or via a secure internet connection. The DRSSW employs 30 photographic teams consisting of a health care professional and accredited photographer who conduct the screening at 220 locations throughout Wales. The Canon DGi digital camera is used to acquire the digital images which are centrally graded using a standardised grading protocol (table 1). All the key elements are subject to quality control procedures. At the time of screening all persons are asked to sign a two part consent form. The first part is to give consent mydriasis to be instilled and for retinal photographs to be taken. The second part is for consent for their anonymised data and images to be used for teaching and research purposes. Only the data for those individuals who provided both consents were included in this study.

Table 1 A comparison of grading protocols for diabetic retinopathy

ETDRS scale(28)		NSC(29)		DRSSW	
10	No Diabetic Retinopathy	RO	No Diabetic Retinopathy	RO	No Diabetic Retinopathy
20 - 35	Very mild – Mild Non Proliferative Diabetic Retinopathy	R1	Background Diabetic Retinopathy	R1.1	Minimal Background Diabetic Retinopathy
				R1.2	Moderate Background Diabetic Retinopathy
43 - 53	Moderate – Severe Non Proliferative Diabetic Retinopathy	R2	Preproliferative Diabetic Retinopathy	R2	Preproliferative Diabetic Retinopathy
≥61	Proliferative Diabetic Retinopathy	R3	Proliferative Diabetic Retinopathy	R3	Proliferative Diabetic Retinopathy
		M0	No Maculopathy	M0	No Maculopathy
		M1	Maculopathy	M1	Possible Maculopathy
				M2	Definite Maculopathy

Key: ETDRS – Early treatment of diabetic retinopathy study; NSC – National Screening Committee (UK); DRSSW – Diabetic retinopathy screening service for Wales

Persons with diabetes aged 12 years or above who are registered with a general practice (GP) in Wales and not already under the care of HES for DR related reasons, are required to be referred to the DRSSW accompanied by demographic and diagnostic information. These referrals from GP's form the single collated list of persons for screening. On a monthly basis the lists are complied and sent to each GP practice for validation. 8.4% of those known to have diabetes in Wales were ineligible for screening as 6.5% were already under the care of HES for DR related reasons, 1.6% were excluded due to medical reasons and 0.4% were under the age of 12 years (19.3% of those who were eligible for screening did not attend appointments). All persons invited for screening are sent an appointment letter with a date, time and venue for screening. All letters have a reminder that all appointments and venue can be changed to a time and place more suitable for the individual. The DRSSW currently (2013) has an uptake rate of 80% for screening. Any person who does not attend a screening appointment are sent additional appointments within 3 months and their GP's are informed of

their non-attendance and are asked to remind their patients of the importance of attending screening.

DRSSW utilise a grading protocol which evolved from the European handbook for screening(9) and all subsequent changes were made by consensus with ophthalmologists across Wales as part of the All Wales Ophthalmology group who provide advice and guidance to the DRSSW on DR and referrals to the HES. Subjects with DR were sub-divided into two groups: non sight-threatening DR (NSTDR) which included those with background DR (BDR) and pre-proliferative DR (PPDR); and sight-threatening DR (STDR) i.e. maculopathy and/or proliferative DR (Table 1). As retinal thickening or clinically significant macular oedema is not discernible on non-stereoscopic images, maculopathy was defined as definite exudates or haemorrhages (with an unexplained VA of worse than 6/12) within 1 disc diameter of the fovea. Both eyes were assessed for DR and the worse grade from the two eyes used in the analysis. All persons with unassessable images in one or both eyes that had not previously been seen by an ophthalmologist were referred to HES for assessment. Where only one eye was assessable the presence or absence of DR relied on this eye as was the grading of DR if present. The NSC definition of unassessable images is used by the DRSSW.(30)

Characteristics of the study population were described using means (SD) for continuous variables with percentages for categorical variables. For comparisons, T-tests and chi-squared tests were used respectively with a p-value of <0.05 used to indicate statistical significance. Logistic regression analyses were performed to assess the association of the routinely collected variables with retinopathy status, separately for each type of diabetes. The continuous variables of age at diagnosis of diabetes and duration of diabetes were

categorised to avoid assuming linearity, with different categories used for type 1 and type 2 diabetes to ensure equal distribution among the groups. For type 1 diabetes, age at diagnosis was divided into sub groups ≤12 yrs, 13 to 23 yrs and ≥24 yrs and diabetes duration into sub groups <10 yrs, 10 to 19 yrs and ≥20 years. For type 2 diabetes the sub groups for age at diagnosis were ≤55 yrs, 56 to 66 yrs and ≥67 yrs and for diabetes duration were <5 years, 5 to 9 years and ≥10 years respectively. Odds ratios (OR) and 95% confidence intervals (CI) for each were calculated.

RESULTS

From January 2005 to November 2009, 91,393 persons with type 1 or type 2 diabetes were screened by the DRSSW. The demographic characteristics of the participants are in included in table 2. The overall prevalence of any DR within this population was 32.4% (95% CI 32.1, 32.7), NSTDR 29.0% (95% CI 28.7, 29.3) and STDR 3.4% (95% CI 3.3, 3.5). The prevalence of any DR was 56.3% in persons with type 1 diabetes and 30.9% in persons with type 2 diabetes. NSTDR prevalence was 45.1% in type 1 diabetes and 28.1% in type 2 diabetes. For STDR the prevalence in type 1 diabetes was 11.2% and in type 2 diabetes was 2.9%. The prevalence's of the different categories of DR are shown in table 2.

Table 2 Characteristics of study participants at the occasion of first screening event.

	Type 1 diabetes	Type 2 diabetes
n	5,003	86,390
Age years	36.5 (16.4)	65.3 (11.7)
Gender n (%):		
Male	2,721 (54.7)	48,490 (56.4)
Female	2,257 (45.3)	37,446 (43.6)
Known duration of diabetes years	16.7 (13.2)	5.3 (5.6)
Treatment of diabetes:		
Diet only	0	26,025 (30.5)
OHA	0	51,071 (59.9)
Insulin	5,003 (100)	8,226 (9.5)
Age at diagnosis of diabetes years	19.7 (13.7)	60.0 (11.9)
Unassessable images % (95% CI)	0.5 (0.3, 0.7)	2.1 (2.0, 2.2)
DR status: % (95% CI)		
No DR	43.8 (42.4, 45.1)	69.0 (68.7, 69.3)
BDR	39.8 (38.4, 41.2)	26.5 (26.3, 26.9)
PPDR only	5.2 (4.6, 5.9)	1.5 (1.4, 1.6)
NSTDR	45.1 (43.7, 46.4)	28.1 (27.8, 28.4)
Maculopathy (with BDR)	4.2 (3.7, 4.8)	1.4 (1.3, 1.5)
PPDR with maculopathy	2.9 (2.5, 3.4)	0.97 (0.91, 1.04)
PDR only	2.6 (2.2, 3.1)	0.31 (0.28, 0.35)
PDR with maculopathy	1.5 (1.2, 1.9)	0.23 (0.20, 0.27)
STDR	11.2 (10.4, 12.1)	2.9 (2.8, 3.0)

Some subjects had missing values for gender and treatment. Numbers are mean (±SD) or n (%) unless otherwise stated Key: diabetes – Diabetes mellitus; OHA – Oral hypoglycaemic agents; 95% CI – 95% confidence intervals; No DR - No evidence of diabetic retinopathy; BDR – Background diabetic retinopathy; PPDR – Pre-proliferative diabetic retinopathy; NSTDR – Non sight-threatening diabetic retinopathy; PPDR with maculopathy – pre-proliferative diabetic retinopathy with exudates less than 1 disc diameter from the fovea; PDR – Proliferative diabetic retinopathy; PDR with maculopathy – Proliferative diabetic retinopathy with exudates within 1 disc diameter of the fovea; STDR – Sight-threatening diabetic retinopathy.

The characteristics of subjects with and without DR at initial screening are compared in table 3, with the former group divided into NSTDR and STDR. In subjects with Type 1 diabetes, those with STDR were more likely to be male, younger at the time of diagnosis, with a longer duration of diabetes and therefore older at first screening compared to those without DR. Participants with type 2 diabetes and STDR were also more likely to be male, younger at both the screening event and diagnosis of diabetes, with a longer duration of diabetes and in addition were more likely to be receiving insulin therapy compared to those without DR.

Table 3 Characteristics for subjects with type 1 and 2 diabetes presenting either without DR, with any DR, NSTDR or

	Type 1 diabetes				Type 2 diabetes	
	NDR (Reference)	Any DR	NSTDR	STDR	NDR (Reference)	Any
n	2,177	2,802	2,243	559	58,389	26,
Age years	34.5 (19.2)	37.9 (13.5)*	37.5 (14.0)*	39.1 (11.5)*	64.6 (11.7)	66.
Gender						*
Male	1,182 (54.5)	1,524 (54.7)	1,170 (52.5)	354 (63.4)*	32,162 (55.4)	15,
Female	985 (45.5)	1,264 (45.3)	1,060 (47.5)	204 (36.6)	25,886 (44.6)	10,
Duration of diabetes years	9.4 (10.5)	22.3 (12.2)*	21.9 (12.6)*	24.2 (10.5)*	4.3 (4.5)	7.6
Treatment of diabetes					*	*
Diet only	N/A	N/A	N/A	N/A	20,379 (35.3)	5,0
OHA	N/A	N/A	N/A	N/A	33,578 (58.2)	16,
Insulin	N/A	N/A	N/A	N/A	3,744 (6.5)	4,3
Age at diagnosis of diabetes years	25.2 (17.2)	15.5 (7.9)*	15.7 (7.9)*	14.9 (7.9)*	60.3 (11.7)*	58.

Numbers are mean (±SD) or n(%). Key: *P values <0.0001; N/A not applicable; diabetes – Diabetes mellitus; OHA – evidence of diabetic retinopathy; Any DR – any diabetic retinopathy; NSTDR – Non sight-threatening diabetic retinop retinopathy

The results of the logistic regression analysis are shown in Table 4. For type 1 diabetes subjects the odds ratio for each type of DR was significantly higher in those aged 12 to 23 years at diagnosis and significantly lower in those aged over 23 years when compared to those aged below 12 at diagnosis. Males also had an increased odds of all severities of DR compared to females. The odds ratio of all severity grades of DR increased sharply with duration of diabetes. There was a 7.90 and 20.60 fold increased odds of any DR associated with a duration of diabetes of 10-19 years and ≥20 years compared to <10 years and a 28.22 and 85.84 fold increased odds of STDR in the same sub-groups respectively. For type 2 diabetes the odds ratio of any DR and NSTDR was significantly higher (1.18 and 1.24 respectively) in those aged over 66 years at diagnosis of diabetes than in subjects aged 55 years or less at diagnosis. However the odds ratio of STDR decreased (0.60 and 0.58) with increasing age at diagnosis of diabetes. Males had an increased odds of all grades of DR compared to females. The odds of all grades of DR increased with increasing duration of diabetes for any DR the odds increased by a factor of 1.60 with a known duration of diabetes of 5-9 years and almost 3.71 fold of 10 years or more compared to less than 5 years and for STDR the odds increased from 1.83 to 6.76 fold in the same subgroups respectively. The use of insulin had ORs of 2.77 for any DR and 7.24 for STDR compared to those using diet alone.

Table 4 Multivariate logistic regression analysis for the association between age, gender and duration of diabetes with in persons with type 1 and type 2 diabetes.

Type 1 diabetes	n	Any DR OR (95%CI)	NSTDR OR (95%CI)	STDR OR (95%CI)	Type 2 diabetes	n	Any D OR (9
Age at diagnosis of diabetes years:					Age at diagnosis of diabetes years:		
≤12	1,725	1.00	1.00	1.00	≤55	30,184	1.00
13-23	1,703	1.34 (1.12, 1.58)	1.30 (1.09, 1.55)	1.26 (0.95, 1.66)	56-66	29,437	0.97 (
≥24	1,575	0.40 (0.34, 0.47)	0.40 (0.33, 0.47)	0.30 (0.22, 0.40)	≥67	26,599	1.18 (
Male	2,721	1.20 (1.04, 1.38)	1.14 (0.99, 1.32)	2.02 (1.58, 2.57)	Male	48,490	1.17 (
Duration of diabetes years:					Duration of diabetes years:		
<10	1,876	1.00	1.00	1.00	<5	49,390	1.00
10-19	1,341	7.90 (6.69, 9.32)	6.74 (5.68, 8.00)	28.22 (18.04, 44.15)	5-9	21,592	1.60 (
>/=20	1,786	20.60 (17.26, 24.59)	16.91 (14.10, 20.28)	85.84 (55.20, 133.50)	>/=10	15,238	3.71 (
					Treatment of diabetes:		
					Diet	26,025	1.00
					OHA	51,071	1.59 (
					Insulin	8,226	2.77 (

Key: diabetes – Diabetes mellitus; Any DR – any diabetic retinopathy; NSTDR – Non sight-threatening diabetic retino retinopathy; OR – Odds ratio; 95% CI – 95% confidence interval; OHA – Oral hypoglycaemic agent.
No DR is the reference group NSTDR group excludes STDR and STDR group excludes NSTDR

DISCUSSION

This study provides estimates of the baseline prevalence of DR for subjects over the age of 12 years and not receiving care at the hospital eye services for DR related reasons, when attending for the first time at the DRSSW. In the population studied the prevalence of any DR, NSTDR and STDR in subjects with type 1 diabetes were 56.3, 45.0 and 11.2% respectively and in type 2 diabetes were 30.9, 27.7 and 2.9% respectively. The presence of both NSTDR and STDR were strongly associated with increasing duration of diabetes with either type 1 or type 2 diabetes and was also associated with insulin therapy in those with type 2 diabetes.

The strength of this study is the large population size who underwent systematic screening using standardised quality assured procedures and equipment for both photography and grading. Both graders and photographers were accredited. The exclusion of subjects who did not participate in screening is a limitation. The exclusion of those persons with diabetes under the care of the HES because of DR is likely to lead to an under-estimation, however currently the extent of this difference is not known. Although PPDR is the level at which referral to HES is required by screening programmes in the UK, it was excluded from the category of STDR in this study so that it was more comparable to the category of STDR reported in previous studies. Also the limited availability of putative risk factors which included only duration and treatment of diabetes with glycaemic control, blood pressure and lipid status not collected by the DRSSW is a limitation and will be addressed in future studies.

The comparison of the prevalence rates for DR between studies is inherently difficult due to the changing classification of diabetes over time and the different grading protocols employed, as well as differences in population characteristics (8, 27, 31-34).

Web appendix 1 shows the prevalence rates found in previous studies worldwide. In other UK screening programmes the prevalence of any DR has been reported at 53.5% for type 1diabetes,(33) and 19.2 to 25.3% for type 2 diabetes,(3, 32, 33) which were lower than that seen in our study population at 56.0% and 30.3% respectively. Also in comparison, in Iceland the prevalence of DR was slightly lower in type 1 diabetes and higher in type 2 diabetes at 51.7%,(34) and 41.0%,(31) respectively. A recent meta-analysis found a much higher prevalence of DR in type 1 diabetes at 77.3%,(27) and a slightly lower prevalence in type 2 diabetes at 25.2%.(27) Retinal image capture (number of images and the use or not of mydriasis) may contribute to some of these differences as well as duration of diabetes. Our study clearly demonstrates that increased duration of diabetes is associated with a higher prevalence of DR. The prevalence of STDR previously reported in the UK has been 16.4% in type 1 diabetes and 1.9% and 6.0% in type 2 diabetes.(3, 32, 33) In our study the prevalence of STDR was a little lower in persons with type 1 diabetes at 11.2% Differences in the classification of STDR such as the inclusion or exclusion of PPDR and definitions of maculopathy may explain the differences.(32, 33) We had essentially similar prevalence's of STDR at 2.9% in type 2 diabetes. The Scottish screening programme reported the prevalence in 47,090 newly diagnosed type 2 diabetes and this short duration is likely to be the reason for the low prevalence of DR reported at 19.3% for any DR and 1.9% RDR.(3)

Increasing duration of diabetes was the most significant risk factor for the presence of any DR, NSTDR and STDR in subjects with both types 1 and type 2 diabetes. The odds ratios were much higher in type 1 diabetes compared to type 2 diabetes, however the duration of diabetes were also longer with subgroups of <10, 10-19 and ≥20 years compared to <5, 5-9 and ≥10 years respectively. The risk of all grades of DR increased

with duration of diabetes being particularly high in those with diabetes duration of 20 years or more for type 1 diabetes and 10 years or more for type 2 diabetes.
In our study we observed an increased risk of all severities of DR associated with the use of insulin after adjusting for all other confounders. For type 2 diabetes this may reflect a more advanced disease state and we interpret this as likely to be an epi-phenomenon and not a direct result of insulin therapy. Both glycaemia and duration of diabetes have previously been shown to be highly associated with the presence of DR along with elevated blood pressure and cholesterol levels.(4, 8, 33, 35-38)

To date this study represents the largest reported community-based national DR screening programme for detecting the presence of DR, especially STDR. The findings will provide our policy makers with important information for planning eye care services, with the proviso that the prevalence of STDR may be underestimated because of those already within hospital eye services. The strong association with disease duration demonstrates the importance of early detection and referral to a screening programme. The detection of STDR at an early stage is essential to ensure timely onward referral for further assessment and possible treatment to improved outcome. Detection of NSTDR provides the physician with an opportunity to improve, where necessary, glycaemic and blood pressure control to prevent the progression of DR. A structured screening programme is expected to reduce blindness by 40% within 4 years.(29) Addressing issues of non-attendance currently at approximately 20% will contribute greatly to the success of such programmes to ensure optimal cost benefit of any DR screening service, especially poignant in times of austerity.

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Ethics All data from those persons who consented at screening for their anonymous data to be used in research was anonymised at source by the data manager prior to being provided to the study team for analysis. R&D and ethics approval was sought for this study however both panels decided the study was a service evaluation and not research and as such R&D and ethical approval was not required.

Contributors All authors contributed to the writing of this report. R Thomas processed, analysed and interpreted the data. F Dunstan provided statistical advice and analysis. DR Owens, S Luzio and R Gibbins contributed to the conception, study design, interpretation of the data. S Roy Chowdhury contributed to processing and interpreting the data and S Hale and R North provided expert advice. All authors revised and approved the final version of this manuscript. DR Owens had full access to all of the data in this study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Competing interests All authors declare that there are no conflicts of interest.

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