

Diabetic Retinopathy

...What Paediatric MDT should know



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Declarations / Conflicts of Interest

- Although there is no obvious conflict of interest with this talk
- I have received fees from Bayer, Allergan, Roche and Boots Opticians for consultancy work or advisory board participation
- and part of my salary is supported by the NHS Diabetic Eye Screening Programme in Public Health England.

Learning points from talk

- Point 1 - Retinopathy levels at age 12-13 years in Type 1 diabetes
- Point 2 - Facts behind the age at which screening should commence
- Point 3 - The significance of one or more microaneurysms in one eye versus both eyes

Point 1 - Retinopathy levels at age 12-13

Four Nations Collaborative Group

- Data were extracted from 4 English screening programmes and from the Scottish, Welsh and Northern Irish programmes:
- Time from diagnosis of diabetes to first screening
- Age at diagnosis
- Retinopathy level.

Table1a. English NHS DESP retinopathy (R) grading

R Level	Description	Features
R0	No detected DR	
R1	Mild or “background” DR	At least one microaneurysm and/or retinal haemorrhage ± hard exudate ± CWS
R2 (STDR)	Moderate to severe or “pre-proliferative” DR	Presence of multiple deep blot haemorrhages and/or definite intraretinal microvascular abnormality and/or venous beading and/or reduplication
R3 (STDR)	Proliferative DR (any)	Presence of proliferative DR

Table1b. English NHS DESP maculopathy (M) grading

M Level	Description	Features
M0	No referable maculopathy	Absence of any M1 feature below
M1 (STDR)	Referable maculopathy	Any of the following: • exudate within 1 disc diameter (1DD) of the centre of the fovea • circinate or group of exudates within the macula • microaneurysm or haemorrhage within 1DD of the centre of the fovea, but only if associated with a best visual acuity of 0.3 logMAR or worse (equivalent to Snellen 6/12)

Point 1 - Retinopathy levels at age 12-13

- Data were available for **2125 children** with diabetes screened for the first time at age 12 or 13.
- In those diagnosed with diabetes at **2 years of age or less** the proportion with retinopathy in one eye 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 3 children** (aged **8, 10 and 11** at diagnosis of diabetes) had images graded with **referable** retinopathy and of these **2 had non-referable DR** at all subsequent screenings.

Should the screening age be reduced?

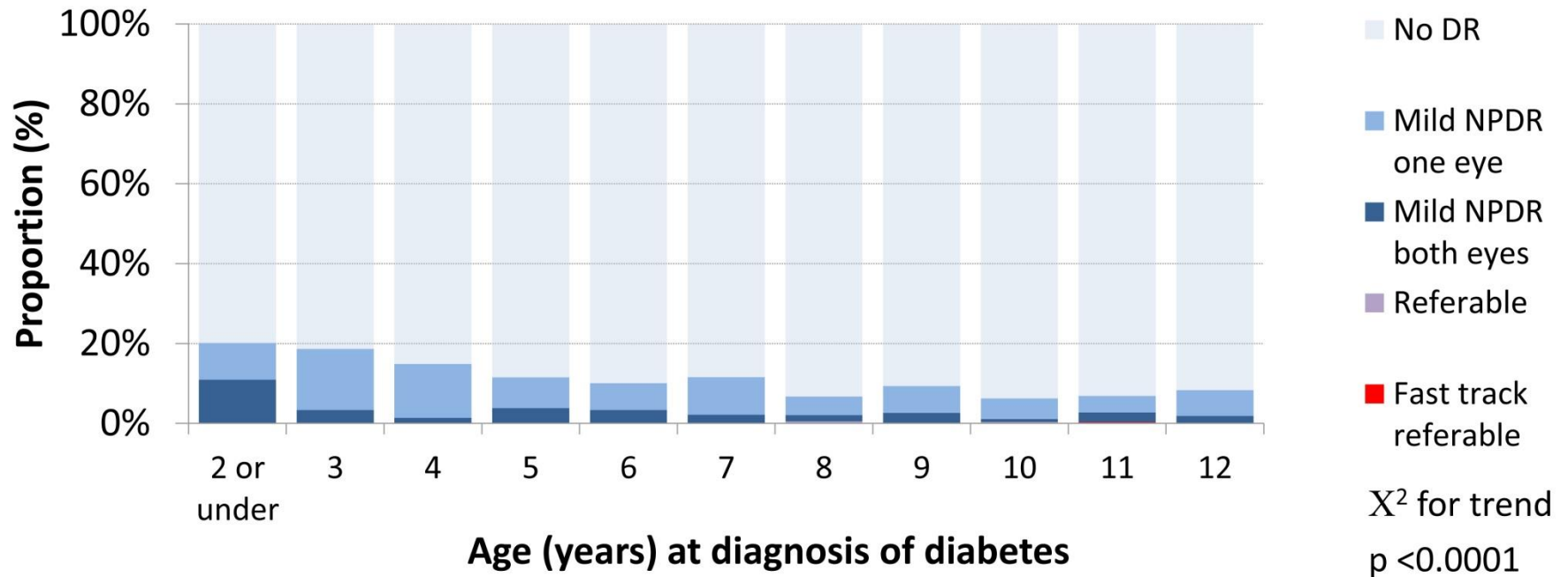
- Making the assumption that screening is to detect referable DR:
- In this large cohort of children diagnosed with diabetes before the age of twelve the low prevalence and incidence rates of referable DR suggest that earlier screening is not necessary in this age group

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

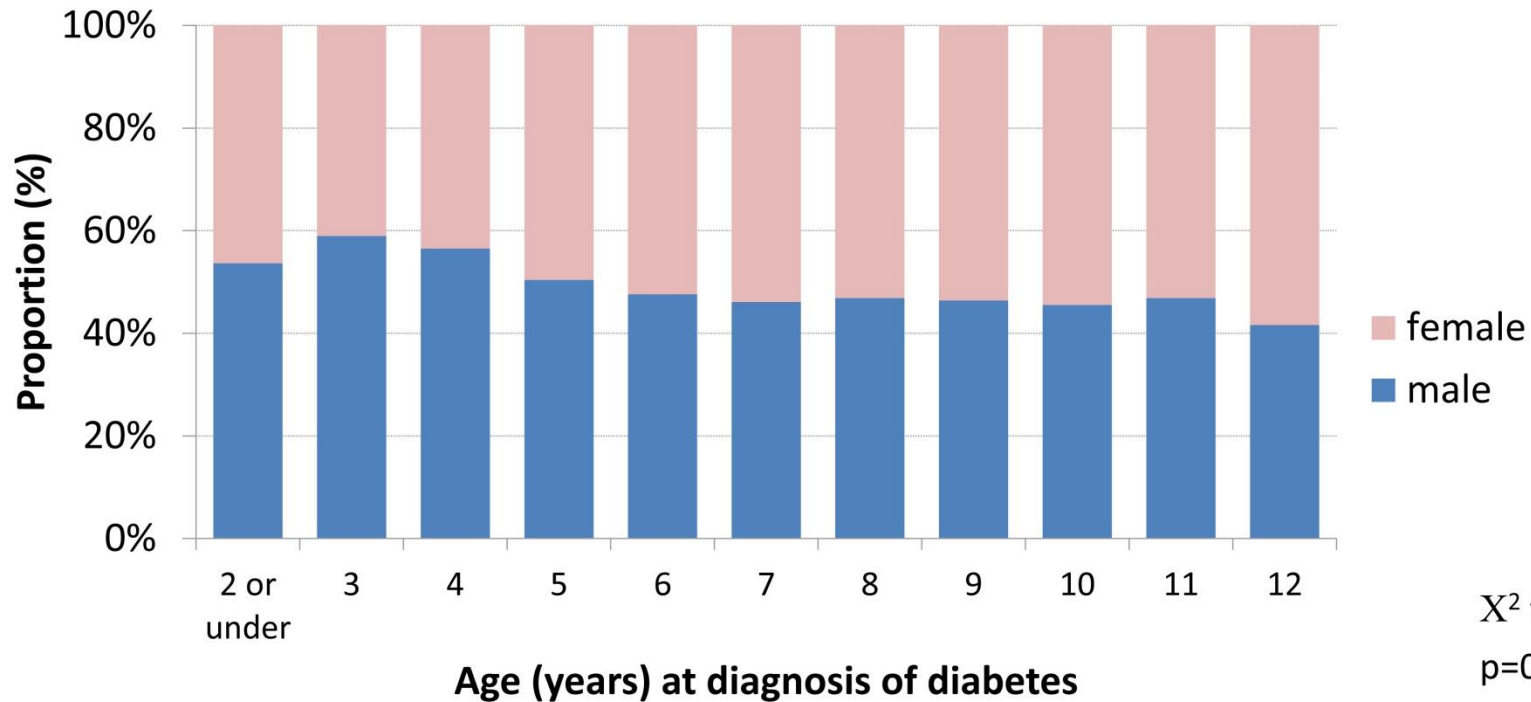
Age at diagnosis of diabetes	Number Total = 2125	Proportion with any DR	Proportion with mild NPDR in one eye	Proportion with mild NPDR in both eyes	Proportion with fast track or referable DR
2 or under	164	20.1%	9.1%	11.0%	0.0%
3	118	18.6%	15.3%	3.4%	0.0%
4	141	14.9%	13.5%	1.4%	0.0%
5	130	11.5%	7.7%	3.8%	0.0%
6	149	10.1%	6.7%	3.4%	0.0%
7	181	11.6%	9.4%	2.2%	0.0%
8	193	6.7%	4.7%	1.6%	0.5%**
9	224	9.4%	6.7%	2.7%	0.0%
10	271	6.3%	5.2%	0.7%	0.4%**
11	290	6.9%	4.1%	2.4%	0.3%**
12	264	8.3%	6.4%	1.9%	0.0%

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

Retinopathy level at first screen when aged 12 or 13



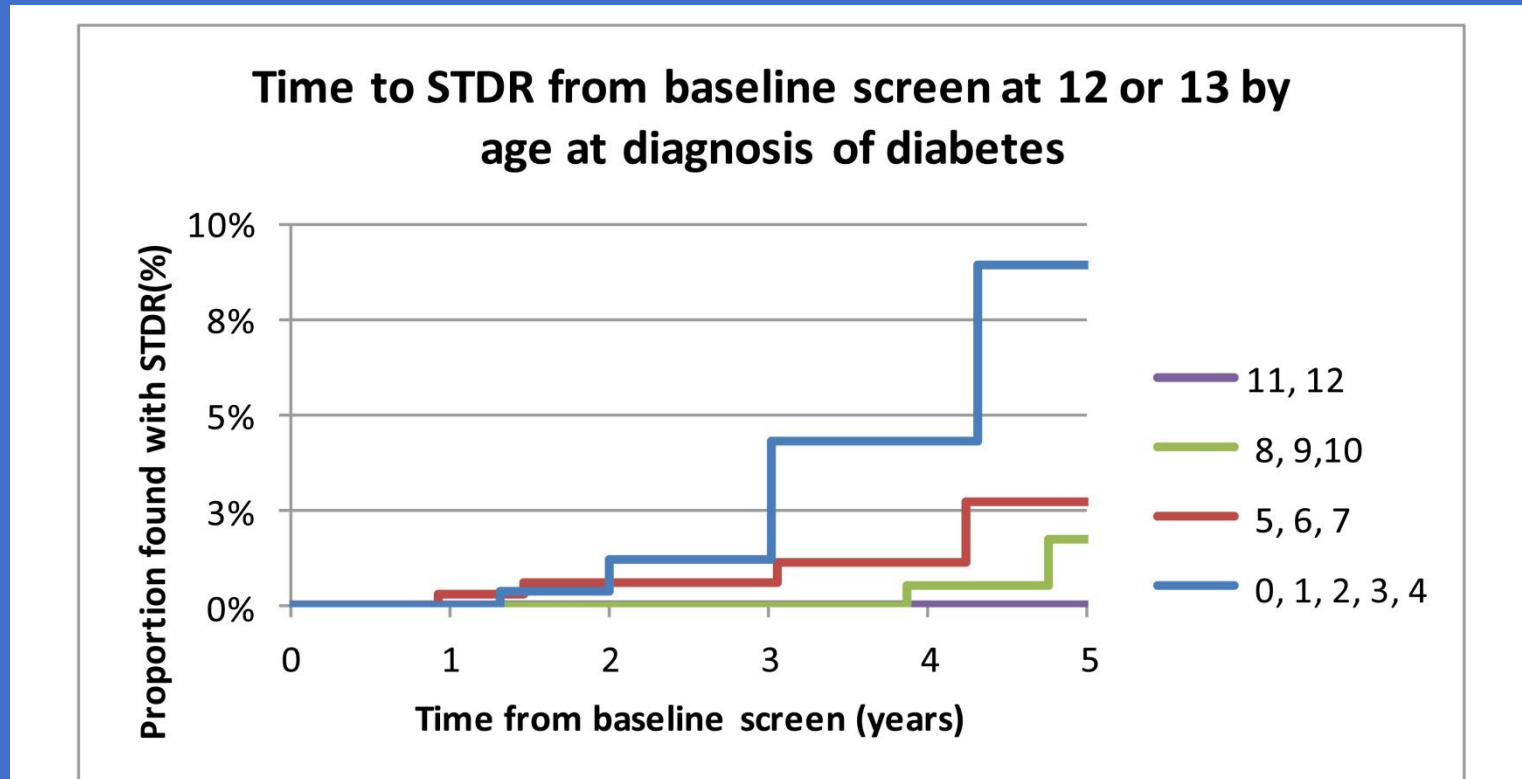
**Gender by age at
diagnosis of diabetes**



Point 1 - Retinopathy levels at age 12-13

- Of **1703 children with subsequent images**
- **25** were graded with **referable DR** over a **mean follow-up of 3.1 years**,
- **incidence rate of 4.7** (95% confidence interval (CI) 3.1-7.0) **per 1,000 per year**.
- Those with **longer duration** of diabetes were at higher risk of progression to referable DR with **hazard ratio of 1.36 per year since diagnosis** of diabetes (95% CI 1.20 to 1.53)

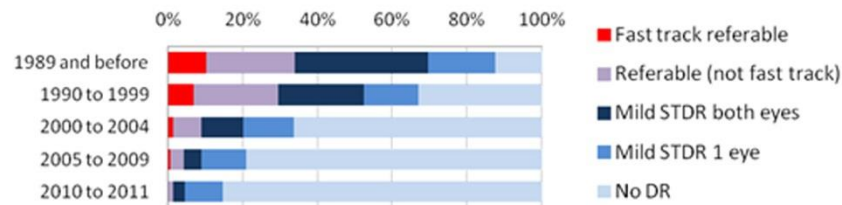
- Time to STDR from baseline screen at 12 or 13 years by age of diagnosis of diabetes



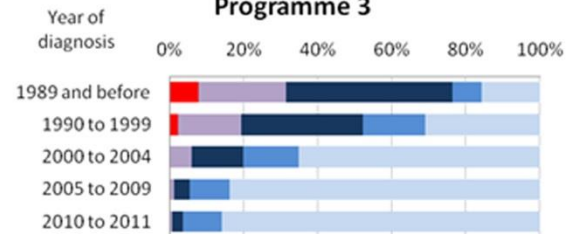
Screening Attendance, Age Group and Diabetic Retinopathy Level at First Screen. Four Nations Collaborative Group

- The time to first screening episode is strongly related to age at registration.
- **Within 18 months** of registration **89%** of 3,958 young people **under 18 years** of age and **81%** of 391,293 people **over 35** were seen.
- In 19,058 people **between 18 and 34 years** of age **80% coverage was not reached until 2 years and 9 months.**
- The **time from diagnosis of diabetes to first screening** is **positively associated with severity of disease** ($p < 0.0001$).

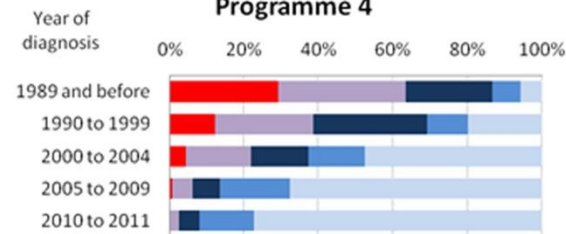
Programme 1



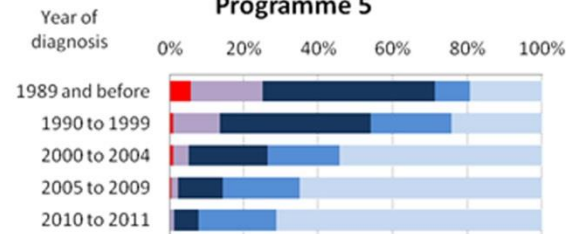
Programme 3



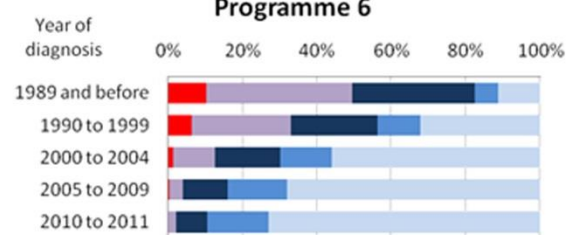
Programme 4

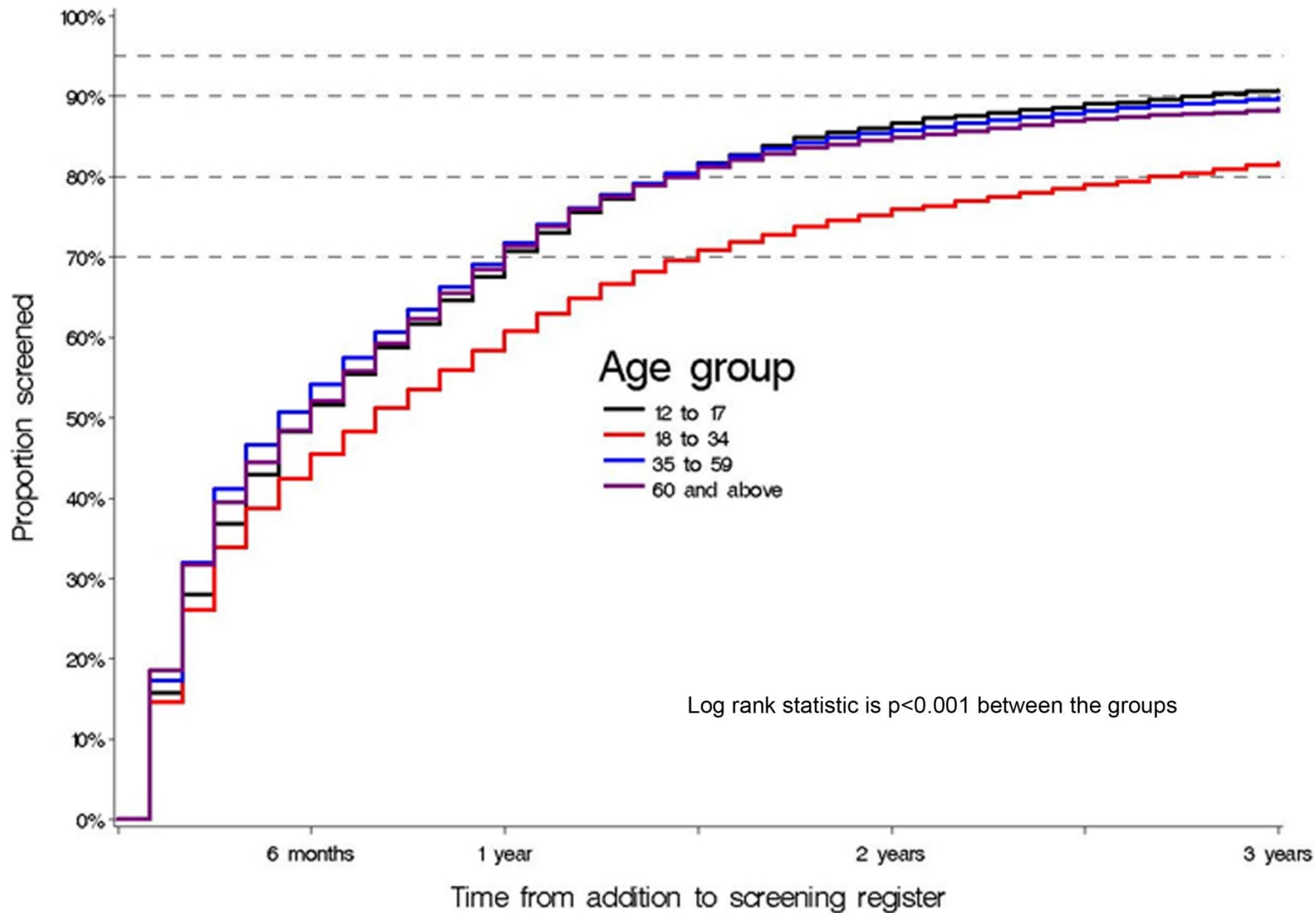


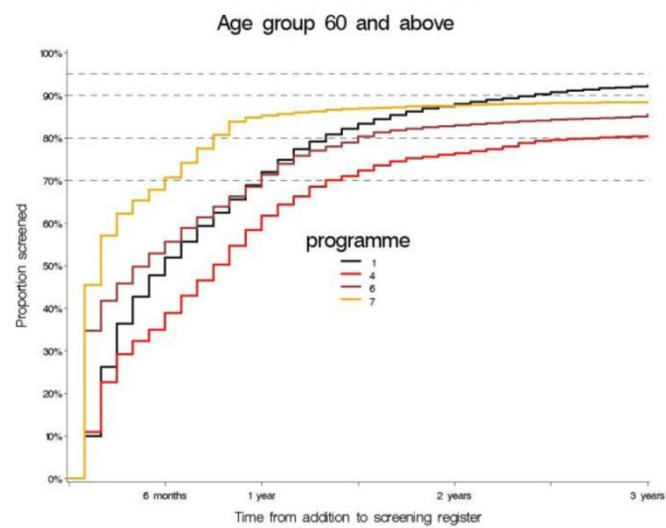
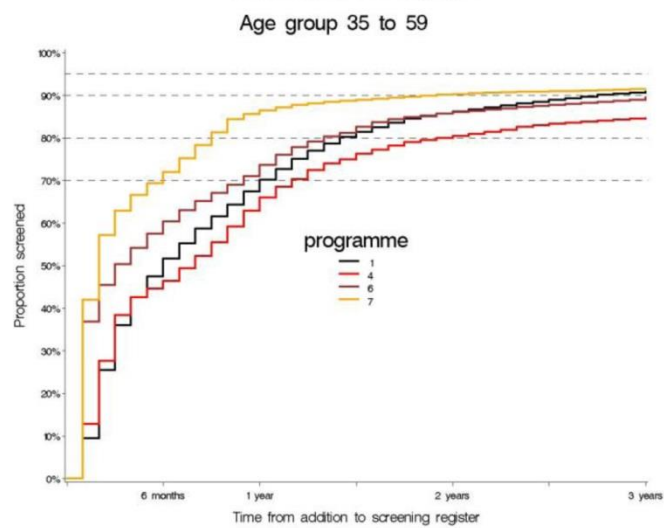
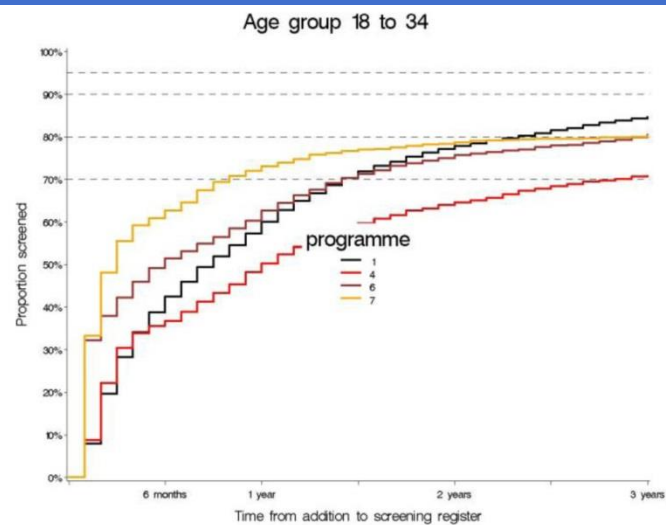
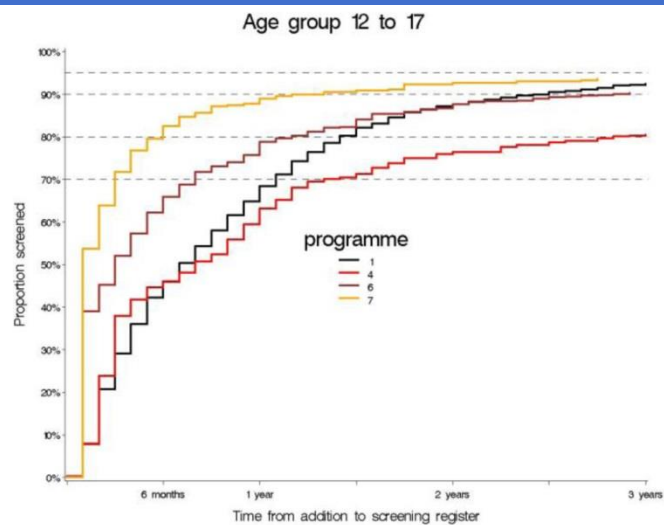
Programme 5



Programme 6







The p value for the difference between the age strata is $p < 0.0001$

Proportion with referable DR

- Between those diagnosed in **2010 or 2011** and those diagnosed **before 1990** the proportion with any diabetic retinopathy increased from **18% to 67%**,
- and the proportion with '**fast track**' referable diabetic retinopathy increased from **0.1% to 8.7%** (Table) (**chi-squared for trend $p < 0.0001$**).
- Those diagnosed with diabetes **before 1990** and first screened in **2010 or 2011** were **19** (95% CI 16 to 21) **times more likely** to have **referable diabetic retinopathy** than those diagnosed in 2010 or 2011 and **69** (95% CI 47 to 101) times more likely to have '**fast track**' referable diabetic retinopathy.

Results of first screening by date of diagnosis of diabetes, at first screening in 2011, all programmes combined.

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

Chi squared for trend for level of DR $p < 0.0001$

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

		Referable retinopathy	Urgent referral to ophthalmology
		Odds ratio and 95% CI	Odds ratio and 95% CI
Duration of diabetes	Up to 5 years (reference)	1	1
	5 to 9 years	3.5 (2.8 to 4.5)	4.5 (2.5 to 8.1)
	10 to 19 years	10.7 (8.6 to 13.2)	17 (10 to 28)
	20 years or more	15.8 (12.3 to 20.4)	33 (20 to 54)
Time from registration to first screen	Up to 2 months	1	1
	2 to 11 months	1.2 (0.9 to 1.4)	1.5 (0.9 to 2.6)
	12 to 35 months	1.9 (1.4 to 2.5)	2.8 (1.4 to 5.4)
	36 months or more	2.9 (2.3 to 3.6)	4.3 (2.6 to 7.1)
Diabetes type	T1DM	1	
	T2DM	0.72 (58 to 0.90)	
Age group	18 to 34 years (reference)	1	1
	35 to 59	1.4 (1.1 to 1.9)	1.1 (0.7 to 1.7)
	60 and above	1.1 (0.8 to 1.5)	0.6 (0.4 to 1.0)
Gender	Male	1	
	Female	0.82 (0.72 to 0.93)	

Fiona Laver thesis

- A thesis submitted in partial fulfilment of the requirements of the degree of Doctor of Clinical Psychology validated by the University of Oxford
- A Grounded Theory Exploration of Young Adults' Non-attendance at Diabetic Retinopathy Screening Appointments

Fiona Laver thesis 2

- **Nine young adults** diagnosed with Type 1 diabetes mellitus were recruited **from two screening services** and **interviewed**.
- Participants had not attended screening for a minimum of one year, during which period they would have received, and not responded to, at least one appointment letter and two reminder letters.

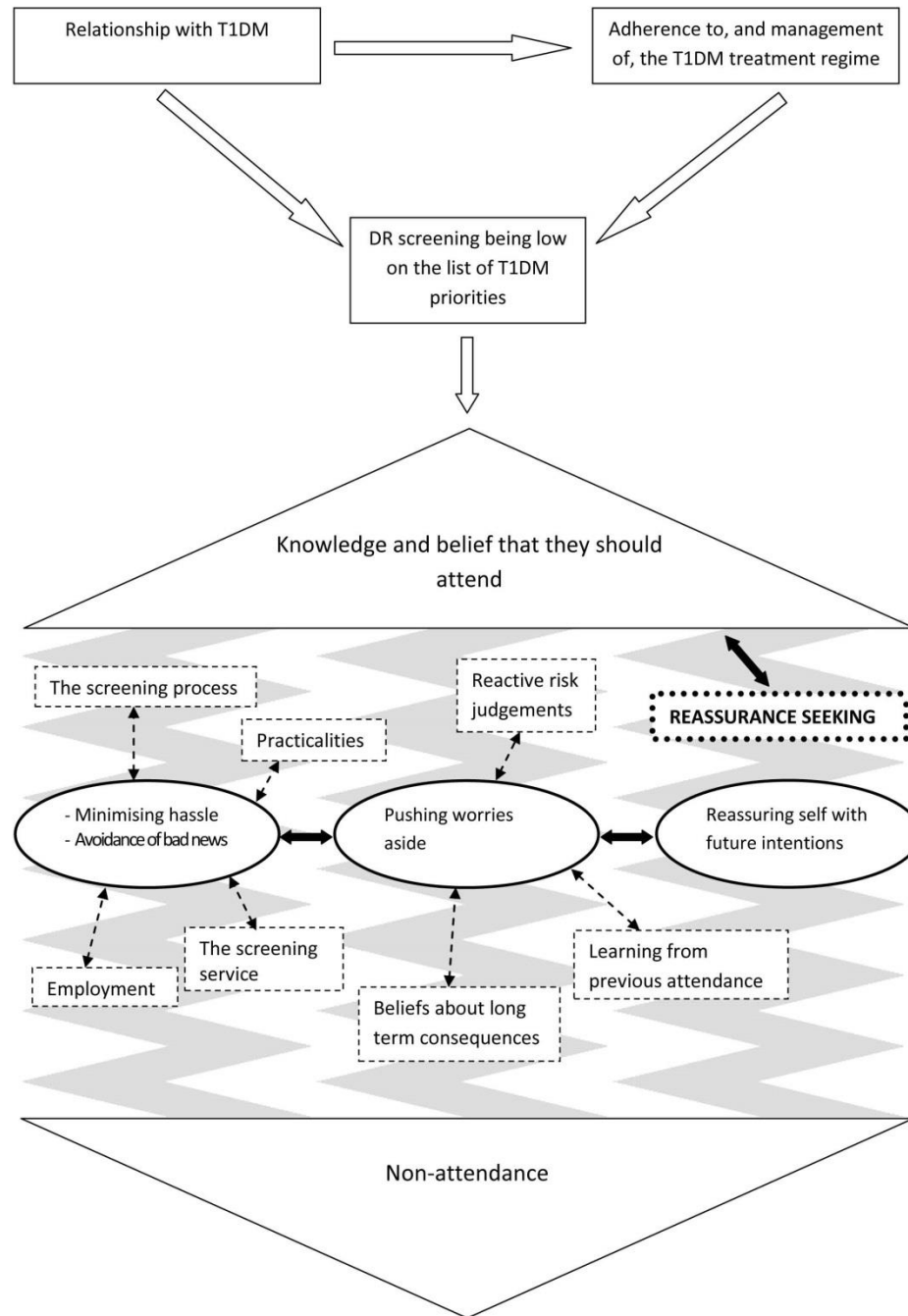


Figure 1. The grounded theory model developed.

The model developed illustrates that participants both **knew and believed they should attend screening.**

This created a conflict with their actual non-attendance behaviour.

Four strategies that participants employed to resolve this conflict were identified;

1. to **minimise 'hassle'** for themselves,
2. **avoid bad news,**
3. **push their worries** about not attending **aside** and
4. **reassure themselves with intention to attend in the future.**

Practical issues

Employment.

- Participants found it difficult to take **time off work** to attend screening appointments and were concerned about how 'time off' would be perceived by their employers and colleagues.
- Some were concerned about the **security of their jobs** in the current economic climate and considered it 'risky' to take time off.

Practicalities.

- **Time and location of appointments** and the need to be **accompanied** to screening were also considered '**hassles**'.
- **Morning appointments** particularly so due participants being '**wiped out**' (referring to the blurry vision they experienced after screening) for the **remainder of the day**.
- Generally participants were **not willing**, or perhaps able, to engage in a lot of **organising and planning** in order to manage the practicalities involved in screening attendance.

Qualitative research 1

Funding body: Research for Patient Benefit Programme PROJECT: 'Understanding factors leading to low uptake of diabetic retinopathy screening in Primary Care'.

End date: Completed in November 2012

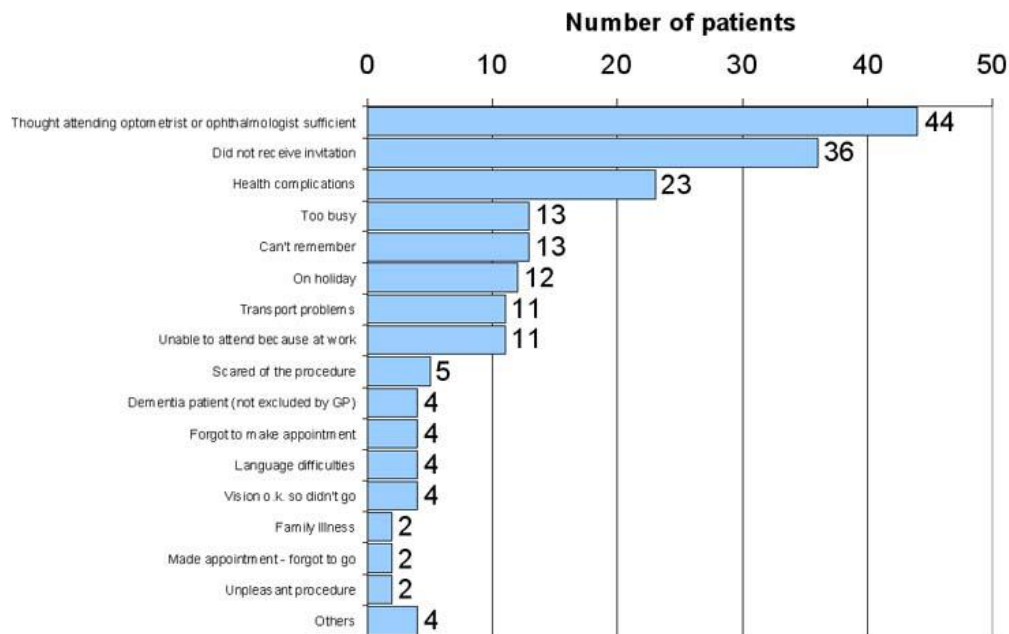
Factors that were seen as enabling or hindering screening uptake

	Practice 1: City	Practice 2: Small town	Practice 3: Small town	Practice 4: Rural	Practice 6: City	Practice 5: Small town	Practice 7: Rural	Practice 8: City	Practice 9: City
Outcome: DRS Uptake	96%	88%	85%	75%	73%	72%	71%	68%	57%
Deprivation (IMD rank out of 32, 482)	Most deprived 3,076	Below average 6,605	Most deprived 1,990	Above average 21,141	Most deprived 4,031	Below average 8,174	Least deprived 27,564	Most deprived 1,182	Most deprived 1,058
Language/ Ethnicity/ Cultural Issues	Neutral	Neutral	Neutral	Neutral	Neutral	Major barrier	Neutral	Major barrier	Major barrier
Transport and access	Minor enabler	Neutral	Minor enabler	Minor barrier	Minor barrier	Minor barrier	Major barrier	Minor barrier	Major barrier
Communication w. screening service	Neutral	Minor enabler	Minor enabler	Minor barrier	Major barrier	Minor barrier	Major barrier	Minor barrier	Minor barrier
Contacting patients pre-post screening	Neutral	Neutral	Minor enabler	Minor enabler	Minor enabler	Minor enabler	Minor enabler	Major enabler	Minor enabler
RPS integrated with other diabetes care	Minor enabler	Major enabler	Minor enabler	Neutral	Minor enabler	Minor barrier	Major enabler	Minor enabler	Major enabler
Integrating the newly diagnosed	Neutral	Minor enabler	Minor enabler	Minor enabler	Neutral	Neutral	Minor enabler	Minor enabler	Minor enabler
Staff describe unengaged patients	Yes	No	No	Yes	No	Yes	Yes	Yes	Yes

Qualitative research 2 (Audit)

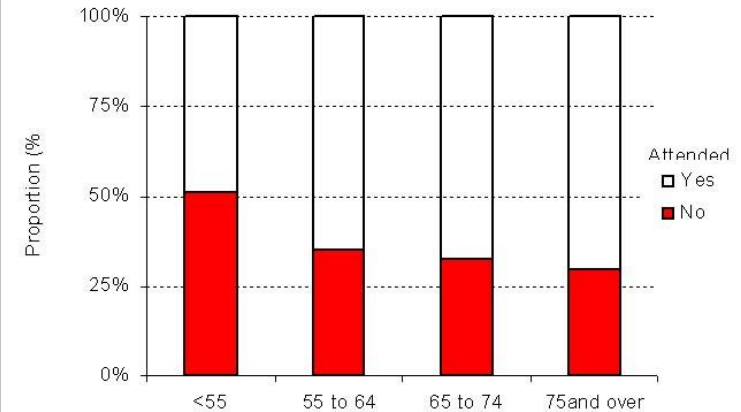
Sachdeva A, Stratton IM, Unwin J, Moreton R and Scanlon PH. Diabetic retinopathy screening: Study to determine risk factors for non-attendance. *Diabetes & Primary Care*. 2012; 14 (5): 308-16.

Reasons for non-attendance at screening



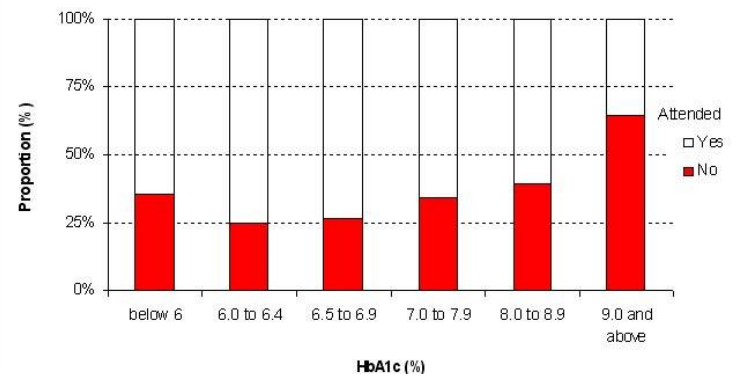
Age

$p < 0.001$ for trend



HbA1c

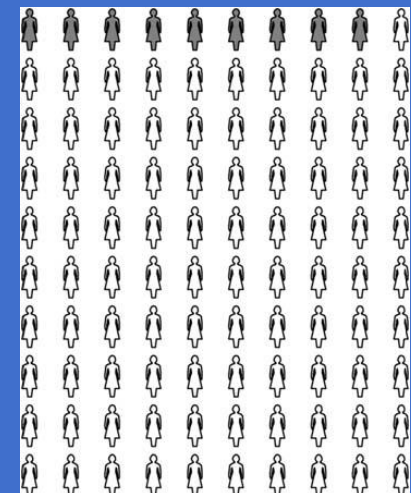
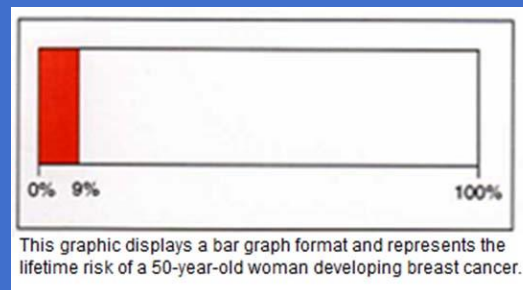
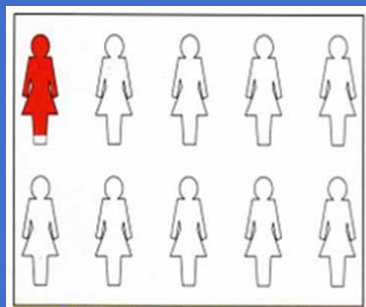
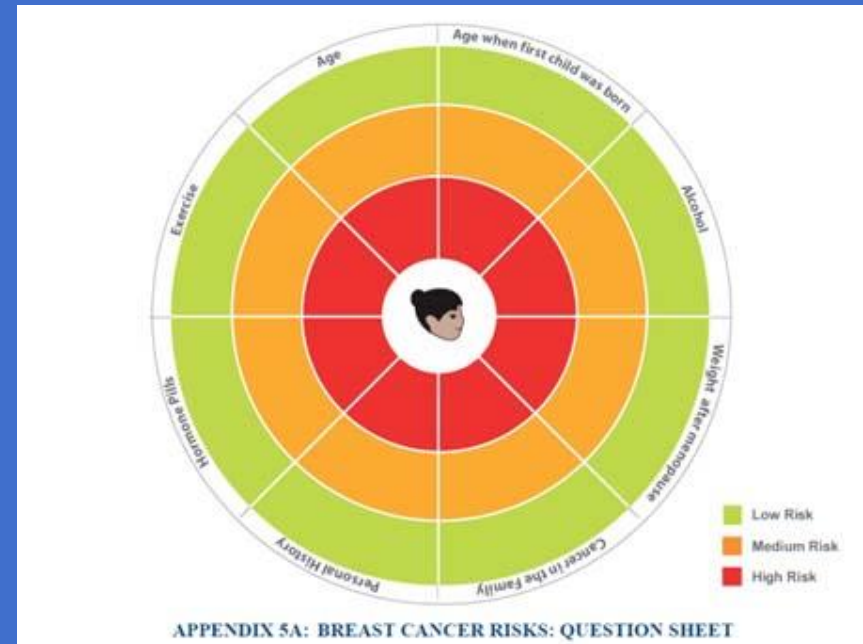
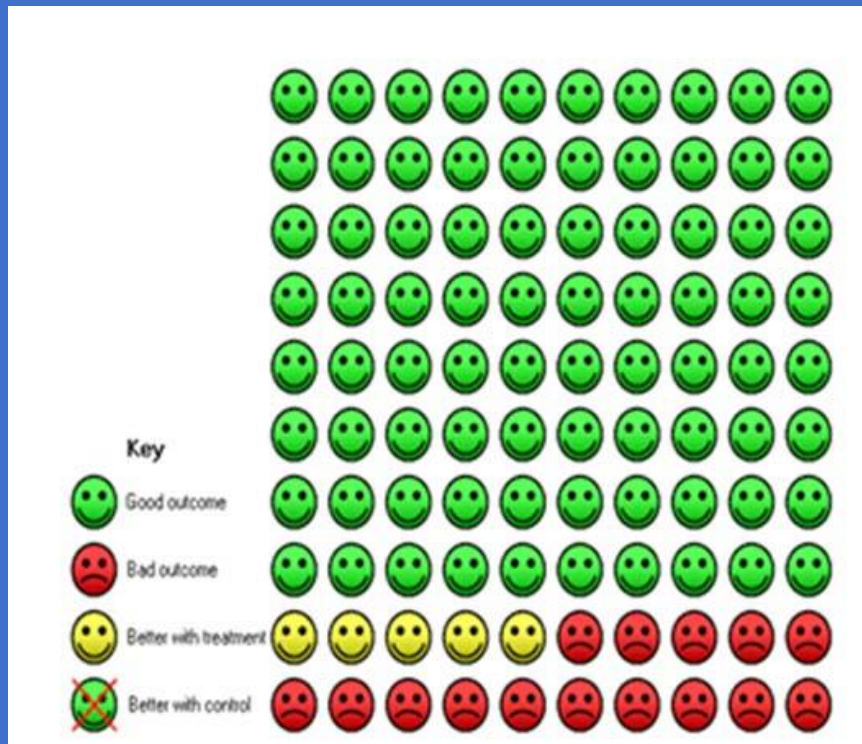
$p < 0.001$ for trend



Qualitative research 3

THE INFLUENCE RISK COMMUNICATION TOOLS ON DIABETES SELF MANAGEMENT

N. Al-Athamneh



Qualitative research 3

THE INFLUENCE RISK COMMUNICATION TOOLS ON DIABETES SELF MANAGEMENT

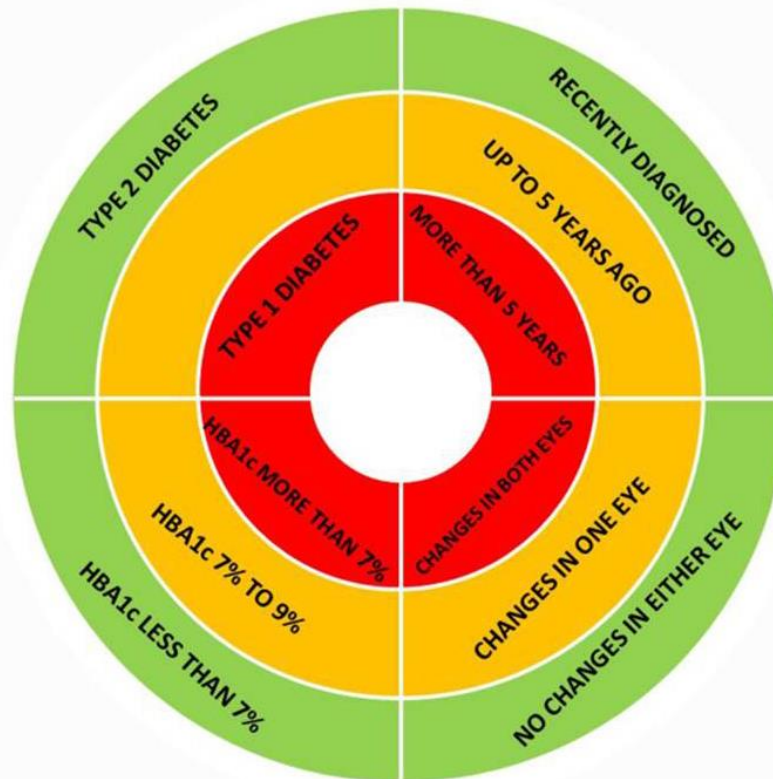
N. Al-Athamneh

"This traffic light system is really good way of explaining the risk factors of diabetic eye, I was a bit worried but now I can see clearly that I am at low risk"

(South Asian Participant)

"Yes I can understand this, green is safe, red is more risk of complications and blindness may be, yes, red is danger"

(South Asian Participant)



"Having scored 4 greens means that I am doing the wright thing, so I should continue the good work and keep my blood sugar under control and look after my diet"

White British Participant

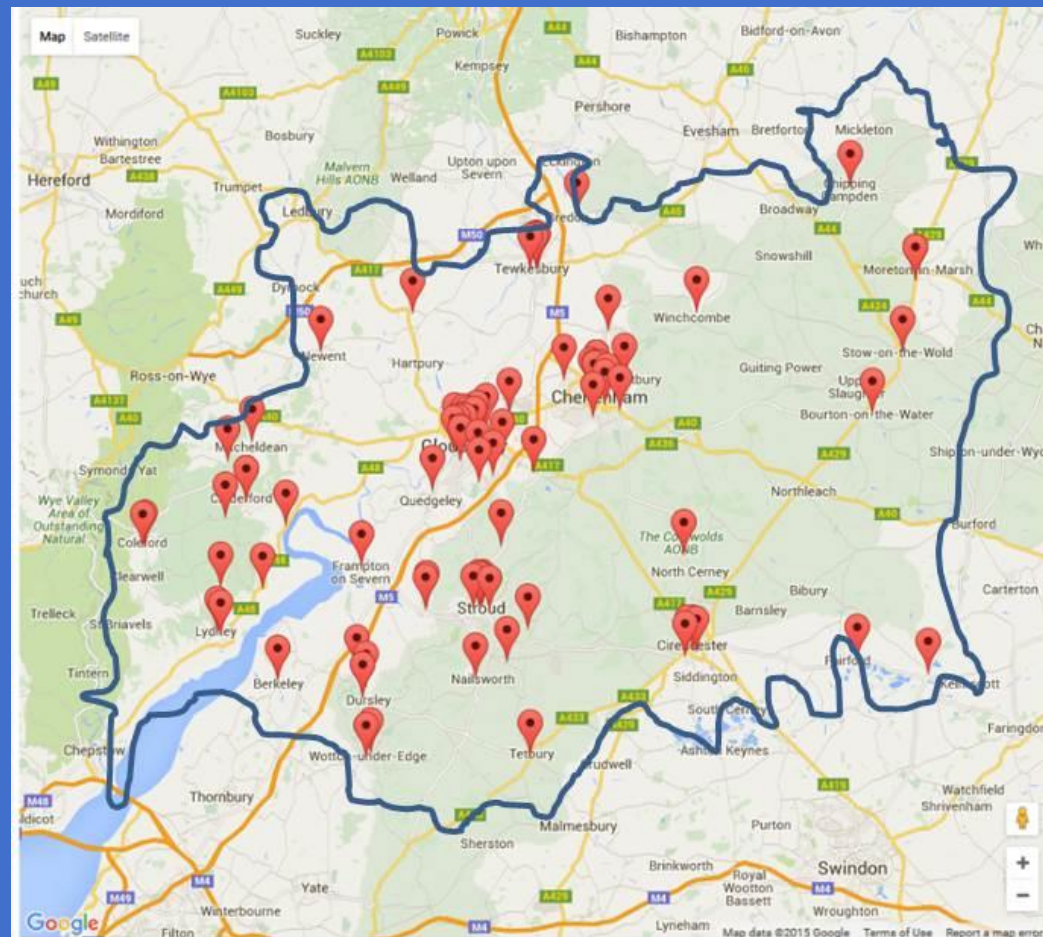
"Doing this test, made me think a lot deeper than I did before,because I have 2 reds and 2 green, I should give more attention to my diabetes to keep my eyes safe"

(White British Participant)

Health Equity Audit – Melanie Little

Gloucestershire Screening sites

31797 eligible patients



Differences in deprivation levels in Gloucestershire

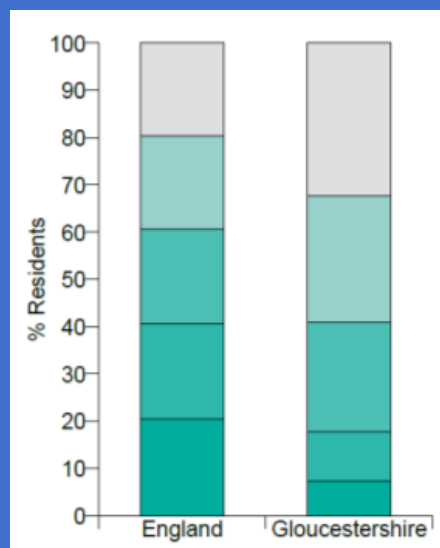
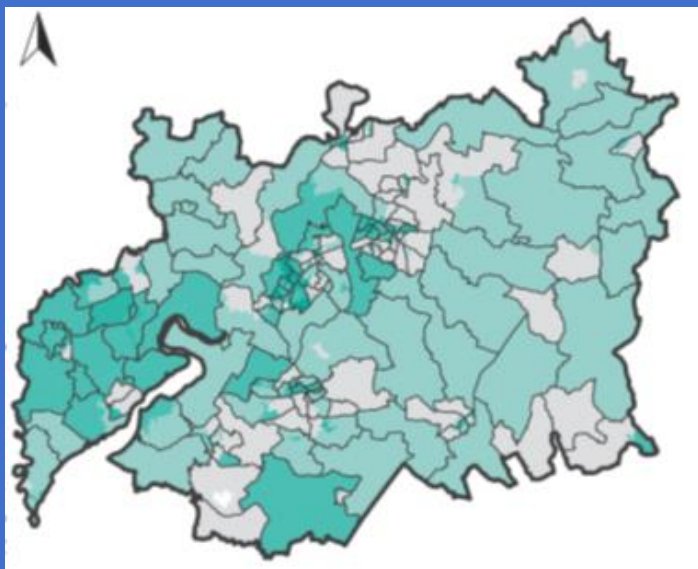
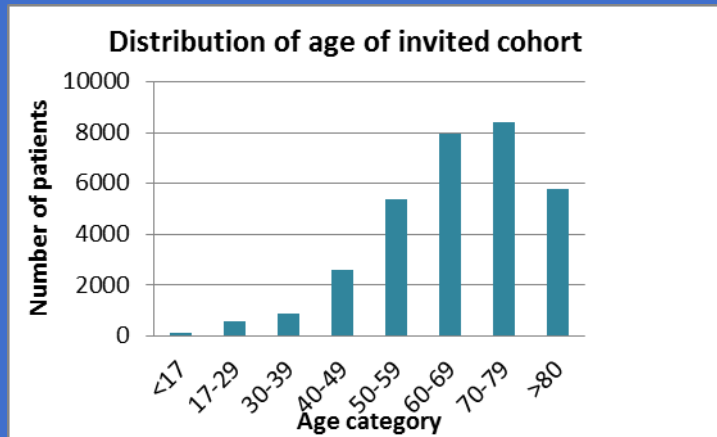
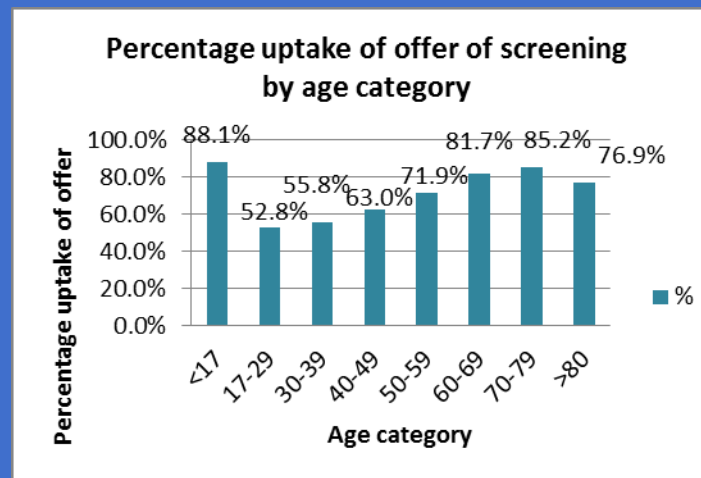


Figure 5: The darkest shaded areas are some of the most deprived areas in England. Using the bars on the right, it is clear that Gloucestershire has fewer of the most deprived areas when compared with the national average. Gloucestershire also contains a significant number of least deprived quintiles.⁽¹⁰⁾

Distribution of age of eligible patients invited for diabetic eye screening

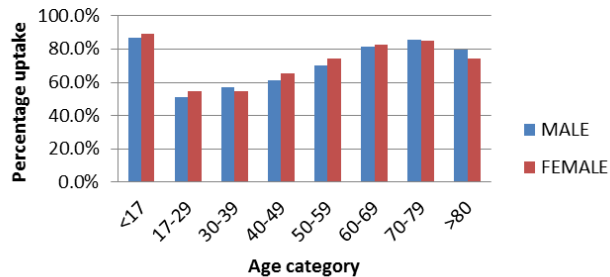


Programme Eligible Patients by Age		
AGE	Invited Count	%
<17	142	0.4%
17-29	580	1.8%
30-39	912	2.9%
40-49	2628	8.3%
50-59	5387	16.9%
60-69	7933	24.9%
70-79	8410	26.4%
>80	5805	18.3%
Total	31797	100.0%

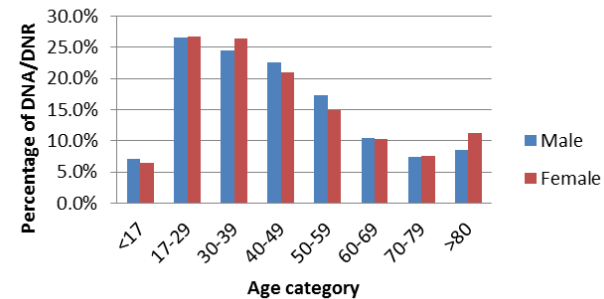


Percentage uptake of screening invitation by age and gender

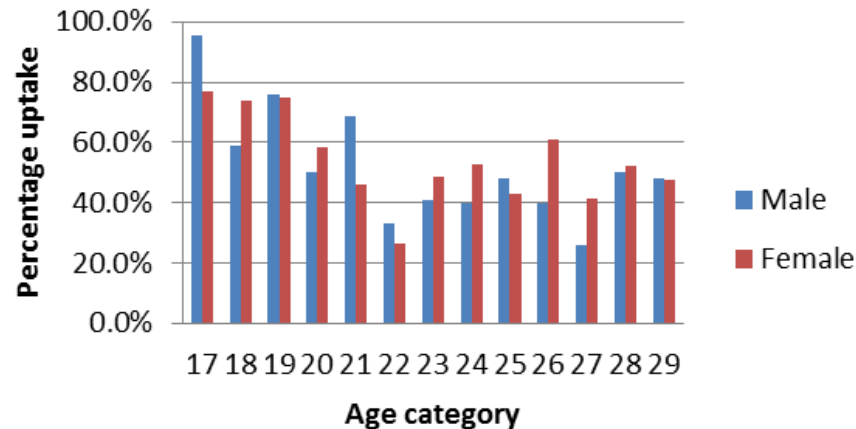
Percentage uptake of screening invitation by age and gender



Percentage of DNA/DNR by age and gender

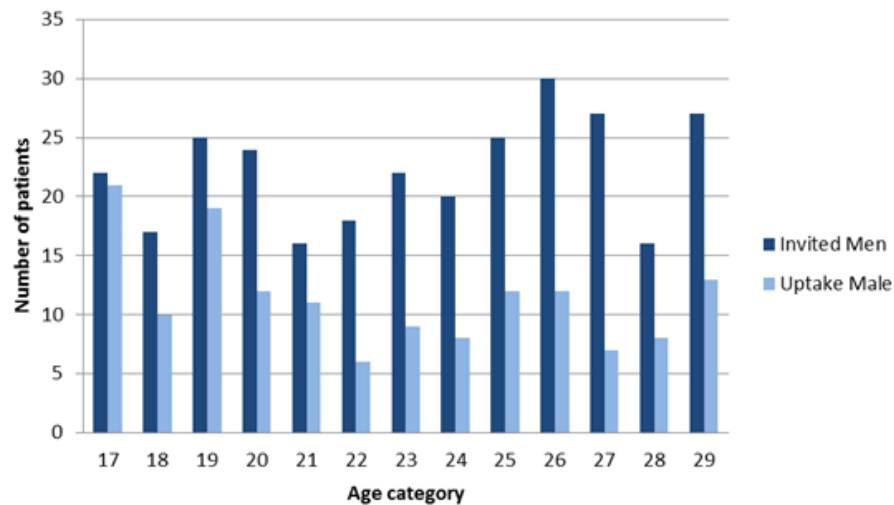


Percentage uptake by age 17-29

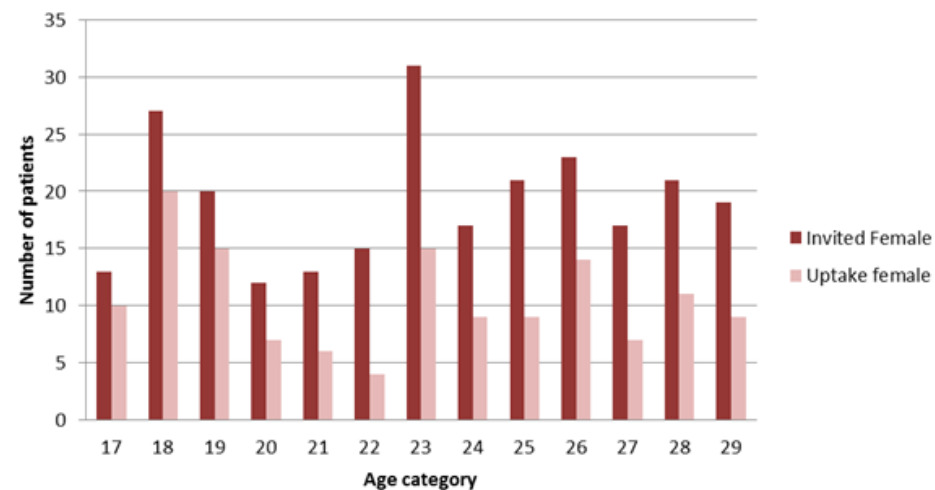


Uptake in males and females aged 17-29

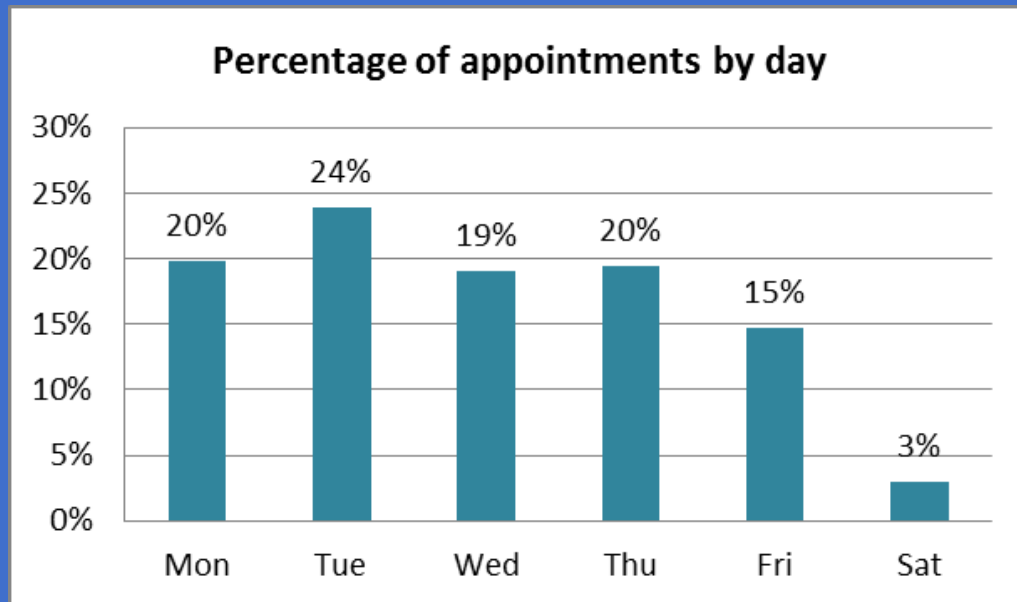
Uptake of screening invitation in males age 17-29



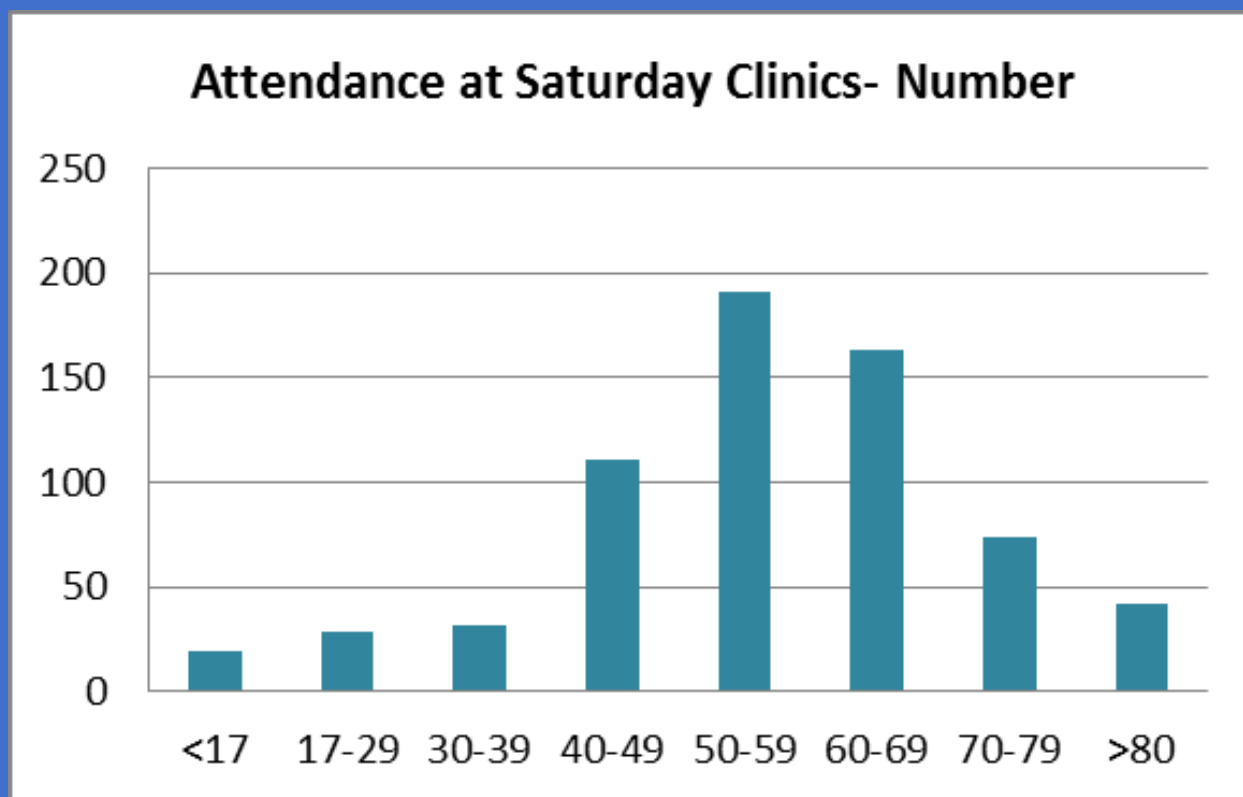
Uptake of screening invitation in females age 17-29



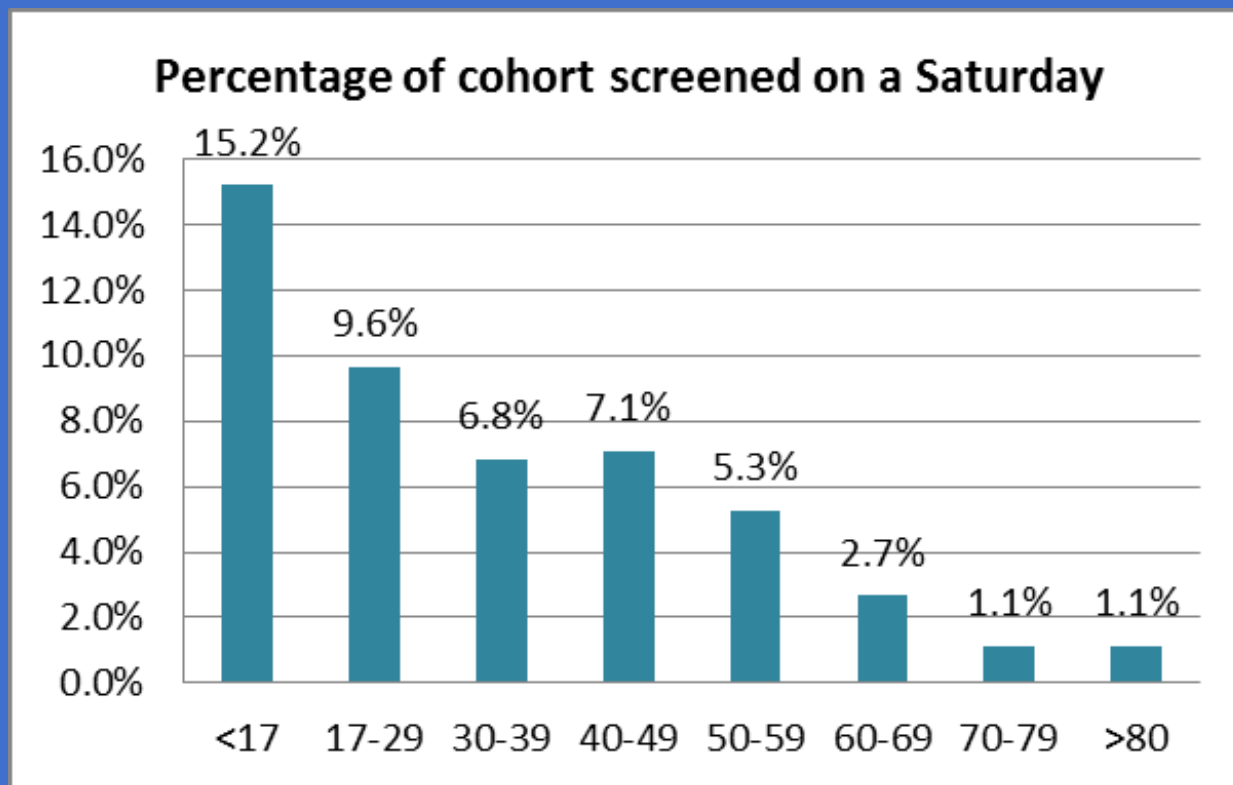
Percentage appointments by day



Attendance on Saturday clinics



Attendance on Saturday clinics



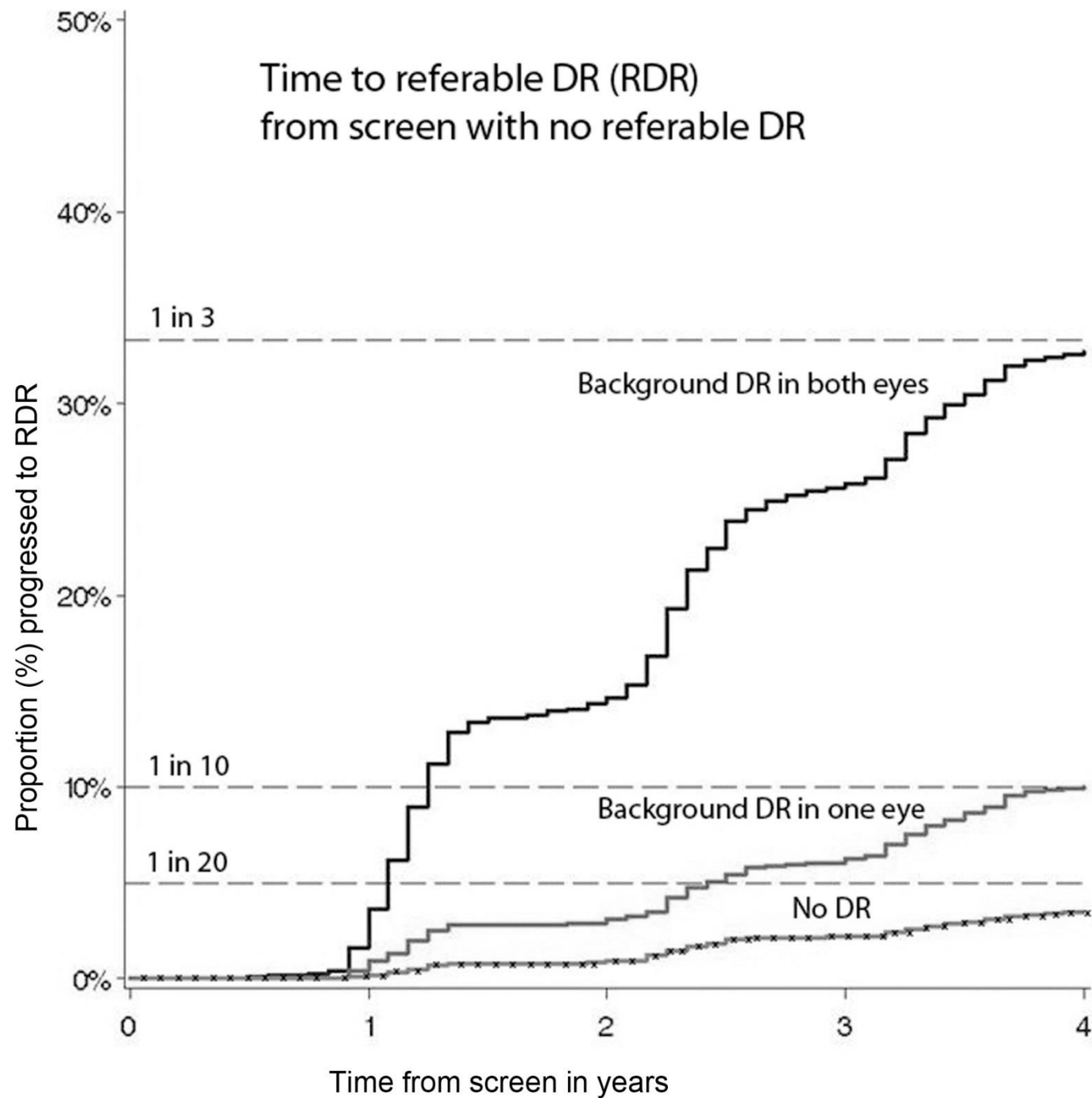
The significance of background DR in one eye versus 2 eyes

- Gloucestershire Population
- 19044 people with diabetes screened on at least 2 occasions between 2005 and 2010
- 56% men,
- age at screening 66 (57 to 74) years (median, 25th, 75th centile).

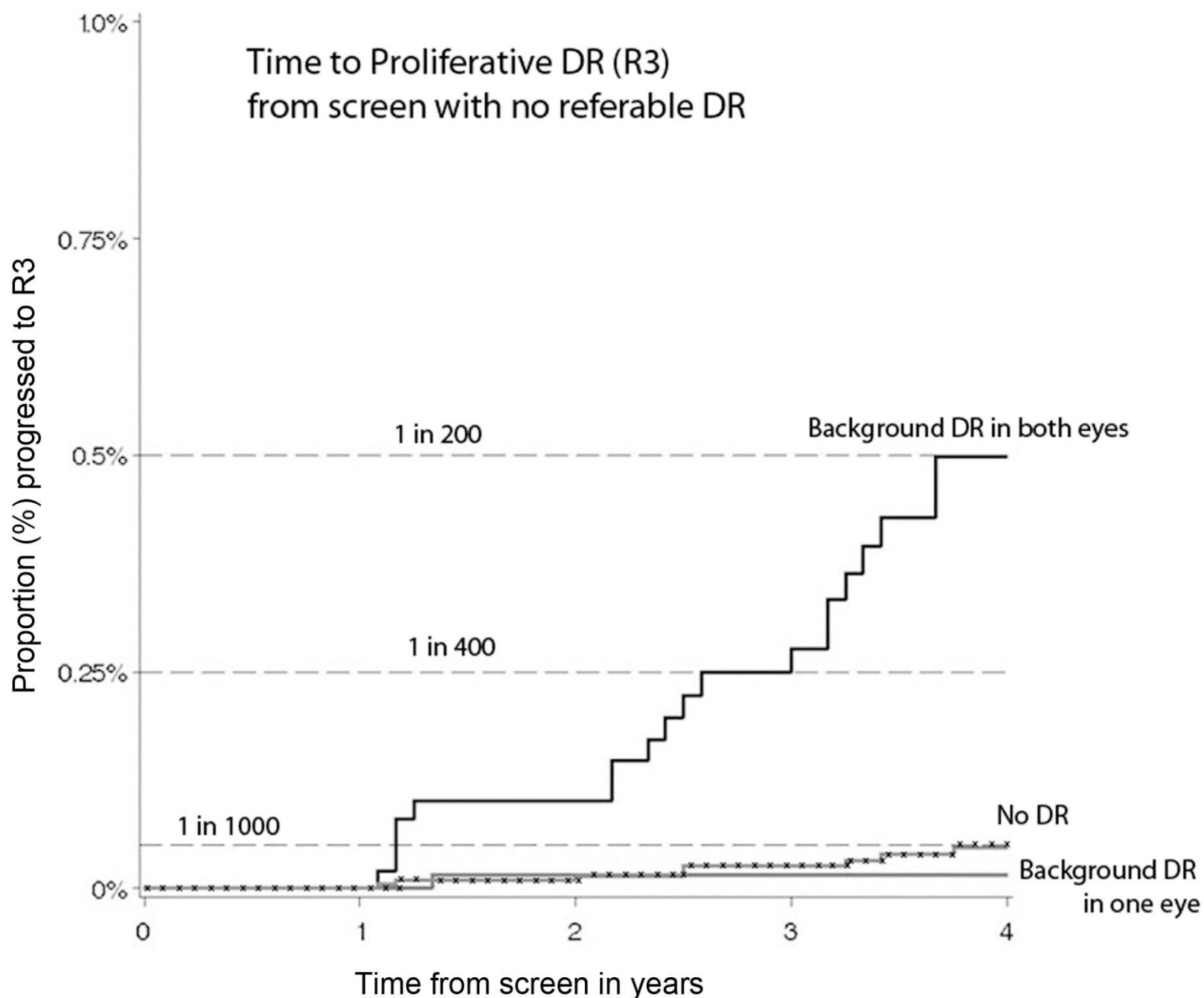
Scanlon P.H. Stratton I.M. Histed. M. Chave S.J. Aldington S.J. The influence of background diabetic retinopathy in the second eye on rates of progression of diabetic retinopathy between 2005 and 2010. *Acta Ophthalmol.* 2013 Apr 1. doi: 10.1111/aos.12074.

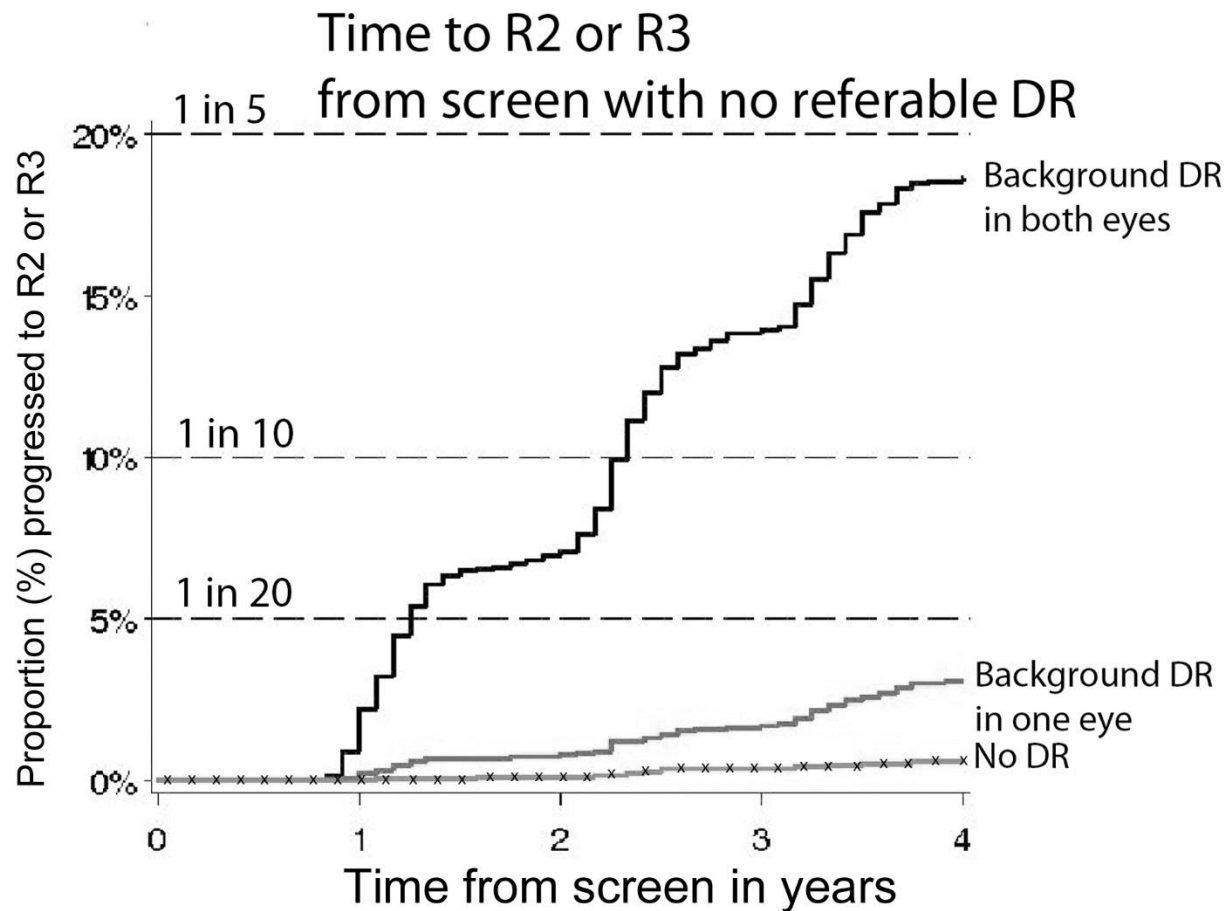
Progression

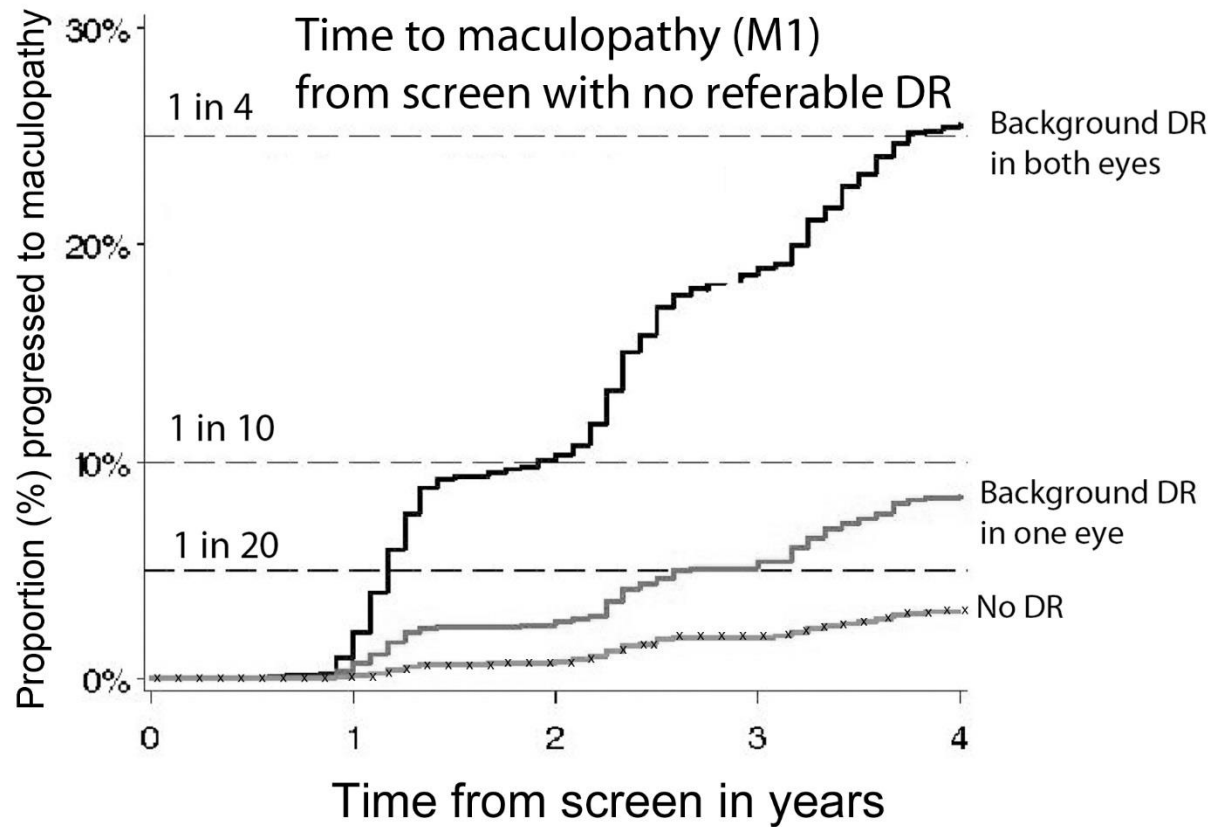
- A total of 8.3% of those with background DR in one eye progressed to referable DR - hazard ratio 2.9 [2.5 – 3.3]
- 28.2% of those with background DR in both eyes progressed to referable DR - hazard ratio 11.3 [10.0 – 12.8].



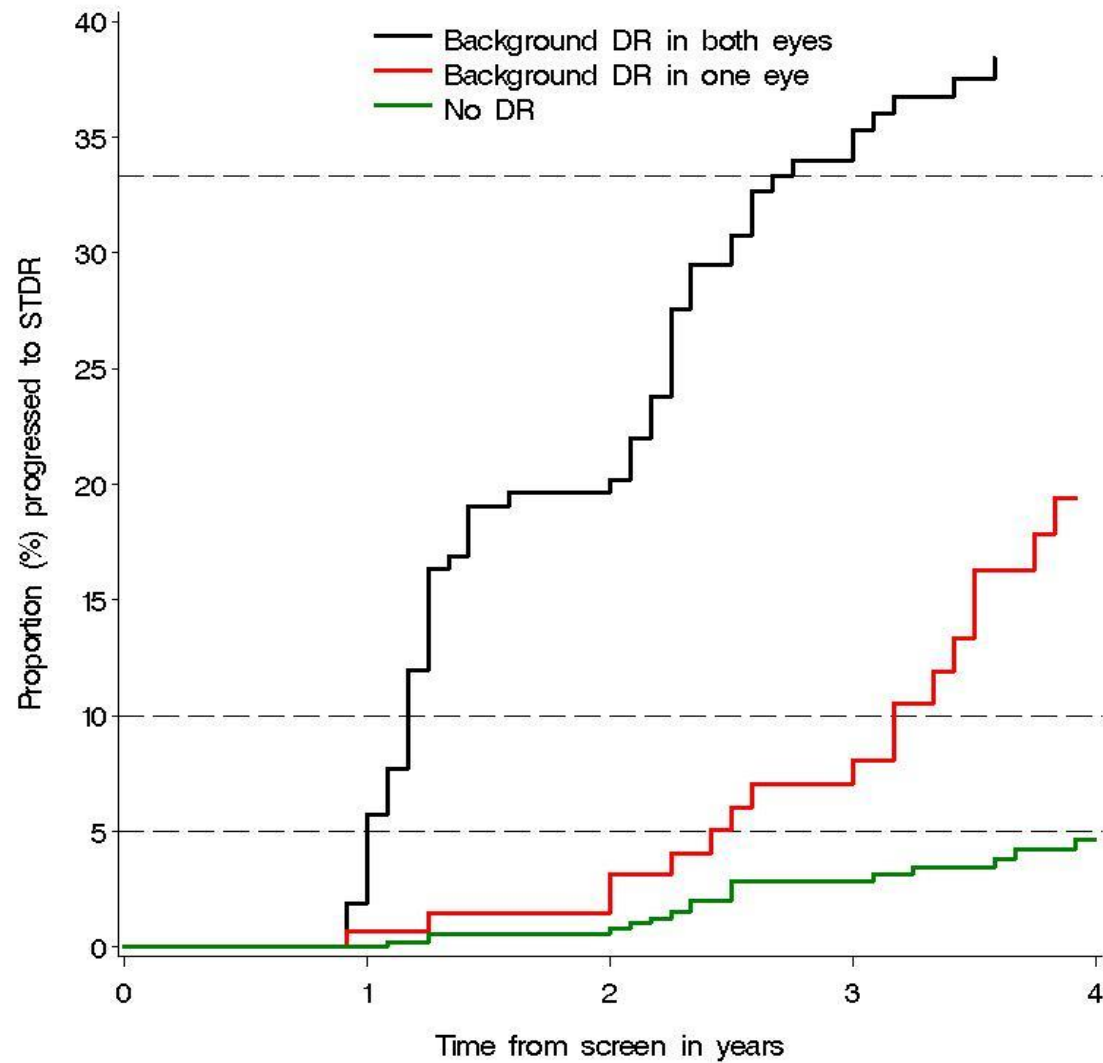
Time to Proliferative DR (R3)
from screen with no referable DR







Time to referable DR
from screen with no referable DR
Age group 12 to 40 years



Jason Oke –the significance of 1 microaneurysm in one eye

		to				
	States	1	2	3	4	5
		No detectable DR	Background DR in one eye	Background DR in both eyes	Referable maculopathy	Referable DR (pre proliferative or proliferative)
From	1	21127 (76%)	4694 (17%)	1723 (6%)	191 (1%)	19 (0%)
	2	4630 (45%)	3466 (34%)	1854 (18%)	219 (2%)	44 (0%)
	3	1446 (16%)	1608 (18%)	4660 (53%)	784 (9%)	285 (3%)
	4	162 (5%)	179 (5%)	582 (16%)	2309 (64%)	349 (10%)
	5	19 (1%)	18 (1%)	192 (15%)	357 (27%)	735 (56%)

Oke JL, Stratton IM, Aldington SJ, Stevens RJ, Scanlon PH. The use of statistical methodology to determine the accuracy of grading within a diabetic retinopathy screening programme. Diabet Med. 2015 Dec 15. PubMed PMID: 26666463

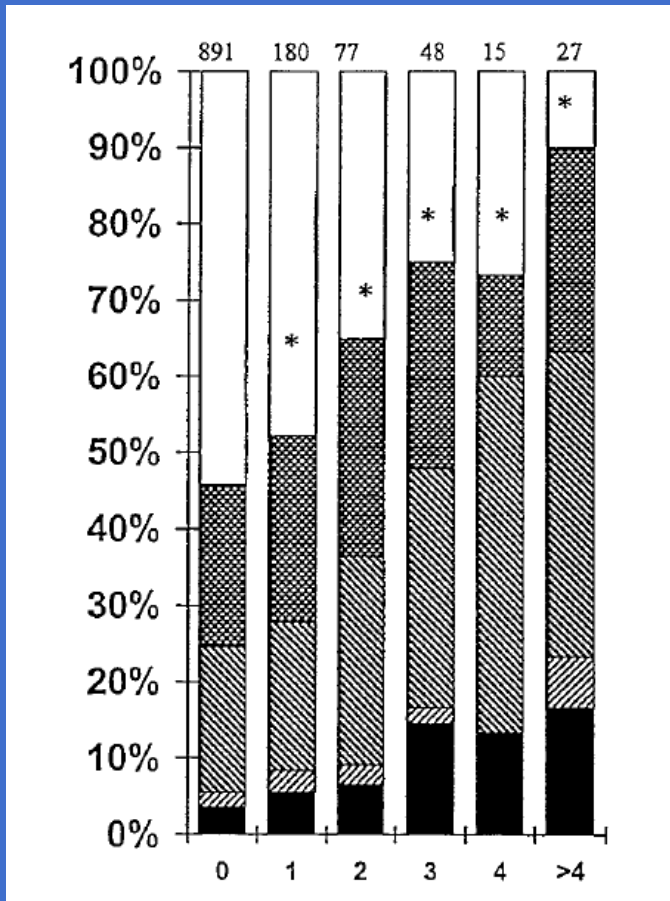
Counting microaneurysms

- The number is linked to the risk of progression



UKPDS paper 42

Retinopathy at 9 years by number of microaneurysms at baseline.



$p < 0.0001$

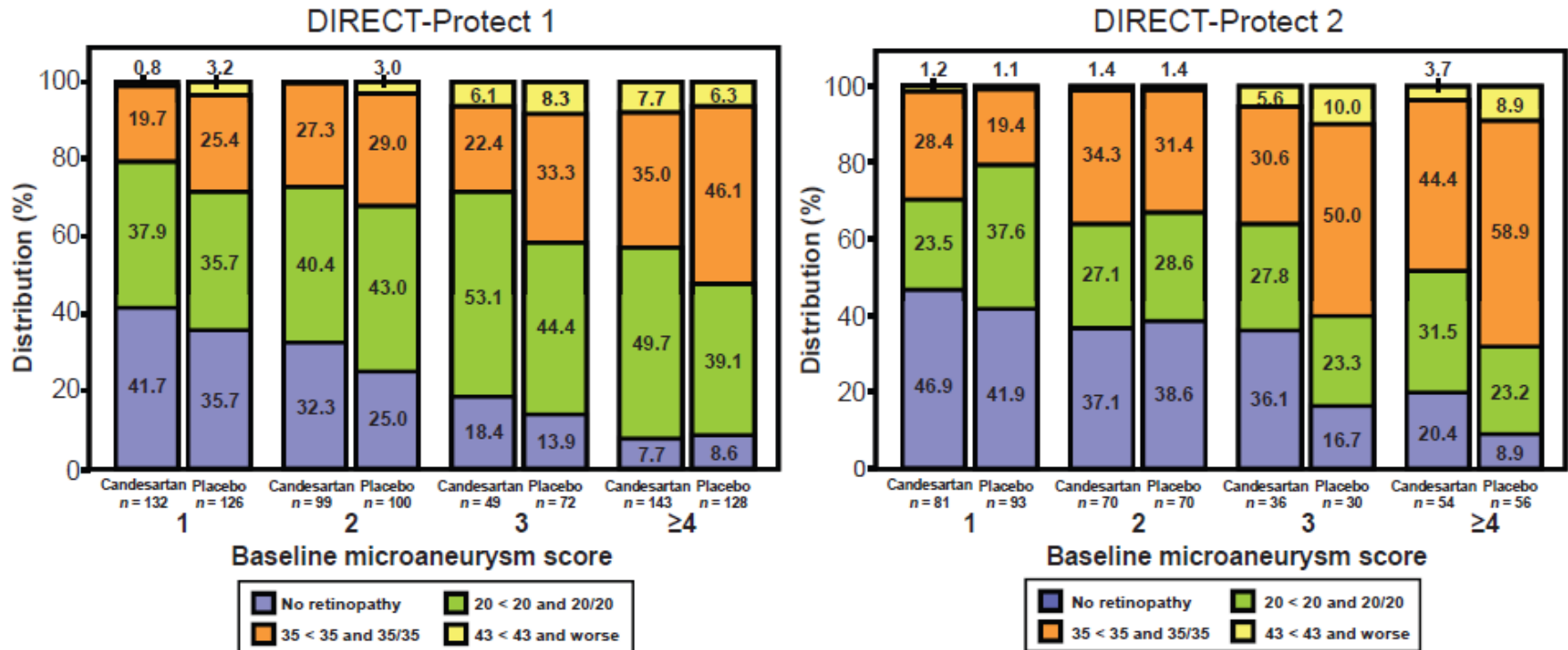
Retinopathy at 9 years by number of microaneurysms at entry. Number above columns shows total number of eyes in that group. Vertical axis shows per cent of eyes in each category indicated in to the right of the columns. Clear part of column with asterisk shows per cent of eyes in which the microaneurysms have disappeared. * – MA disappeared; $\square$ no retinopathy; $\square$ MA only; $\square$ 35 < 35 and 35/35; $\square$ 43 < 43 and worse; $\blacksquare$ photocoagulation or vitreous haemorrhage

Number of MA at baseline (no other DR)

DIRECT MA counts

(Type 1 DM with DR)

(Type 2 DM with DR)

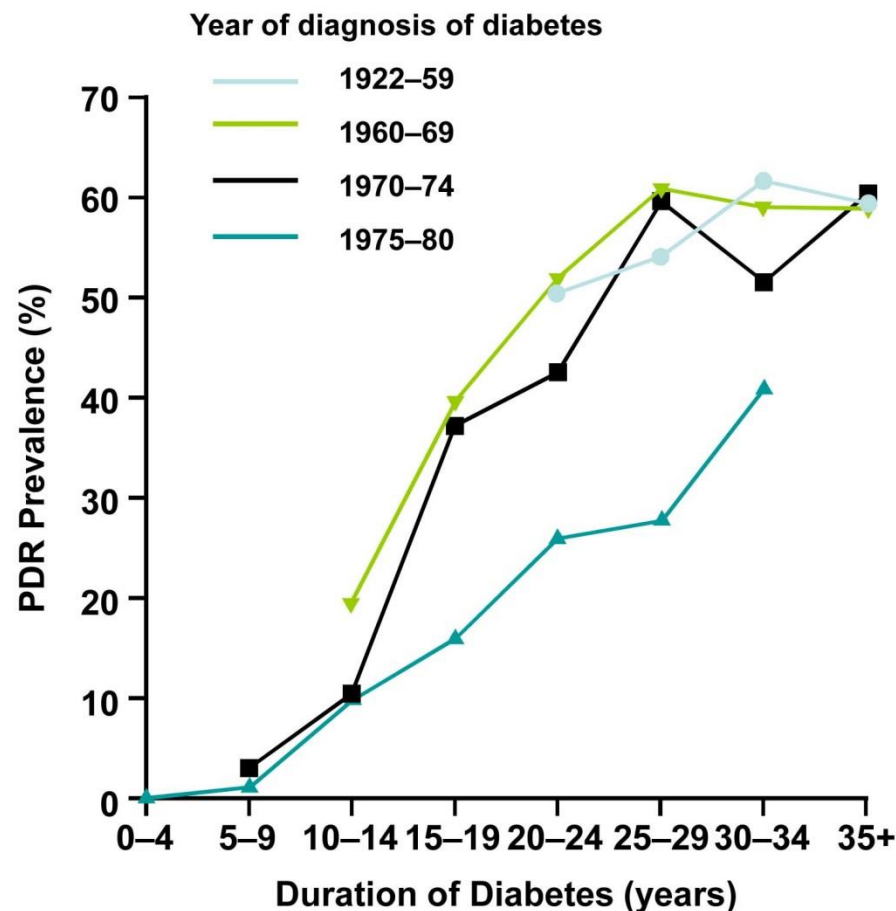


ETDRS category at end of DIRECT-Protect 1 and DIRECT-Protect 2 vs. baseline combined microaneurysm score.

Retinal microaneurysm count predicts progression and regression of diabetic retinopathy. Post-hoc results from the DIRECT Programme. A. K. Sjølie, R. Klein, M. Porta, T. Orchard, J. Fuller, H. H. Parving, R. Bilous, S. Aldington and N. Chaturvedi. Diabet. Med. (2011) 28: 345–351

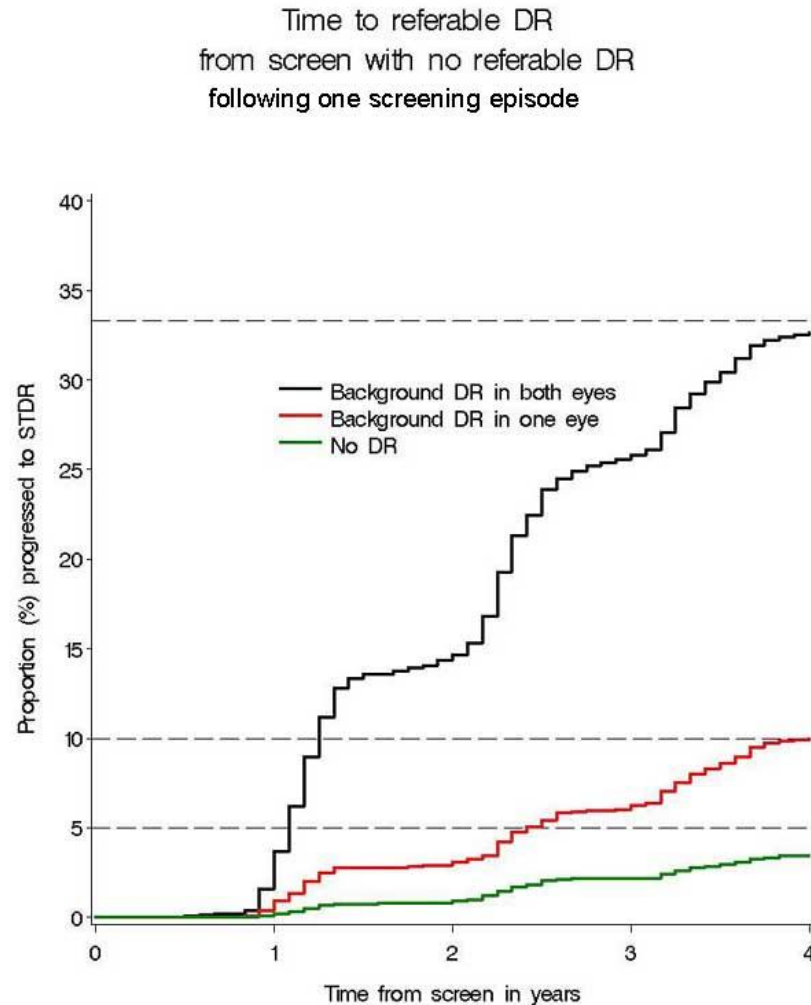
WESDR: Twenty-Five Year Progression of Retinopathy in Patients with T1DM

- Better glycaemic control and to a lesser extent BP control may be beneficial in reducing incidence of PDR and increasing odds of improvement of DR
- Reduction in prevalence of PDR in more recently diagnosed cohorts
- possible benefit of recent changes in management of diabetes



Scanlon P.H. Stratton I.M. Histed. M. Chave S.J. Aldington S.J. The influence of background diabetic retinopathy in the second eye on rates of progression of diabetic retinopathy between 2005 and 2010.

Acta Ophthalmol 91(5): e335-339.



retinopathy. *Diabetes Care*. 2013 Mar;36(3):580-5.



Funding body: HTA. Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. 2012-2014

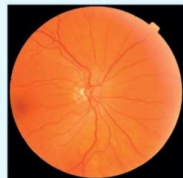
Published September 2015

Using data from the Screening Programmes in Gloucestershire, South London and Nottingham

Gloucestershire Retinal Research Group
and
HERC- Health Economic Research Centre,
University of Oxford
and
The Department of Primary Care Health Sciences,
University of Oxford

THE GRADING REFERRAL CRITERIA

– every image is given an 'R' and an 'M' grade:



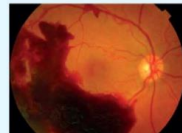
R0
no DR



R1
background DR



R2
pre-proliferative DR

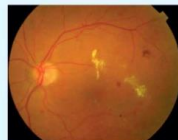


R3
proliferative DR

Leaks also occur in the macular area:



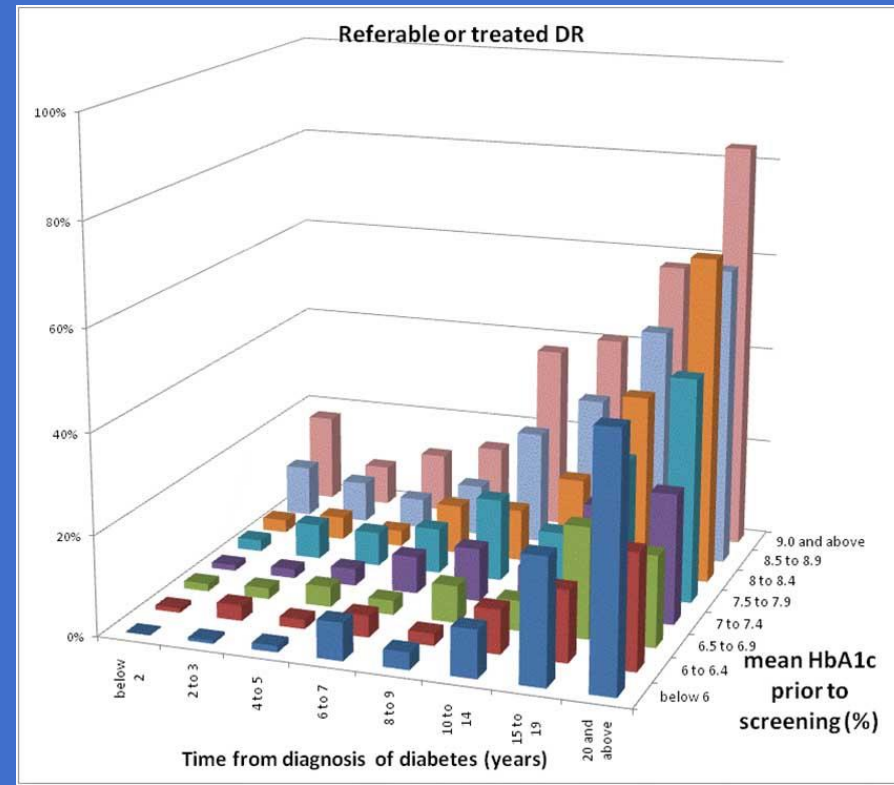
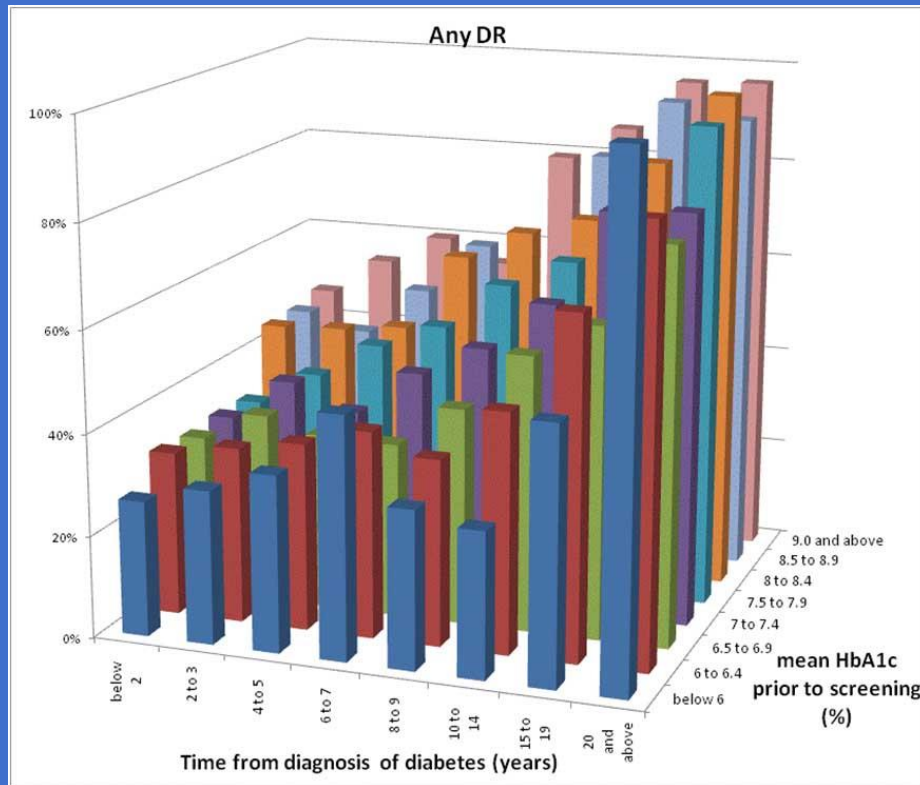
M0
no maculopathy



M1
photographic markers
of maculopathy
e.g. exudate



Adding in different risk factor elements to see if these affect the model



- March 2011. Diabetes UK Conference, London. Stratton IM, Provins E, Histed M, Chave SJ, Scanlon PH. Relationship of diabetic retinopathy levels with duration of diabetes and HbA1c in an English screening programme. Poster presentation

Results of Cox proportional hazards model

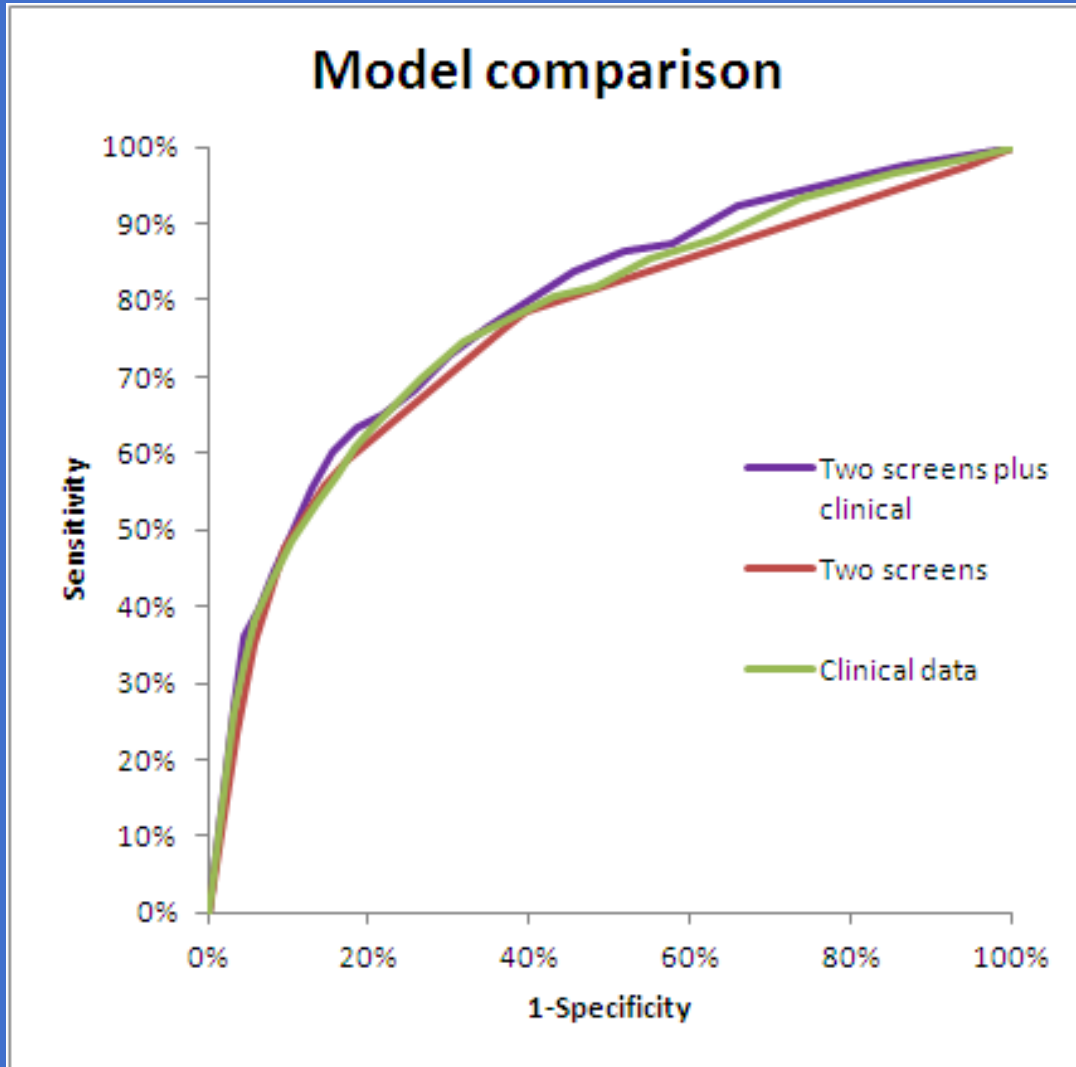
time to STDR (R2, R3 or M1)

	Hazard Ratio	95% CI
Mild NPDR in both eyes at screening visit	7.13	(5.84 to 8.70)
Mild NPDR in one eye at screening visit	2.56	(2.05 to 3.20)
HbA1c (per 10 mmol/mol increase)	1.28	(1.23 to 1.34)
Duration of diabetes (per 5 year increase)	1.20	(1.16 to 1.24)
Total serum cholesterol (per 1 mmol/L)	1.12	(1.05 to 1.19)
Serum creatinine (per 10 μ mol/L)	1.04	(1.01 to 1.07)

Characteristics of highest and lowest risk groups in validation data set

Data items in risk model	Lowest fifth (n=1071)	Highest fifth (n=1195)
Mild NPDR at previous screening episode		
Neither eye	1071 (100%)	53 (4.4%)
One eye	0 (0%)	295 (24.7%)
Both eyes	0 (0%)	847 (70.88)
HbA1c (mmol/mol)	42 (39 to 44)	58 (49 to 72)
Duration diabetes at baseline screen (years)	0.9 (0.5 to 1.75)	6.2 (1.3 to 13.25)
Serum total cholesterol (mmol/L)	4.0 (3.5 to 4.6)	4.3 (3.7 to 5.1)
Serum creatinine (μmol/L)	78 (67 to 91)	84 (72 to 100)

Model comparison



ROC curves compared:

1. Clinical risk factors + 2 screening episode
2. Clinical risk factors + 1 screening episodes
3. 2 screening episodes

	AUC	95% CI
1	0.786	0.759 to 0.813
2	0.774	0.748 to 0.800
3	0.759	0.732 to 0.788

- Scanlon PH, Aldington SJ, Leal J, Luengo-Fernandez R, Oke J, Sivaprasad S, et al. Development of a cost-effectiveness model for optimisation of the screening interval in diabetic retinopathy screening. Health Technol Assess. 2015 Sep;19(74):1-116. PubMed PMID: 26384314.

http://www.journalslibrary.nihr.ac.uk/__data/assets/pdf_file/0006/152943/FullReport-hta19740.pdf

**Development of a cost-effectiveness model for
optimisation of the screening interval in diabetic
retinopathy screening**

*Peter H Scanlon, Stephen J Aldington, Jose Leal, Ramon Luengo-Fernandez,
Jason Oke, Sobha Sivaprasad, Anastasios Gazis and Irene M Stratton*

DOI 10.3310/hta19740


**National Institute for
Health Research**

Conclusions

- Within each of the 3 screening programmes **the risk model discriminates well** between those with **very low risk** and those with **very high risk** of progression to sight threatening diabetic retinopathy.
- The algorithm would be suitable for calculation of **personalised screening intervals**
- The UK NSC has been considering extension of the screening interval to two years for those with 2 negative screens

English National DR Screening Programme

2002

8 reasonable
quality services



5/8 shown



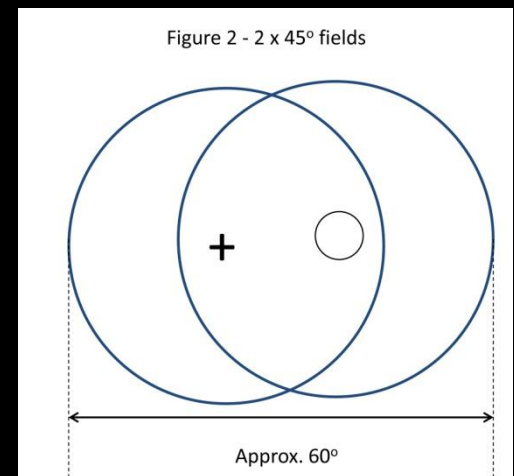
2014 -15

- 83 centres
- 2.8 million with diabetes
- 2.5 million offered
- 2.1 million actually screened
- Increase 120,000 in 12 months

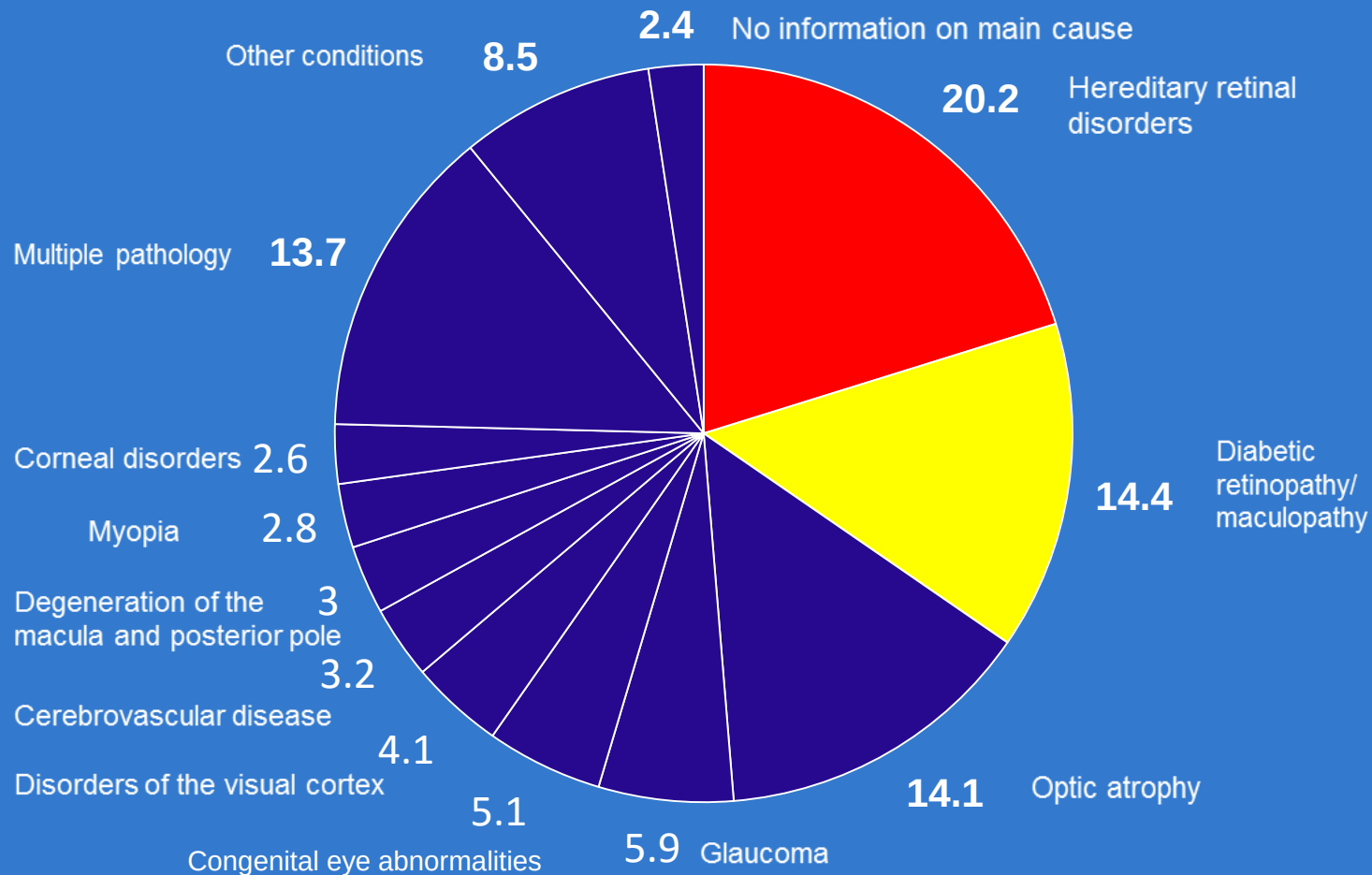


83

2 field digital imaging offered to all people with diabetes in England (2.5 million people offered in 2014-15 and 2.1 million screened)



For the first time in at least five decades, diabetic retinopathy/maculopathy is no longer the leading cause of certifiable blindness (16-64) in England & Wales*



*A comparison of the causes of blindness certifications in England and Wales in working age adults (16-64 years), 1999-2000 with 2009-2010