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Population trends in the ten-year incidence and prevalence of diabetic retinopathy in the UK: a descriptive cohort study in the Clinical Practice Research Datalink 2004-2014

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TITLE PAGE

Title: Population trends in the ten-year incidence and prevalence of diabetic retinopathy in the UK: a descriptive cohort study in the Clinical Practice Research Datalink 2004-2014

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Running Head: Population trends in in the incidence and prevalence diabetic retinopathy in the UK

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ABSTRACT (300 words)

Objectives: To describe trends in the incidence and prevalence of diabetic retinopathy (DR) in the UK by diabetes type, age, sex, ethnicity, deprivation, region, and calendar year between 2004 and 2014.

Design: Analysis of longitudinal electronic health records in the UK Clinical Practice Research Datalink (CPRD).

Setting: UK Primary Care.

Participants: 7.7 million patients aged ≥ 12 contributing to the CPRD between 2004 and 2014.

Primary and secondary outcome measures: Age standardised prevalence and incidence of diabetes, DR and severe DR (requiring photocoagulation) by calendar year and population subgroup. Relative risk of developing DR and severe DR by population subgroup accounting for duration of diabetes.

Results: The prevalence of DR was 48.4% in the population with type 1 diabetes (14,846/30,657) and 28.3% (95,807/338,390) in the population with type 2 diabetes. Prevalence of DR remained stable in both diabetic populations. Among people with type 2 diabetes, incidence of DR increased in parallel with the incidence of type 2 diabetes. Relative risk of developing diabetic retinopathy varied significantly by region, age group and gender, while the relative risk of developing severe retinopathy varied also by ethnicity and deprivation.

Conclusions: This is the largest study to date examining the burden of diabetic retinopathy in the UK. Regional disparities in incidence may relate to differences in screening program delivery and subsequent disease ascertainment. Evidence that increasing deprivation and south Asian ethnicity may be associated with a higher risk of severe DR, when viewed alongside previous evidence of lower retinopathy screening uptake amongst deprived groups, highlights a significant potential health inequality. Findings from this study will have implications for professionals working in the diabetes and sight loss sectors, particularly to inform approaches for diagnosis of retinopathy and campaigning to better tackle the disease for at risk groups.

ARTICLE SUMMARY

Strengths and limitations of this study

- This study constitutes the largest ever sample size to examine trends in the burden of diabetes and diabetic retinopathy in the UK which allowed for sufficient power to detect relationships between population subgroups, which is often unfeasible in smaller studies where population sizes do not allow for such granular comparisons.

- Since recording of screening of diabetic retinopathy was incentivised under QOF from 2004-2014m and QOF indicators are known to have been well recorded by GPs and so we anticipate that screening and identification of DR will have been recorded with a high degree of accuracy during the study period.

- This study relied on coded diagnoses of diabetes and retinopathy as we did not have access to data from other sources such as retinal photography or practitioner letters, which could have been used to validate the diagnoses.

FUNDING STATEMENT

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COMPETING INTERESTS

none declared

INTRODUCTION

Diabetic retinopathy (DR) is the most common form of eye disease amongst individuals with diabetes mellitus. In the UK, within 20 years of diabetes diagnosis nearly all people with type 1 and almost two thirds of people with type 2 diabetes (60%) have some degree of retinopathy.(1) (2) Diabetic retinopathy is the leading cause of visual impairment and blindness in the UK, amongst people of working age; Compared with the general population, risks of cataract and of glaucoma are doubled amongst individuals with established diabetic retinopathy.(3)

Diabetic retinopathy is a progressive disease directly attributable to diabetes, which affects the blood vessels of the retina. The blood vessels can leak, become blocked, or proliferate excessively.(4,5) If untreated, this can lead to retinal damage and visual impairment (21). In order to prevent, delay and better manage diabetic retinopathy, annual screening using digital photography is recommended for all people with diabetes aged 12 and over in the UK. Introduced in 2004, uptake of the screening program has increased steadily, achieving full national coverage in 2008 (6). Implementation of screening varies across each of the four devolved nations of the UK, and can take place in general practices, at specialist diabetes clinics, mobile clinics, and at the high street optician.

Differences in the risk of diabetes by gender, ethnic group, and deprivation have been established both in the UK and worldwide.(7–12) In the UK, the risk of developing type 2 diabetes is elevated approximately twofold in South Asian and African Caribbean communities compared to the White British population.(13,14)

Despite extensive literature detailing the prevalence and incidence of diabetes in the UK, population-wide measures of incidence and prevalence of diabetic retinopathy in a UK context have not been determined. Previous UK focussed research on retinopathy has largely been limited to estimates based on regional screening programmes or small general practices samples.(15–19) Having a more complete understanding of the burden of disease due to diabetic retinopathy across the diverse UK population will help improve future service planning and provision of preventive and therapeutic care. The aim of this study was to generate nationally representative estimates of the incidence and prevalence of diabetic retinopathy in the United Kingdom between 2004 and 2014 using the Clinical Practice Research Datalink (CPRD), and to examine trends according to diabetes type, age, sex, ethnicity, socio-economic deprivation, calendar period, and region.

METHODS

Data Sources

The CPRD is an electronic health database which currently contains longitudinal primary care records for approximately 13.5 million patients from 601 general practices across the UK, of whom 5.5 million are currently active.(20) The CPRD contains anonymised patient level information on demographics, lifestyle data, clinical diagnoses, prescriptions, and preventive care. Continuous observational data has been collected in most practices for over six years yielding over 30 million patient years of observation. Data undergo regular quality checks and practices are deemed to be "up to standard" if their data are deemed to be of research level quality. The Clinical Practice Research Datalink has been found to be representative of the UK population with respect to gender, age and ethnic group. (20,21)

Identification of diabetic retinopathy

Clinical terms to identify diagnoses of diabetic retinopathy were agreed upon via consultation between the research team and clinicians. All diagnoses of diabetic retinopathy were identified by searching for Read clinical terms in the CPRD. Diabetic retinopathy was classified as severe if the codes pertained to laser therapy, advanced retinopathy, pre-proliferative or proliferative retinopathy.

Onset of diabetic retinopathy was defined as the first ever diagnostic Read code entered onto the patient record. Patients with a diagnosis for severe retinopathy at any time were included in a sub-analysis of patients with advanced disease, with onset defined as the earliest ever code of severe DR on the patient record.

Screening for diabetic retinopathy was identified using a set of clinical terms which indicated that a screening event had occurred. Codes indicating that an individual had been invited to or referred for screening were not included. A summary of the clinical terms used to identify diabetic retinopathy and screening can be found in the supplementary material.

Identification of diabetes mellitus

For the purposes of this study, classification of patients into categories of type 1 diabetes or type 2 diabetes was determined using algorithms developed by the UK Biobank study for use in electronic health records.(22) The algorithms initially classify patients according to the presence of diagnostic Read codes for type 1 or type 2 diabetes. The diagnoses are then confirmed if supporting

information such as prescriptions of antidiabetic medications, raised blood glucose, and diabetes process of care measures are present. All individuals identified as having type 1 or type 2 diabetes after successfully passing through the adjudication algorithm were included in the final analysis.

Covariate definition

Age was grouped into ten-year age-bands. Deprivation was classified using the Index of Multiple Deprivation and divided into quintiles (IMD).(23) Each patient in the study was assigned a deprivation score relating to the deprivation value of their general practice. Information on ethnic group was derived from the CPRD record where available and updated using ethnicity recorded in linked Hospital Episode Statistics data if missing in CPRD. Conflicts between the two data sources were resolved using a defined and previously validated algorithm.(24) Ethnicity was grouped into the five categories of the 2011 census, namely, White, South Asian, Black African/Caribbean, Mixed, and Other. Patients with missing ethnicity, or with codes which were unusable were collapsed into a category of unknown ethnicity (See supplementary material for algorithm and Read codes). Duration of diabetes at onset of diabetic retinopathy (expressed in years) was calculated by subtracting the date of the first diagnostic code for diabetes from the date of the first diagnostic code for diabetic retinopathy.

Statistical *Methods*

A prospective cohort study was conducted to examine the prevalence and incidence of diabetic retinopathy in all patients aged 12 years and over registered with the CPRD between January 2004 and December 2014. The prevalence and incidence of diabetes and diabetic retinopathy and severe diabetic retinopathy was examined separately for individuals with type 1 diabetes and type 2 diabetes.

All prevalence and incidence estimates were standardised against the mid-2014 UK population estimates from the Office for National Statistics.(25) The overall age standardised prevalence of diabetic retinopathy stratified by diabetes status, gender, ethnic group, deprivation quintile, and region was calculated for the entire study population. For the study of prevalence over time, the outcome was defined as all individuals with a relevant diagnostic code at the midpoint of each calendar year from January 2004 to December 2014. Point prevalence was calculated by dividing the number of individuals with diabetic retinopathy or severe diabetic retinopathy by the number of patients in the CPRD aged 12 years and over on July 1st of each year.

For the study of disease incidence, the outcome was first diagnosis of diabetic retinopathy or severe diabetic retinopathy between January 2004 and December 2014. Individuals with a first diagnosis of retinopathy prior to 2004 were excluded from the analysis. Incidence was calculated by dividing the number of newly diagnosed patients aged 12 and over by the number of person-years of follow-up of all eligible patients aged 12 and over contributing to the CPRD. Age standardised incidence rates of diabetic retinopathy and severe diabetic retinopathy per 10,000 person years of follow-up time were calculated for all patients in the CPRD.

Cox proportional-hazards regression was used to evaluate the risk of diabetic retinopathy in all patients between January 2004 and December 2014. Hazard Ratios for the relative risk of diabetic retinopathy and severe diabetic retinopathy, mutually adjusted for age, gender, deprivation, ethnic group, region, and duration of diabetes, were calculated separately for individuals with type 1 and type 2 diabetes. The start of follow-up was defined as the latest of practice "up to standard date" (up to standard indicating the practice data meets the range of quality criteria as defined and applied by CPRD) or 12 months after the patients' current registration date. Follow-up time ended at the earliest date of; first diagnosis of diabetic retinopathy, transferring out of the practice, latest data collection, death, or December 31st 2014.

RESULTS

From the entire CPRD population of 13.7 million patients, 7,707,475 patients registered with the CPRD between 2004 and 2014 aged 12 and over were eligible for inclusion in the study. Amongst all patients aged 12 and over, 338,390 patients with type 2 diabetes and 30,657 patients with type 1 diabetes were identified using the diabetes classification algorithms (Table 1).

Table 1. Demographic characteristics of the CPRD population registered between 2004-2014

Population	All CPRD Patients		T1DM Patients		T2DM Patients	
	N	%	N	%	N	%
Total (12+)	7,707,475	100.0%	30,657	100.0%	338,390	100.0%
Gender						
Men	3,790,664	49.2%	17,761	57.9%	187,141	55.3%
Women	3,916,811	50.8%	12,896	42.1%	151,249	44.7%
Ethnic Group						
White	4,006,927	52.0%	19,810	64.6%	205,168	60.6%
South Asian	223,090	2.9%	453	1.5%	15,840	4.7%
Black	142,070	1.8%	373	1.2%	7,186	2.1%
Other	109,402	1.4%	254	0.8%	3,891	1.2%
Mixed	50,363	0.7%	152	0.5%	1,095	0.3%
Unknown	3,175,623	41.2%	9,615	31.4%	105,210	31.1%
IMD Quintile						
1 (most affluent)	1,338,388	17.4%	5,280	17.2%	52,280	15.5%
2	1,496,051	19.4%	5,934	19.4%	61,008	18.0%
3	1,621,330	21.0%	6,517	21.3%	71,982	21.3%
4	1,723,122	22.4%	6,910	22.5%	79,130	23.4%
5 (least affluent)	1,470,726	19.1%	5,833	19.0%	72,094	21.3%
Region						
North East	121,334	1.6%	516	1.7%	5,465	1.6%
North West	803,853	10.4%	3,226	10.5%	40,255	11.9%
Yorkshire & The Humber	269,265	3.5%	1,050	3.4%	10,888	3.2%
East Midlands	296,884	3.9%	1,182	3.9%	12,489	3.7%
West Midlands	654,656	8.5%	2,451	8.0%	30,710	9.1%
East of England	752,786	9.8%	3,041	9.9%	29,139	8.6%
South West	651,327	8.5%	2,601	8.5%	30,330	9.0%
South Central	853,405	11.1%	3,242	10.6%	33,416	9.9%
London	1,017,747	13.2%	3,150	10.3%	39,281	11.6%
South East	792,775	10.3%	3,123	10.2%	33,399	9.9%
Northern Ireland	199,509	2.6%	937	3.1%	9,322	2.8%
Scotland	711,397	9.2%	3,601	11.7%	31,387	9.3%
Wales	582,537	7.6%	2,537	8.3%	32,309	9.5%
Retinopathy screen 2004-2014	710,445	8.7%	24,828	79.3%	279,495	82.6%
Retinopathy screen in last 15 months	336,960	4.1%	15,788	50.4%	180,268	53.3%
Diabetic Retinopathy	144,362	1.9%	14,846	48.4%	95,807	28.3%
Severe Diabetic Retinopathy	13,873	0.2%	3,142	10.3%	8,158	2.4%
Mean duration of diabetes at DR onset (years, SD)			14.7	(12.2)	5.9	(6.9)
Mean duration of diabetes at Severe DR onset (years, SD)			20.9	(12.7)	10.4	(8.7)

Overall Prevalence of diabetic retinopathy

Over the ten-year study period, 79.3% of individuals with type 1 diabetes and 82.6% of individuals with type 2 diabetes had evidence of ever having had a diabetic retinopathy screen completed, with over 50% having had their latest screen in the 15 months prior to the end of their follow-up period.

A total of 144,362 prevalent cases of diabetic retinopathy were identified between 2004 and 2014, giving a crude 10-year period prevalence of 1.9% in the entire CPRD population, 48.4% in the population with type 1 diabetes, and 28.3% in the population with type 2 diabetes. The crude 10-year period prevalence of severe diabetic retinopathy was 0.2% in the CPRD population, 10.3% in the population with type 1 diabetes and 2.4% in the population with type 2 diabetes (Table 1).

Mean duration of diabetes at time of DR onset ranged from 6 years for people with type 2 diabetes to 15 years for people with type 1 diabetes, with duration approximately 5 years longer for onset of severe diabetic retinopathy.

Age standardised prevalence and incidence of diabetic retinopathy over time

The age standardised prevalence of diabetic retinopathy remained relatively stable over time, while age standardised incidence varied more extensively. Amongst patients with type 2 diabetes, the prevalence of diabetic retinopathy reduced from 24.6% in 2004 to 23.1% in 2014. The incidence of diabetic retinopathy increased in parallel with the incidence of type 2 diabetes, increasing from 113.2 events per 10,000 person-years in 2004 to 408.6 events per 10,000 person-years in 2011 and declining thereafter (annual increase of 26 events per 10,000 person-years, CI95% 13.2 to 39.3, p=0.001). The prevalence of severe diabetic retinopathy also remained stable over time, reducing from 2.1% in 2004 to 1.9% in 2014. The incidence of severe diabetic retinopathy decreased from 13.8 events per 10,000 person years in 2004 to 7.6 events pre 10,000 person years in 2014 (no trend over time p=0.350) (Figure 1).

Amongst patients with type 1 diabetes the age standardised prevalence of diabetic retinopathy remained stable at 55% (no trend over time p=0.917). The age standardised incidence of diabetic retinopathy increased from 514.7 events per 10,000 person-years in 2004 to 832 events per 10,000 person-years in 2009 and declined thereafter (annual increase of 55.6 events per 10,000 person-years from 2004-2009, CI95% 29.6-81.7, p=0.004) The prevalence of severe diabetic retinopathy increased from 11.7% in 2004 to 12.5% in 2014 (annual increase of 0.1%, CI95% 0.04% to 0.12%, p=0.001). The incidence of severe diabetic retinopathy decreased from 97.8 events per 10,000

person-years in 2004 to 30.1 events per 10,000 years in 2014 (annual decrease of 6.4 events per 10,000 years, CI95 -9.0 to -3.9, p<0.001) (Figure 1).

(Insert Figure 1 here)

In 2014, the final year of the study period, 73,637 prevalent cases of diabetic retinopathy were identified, giving an age-standardised point prevalence of 2.2% (CI95% 2.18% to 2.21%) in the entire CPRD population, 55.4% (CI95% 54.2% to 56.7%) in the population with type 1 diabetes and 23.1% (CI95% 22.4% to 23.9%) in the population with type 2 diabetes (Table 2).

Table 2. Age standardised prevalence of Diabetic Retinopathy in the CPRD 2014

		Diabetic Retinopathy						Severe Diabetic Retinopathy					
		T2DM Population			T1DM Population			T2DM Population			T1DM Population		
	Denominator (12+)	**163,884**			**13,343**			**163,884**			**13,343**		
		N	%	p.val	N	%	p.val	N	%	p.val	N	%	p.val
Overall	*Prevalence (CI95)*	***50,459***	***23.1 (22.4-23.9)***		***7,704***	***55.4 (54.2-56.7)***		***4,027***	***1.9 (1.7-2.1)***		***1,758***	***12.5 (119-13.1)***	
Gender	Men	29,032	23.9	<0.001	4,470	55.2	0.611	2,549	2.2	<0.001	1,052	12.8	0.008
	Women	21,427	22.0		3,244	56.2		1,478	1.5		706	12.2	
Age Group	12-29	101	13.1	<0.001	1,045	29.4	<0.001	7	0.9	0.001	118	3.3	<0.001
	30-49	3,416	21		2,882	59.00		311	1.9		712	14.6	
	50-69	21,493	29.1		2,875	69.5		1,892	2.6		729	17.6	
	70+	25,449	34.9		902	69.3		1,817	2.5		199	15.3	
Ethnic Group	White	31,608	23.7	<0.001	5,112	56.1	<0.001	2,286	1.8	<0.001	1,200	13.0	<0.001
	South Asian	2,616	25.0		97	46.7		301	2.3		12	5.6	
	Black	1,216	25.7		60	46.6		138	2.5		13	13.6	
	Other	613	31.3		47	46.8		45	1.5		8	9.1	
	Mixed	165	20.8		22	41.5		24	2.9		5	13.2	
	Unknown	14,781	21.2		2,366	55.6		674	1.8		520	12.1	
IMD Quintile	1 (most affluent)	7,566	20.2	0.006	1,525	55.8	<0.001	493	1.5	<0.001	323	11.8	0.230
	2	10,084	23.9		1,588	55.8		779	1.6		354	12.3	
	3	10,171	23.1		1,569	56.8		765	1.9		361	12.7	
	4	12,421	26.3		1,712	56.5		1,046	2.5		45	13.5	
	5 (least affluent)	9,688	20.9		1,251	52.3		867	1.8		292	12.3	
Region	North East	585	26.3	<0.001	74	58.3	<0.001	48	2.5	<0.001	16	12.1	<0.001
	North West	4,987	19.9		687	49.5		303	1.2		164	11.8	
	Yorkshire & Humber	426	21.3		80	53.0		45	2.5		23	14.3	
	East Midlands	218	44.4		17	68.1		8	1.3		8	32.2	
	West Midlands	4,436	22.1		560	55.4		338	1.7		113	10.4	
	East of England	2,624	19.7		502	54.5		216	1.5		86	9.2	
	South West	4,491	25.9		595	57.0		398	2.2		179	16.8	
	South Central	5,817	23.7		960	54.8		429	1.9		219	12.1	
	London	6,561	23.9		720	51.2		603	1.9		164	11.4	
	South East	4,501	17.9		782	49.6		258	1.3		145	9.1	
	Northern Ireland	822	10.5		245	40.6		117	1.1		54	8.7	
	Scotland	8,221	33.2		1,509	67.8		662	2.9		306	14.1	
	Wales	6,770	23.6		973	59.5		602	2.4		261	15.7	

*All figures standardised against the UK Mid-2014 population, p.values from chi-squared test for unordered categorical variables, from test for trend for ordered categorical variables (age group and IMD quintile)

Prevalence trends in population sub-groups with Type 2 diabetes

Amongst patients with type 2 diabetes, the age-standardised prevalence of diabetic retinopathy and severe diabetic retinopathy was higher amongst men and those of non-White ethnicity. Age-standardised prevalence of diabetic retinopathy increased with age and with deprivation until quintile 4 and varied substantially by geographic region.

Prevalence trends in population sub-groups with Type 1 diabetes

Amongst patients with type 1 diabetes, the prevalence of diabetic retinopathy was comparable between men and women, and highest in the White ethnic group compared to all other ethnic groups. Prevalence of diabetic retinopathy, but not severe retinopathy increased with deprivation. Prevalence of both diabetic retinopathy and severe retinopathy varied substantially by geographic region.

Relative risk of retinopathy in patients with Type 2 diabetes

Median follow-up time for patients with type 2 diabetes was 9.1 years (IQR 5.4-10.9 years). Within this population, fully adjusted hazard ratios from Cox-proportional hazards regression showed that the risk of developing both diabetic retinopathy and severe diabetic retinopathy was reduced in women compared to men (HR 0.93, CI95% 0.92-0.95 for DR and HR 0.78, CI95% 0.73-0.84 for Severe DR).

Relative to those aged 55-64, the risk of developing diabetic retinopathy was reduced in the youngest and oldest age groups. In the analysis of severe diabetic retinopathy, risk was increased in those aged 35-44 and 45-54 relative to those aged 55-64 and reduced in all older age groups.

Risk of diabetic retinopathy was equivalent between ethnic groups in the main analysis, and raised for the South Asian group relative to the White group in the analysis of severe diabetic retinopathy (HR 1.28 CI95% 1.10-1.48).

Though no clear relationship between deprivation and retinopathy was clear in the main analysis of diabetic retinopathy; In the analysis of severe diabetic retinopathy, risk was increased in all deprivation quintiles relative to the most affluent quintile.

Risk of diabetic retinopathy varied substantially by geographic region, with differences attenuated for severe retinopathy. In comparison to London (the reference region), risk of retinopathy was reduced in Northern Ireland and the East of England, and increased in most other regions of the UK.

Each 5-year increase in the duration of diabetes at baseline was associated with a 17% increase in the risk of diabetic retinopathy (CI95% 1.16-1.18) and a 41% increase in the risk of severe diabetic retinopathy (CI95% 1.38-1.43) after adjustment for all other factors (Figure 2).

Relative risk of retinopathy in patients with Type 1 diabetes

Median follow-up time for patients with type 1 diabetes was 7.1 years (IQR 4.0-10.9 years). Within this population, fully adjusted hazard ratios from Cox-proportional hazards regression showed no evidence for differences in the risk of developing diabetic retinopathy or severe diabetic retinopathy by gender, ethnic group, or deprivation.

Relative to those aged 55-64, the risk of developing diabetic retinopathy was reduced in the both older age groups. In the analysis of severe diabetic retinopathy, risk was increased in those aged 35-44 and 45-54 relative to those aged 55-64 and reduced in all older age groups.

Regional differences in the risk of retinopathy and severe retinopathy for patients with type 1 diabetes mirrored those found in the analysis of patients with type 2 diabetes.

Each 5-year increase in the duration of diabetes at baseline was associated with a 10% increase in the risk of diabetic retinopathy (CI95% 1.09-1.11) and a 22% increase in the risk of severe diabetic retinopathy (CI95% 1.18-1.25) after adjustment for all other factors (Figure 3).

(Insert Figures 2 and 3 about here)

DISCUSSION

Main findings

The study has shown that while prevalence and incidence of diabetic retinopathy has remained stable over time for patients with type 1 diabetes; amongst patients with type 2 incidence of diabetic retinopathy has increased over time in parallel to the incidence of type 2 diabetes. The study has further demonstrated that the relative risk of developing diabetic retinopathy varies by region, age group and gender, while the relative risk of developing severe retinopathy varies also by ethnicity and deprivation.

The overall prevalence of diabetic retinopathy found in our CPRD population is comparable to that of contemporaneous studies. A 2015 study of the Welsh National Diabetic Retinopathy Screening Service has reported that the prevalence of diabetic retinopathy is 56% in those with type 1 diabetes and 30.3% in those with type 2 diabetes. (4) These figures tally closely with the respective ten-year prevalence figures of 48.4% for patients with type 1 diabetes and 28.3% for patients with type 2 diabetes from our study. Similarities extend to severe diabetic retinopathy also; the same study reports prevalences of 11.2% in those with type 1 diabetes and 2.9% in those with type 2 diabetes. Our study has found the prevalence to be 10.3% and 2.4% respectively. A recent review of diabetic retinopathy studies in western countries has reported the prevalence of diabetic retinopathy in to be 28.7% across all diabetic populations, further lending credence to our findings.(26)

The overall incidence of retinopathy increased to a peak partway through the study before decreasing again. Increases in the incidence of retinopathy are likely to be related to increasing incidence of type 2 diabetes and increased ascertainment of retinopathy through nationwide screening programs, which increased in coverage over the duration of the study period. Annual incidence figures obtained in our study are largely in line with incidence figures reported in the Liverpool Diabetic Eye Study, which examined incidence amongst patients with type 2 diabetes.(18)

A key finding of the study was large regional variations in the relative incidence of retinopathy, after accounting for age, gender, deprivation, and ethnicity. Regional differences in incidence may relate to differences in the organization and delivery of screening programs, and subsequent ascertainment of disease. It has been suggested that uptake of screening, and as a result, opportunities for diagnosis, may be lower in rural versus urban areas, due to decreased accessibility of screening services.(19) Qualitative research elucidating the influence of practice levels factors on attendance at screening has also identified challenges in identifying diabetic retinopathy including

communication with screening services, communication with patients, integration of screening services with other aspects of clinical care, and ethnically diverse patient populations.(27,28)

The increased risk of severe diabetic retinopathy for South Asian individuals with type 2 diabetes relative to the White group mirrors ethnic differences in diabetes prevalence, and may be due to the same underlying genetic and biological factors which predispose South Asian groups to insulin resistance. Similarly, increased risk of severe diabetic retinopathy in the more deprived quintiles relative to the least deprived quintile is consistent with existing literature around socio-economic disparities in diabetes.(19,29)

Turning to patients with type 1 diabetes, the stability of the prevalence of retinopathy was to be expected as the prevalence and incidence of type 1 diabetes is not subject to large increases resulting from an increasingly obesogenic environment, as is the case with the current epidemic of type 2 diabetes.

The differences in prevalence by gender and ethnic group found here confirm those of recent smaller UK based studies. In 2012, Sivaprasad et al. reported reduced odds of prevalent retinopathy in women compared to men (OR 0.93 CI95% 0.90-0.97) and raised odds in South Asian and Black African/Caribbean groups compared to White (South Asian OR 1.10 CI95% 1.02-1.18, Black OR 1.79, CI95% 1.70-1.89) amongst individuals with diabetes in the UK. (8)

Strengths

This study made use of high levels of ethnicity recording and linkage with deprivation data provided by the ONS to describe patterns by ethnicity and Index of Multiple Deprivation. This study constitutes the largest ever sample size to examine trends in the burden of diabetes and diabetic retinopathy in the UK. This allowed for sufficient power to detect relationships between populations stratified by gender, ethnic group, geographic region and deprivation, which is often unfeasible in smaller studies where population sizes do not allow for such granular comparisons. At the time of publication, this is the only national study to examine ethnicity and deprivation in relation to the prevalence and incidence of diabetic retinopathy.

Since 2004 it has been a requirement of the UK Quality and Outcomes Framework (QOF) that patients with diabetes should be screened annually for diabetic retinopathy, and that screening should be recorded by general practitioners in patient records. QOF indicators are known to have

been well recorded by GPs and so we anticipate results of screening will have been recorded with a high degree of accuracy during the study period.(30,31)

The advantage of routine electronic health databases is that they are regularly updated and can be used to provide timely information on the demographic makeup of the general population and on areas of growing healthcare need.

The data in the CPRD are prospectively collected and, as a result, the data are not subject to recall bias (the presence of a disease outcome affects the reporting of exposure status) or observer bias (the knowledge of the patient's disease status influences ascertainment or recording of exposure).

Limitations

The primary purpose of the clinical data held in the CPRD is for patient care, rather than research. By its nature it only includes information gathered at consultation and is thus routinely collected rather than researcher-led. As a result, the completeness and accuracy of data are subject to temporal changes in coding practices, health priorities and population need. Anything not reported to the general practitioner is necessarily not recorded. The absence of a code does not necessarily mean that an individual is free from that condition, but could also be interpreted as being unknown.

In addition to incomplete data, a further potential problem with routine electronic health records is incorrect coding stemming from errors in the way data is entered. A wide range of studies have found the validity of diagnoses and process of care measures in CPRD to be high.(32–34) Combined with the fact that the CPRD data are subject to ongoing internal quality checks and that concerns with data quality are fed back to the general practices, researchers can be reassured that errors which do occur in the database are kept to a minimum.

This study relied solely on the coded diagnoses of diabetes, retinopathy, eye disease, and visual impairment. We did not have access to data from other sources such as retinal photography or practitioner letters, which could have been used to validate the diagnoses.

The use of multiple testing across a range of population subgroups meant that some of the observed associations may have arisen due to chance.

Clinical trials have established duration of diabetes, hyperglycaemia, and hypertension as key risk factors in the development of diabetic retinopathy.(35,36) Further work examining the role of pharmacological treatment and risk factor management will be essential in elucidating patterns of diabetic retinopathy further, particularly as the UK population ages and the burden of diabetes grows.

Policy Implications

According to the Office for National Statistics, the size of the UK population at the midpoint of 2014 was 64.6 million people.(37) Given that the CPRD is representative of the UK population structure, we estimate that the absolute number of people with any form of diabetic retinopathy in the UK is approximately 1.5 million and that the absolute number of people with severe diabetic retinopathy is around 140,000. Increases in prevalence of DR are likely to be related to increasing prevalence of T2DM and potentially increased ascertainment through national screening programs.

Findings from the 2013-2014 Screening Programmes in England Report highlighted the success of diabetic retinopathy screening programmes in reducing the burden of diabetic retinopathy in the UK, to the point where, it is now, no longer the leading cause of blindness amongst working age people in the UK.(38) In 2014, attendance at diabetic retinopathy screening was removed from the Quality and Outcomes Framework, meaning that this important indicator will no longer be collected to such a high accuracy for all diabetic patients. Not only will this impact on future research into retinopathy, it is likely to have serious negative implications on service planning for diabetic patients unless the indicator is reinstated.

Findings from this study will have implications for professionals working in the diabetes and sight loss sectors, particularly to inform approaches for diagnosis of retinopathy and campaigning to better tackle the disease for at risk groups. Evidence that deprivation may be associated with a higher risk of retinopathy, when viewed alongside previous evidence of lower retinopathy screening uptake amongst deprived groups, highlights a significant potential health inequality.(39) The national diabetic retinopathy screening programme and other stakeholders need to target and improve access to screening and support around self-management of diabetes for people living in deprived areas to avoid increasing inequalities.

Author Contribution

HL and EE provided the original remit for the study. The study was conceived and supervised by ID. ID and RM designed the study. RM extracted the data, conducted the statistical analysis and drafted the manuscript. EE HL LS KB NS contributed to interpretation of the findings, further drafts and approved the final manuscript. ID is guarantor.

Ethical approval

The pre-specified study protocol was approved by the Independent Scientific Advisory Committee for MHRA Database Research (ISAC). Approval was also received from the London School of Hygiene and Tropical Medicine ethics committee.

Data Sharing Statement

The data were obtained from the Clinical Practice Research Datalink (CPRD). CPRD is a research service that provides primary care and linked data for public health research. CPRD data governance and our own license to use CPRD data do not allow us to distribute or make available patient data directly to other parties. Researchers can apply for data access at www.cprd.com, and must have their study protocol approved by the Independent Scientific Advisory Committee for MHRA database research (details at www.cprd.com/isac).

REFERENCES

1. Diabetes UK. Key statistics on diabetes. 2010.
2. Diabetes UK. Eyes (Retinopathy). 2015.https://www.diabetes.org.uk/Guide-to-diabetes/Complications/Retinopathy/
3. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405–12.
4. Engerman RL. Pathogenesis of diabetic retinopathy. Diabetes. 1989;38:1203–6.
5. Harney F. Diabetic retinopathy. *Medicine (Baltimore)* 2006;34:95–8.
6. Harris M, Lead C, Warehouse V, Docks T. The NHS Diabetic Eye Screening Programme: New Common Pathway. 2012;:5–6.
7. Hayward LM, Burden ML, Burden AC, Blackledge H, Raymond NT, Botha JL, *et al.* What is the prevalence of visual impairment in the general and diabetic populations: are there ethnic and gender differences? *Diabet Med*;19:27–34.
8. Ethnic variations in the prevalence of diabetic retinopathy in people with diabetes attending screening in the United Kingdom (DRIVE UK). *PLoS One* 2012;7. doi:http://dx.doi.org/10.1371/journal.pone.0032182
9. Wong TY, Klein R, Islam FMA, Cotch MF, Folsom AR, Klein BEK, *et al.* Diabetic retinopathy in a multi-ethnic cohort in the United States. *Am J Ophthalmol*;141:446–55.
10. Cappuccio FP, Barbato A, Kerry S. Hypertension, diabetes and cardiovascular risk in ethnic minorities in the UK. Br. J. Diabetes Vasc. Dis. 2003;3:286–93.
11. Tillin. T, Hughes AD, Whincup P, Forouhi NG, Godsland IF, Sattar N, *et al.* Excess diabetes in ethnic minorities-incidence and predictors. *Diabetologia* 2011;Conference:47th Annual Meeting of the European Association fo.
12. Bakker LE, Sleddering MA, Schoones JW, Meinders AE, Jazet IM. Pathogenesis of type 2 diabetes in South Asians. *Eur J Endocrinol* 2013;169:R99–114.
13. Bhopal RS. A four-stage model explaining the higher risk of Type 2 diabetes mellitus in South Asians compared with European populations. *Diabet Med* 2013;30:35–42.
14. Davis TME, Coleman RL, Holman RR. Ethnicity and long-term vascular outcomes in Type 2 diabetes: A prospective observational study (UKPDS 83). *Diabet Med* 2014;31:200–7.
15. Kostev K, Rathmann W. Diabetic retinopathy at diagnosis of type 2 diabetes in the UK: A database analysis. *Diabetologia* 2013;56:109–11.
16. Looker HC, Cromie D. Diabetic retinopathy at diagnosis of type 2 diabetes in Scotland. Diabetes. 2011;60:A183.
17. Thomas RL, Dunstan FD, Luzio SD, Chowdhury SR, North R V., Hale SL, *et al.* Prevalence of diabetic retinopathy within a national diabetic retinopathy screening service. *Br J Ophthalmol* 2015;99:64–8.
18. 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;361:195–200.
19. Leese GP, Boyle P, Zhiqiang F, Emslie-Smith A, Ellis JD. Screening uptake in a well-established diabetic retinopathy screening program the role of geographical access and deprivation. *Diabetes Care* 2008;31:2131–5.
20. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, *et al.* Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* Published Online First: 6 June 2015. doi:10.1093/ije/dyv098
21. Mathur R, Bhaskaran K, Chaturvedi N, Leon DA, vanStaa T, Grundy E, *et al.* Completeness and usability of ethnicity data in UK-based primary care and hospital databases. *J Public Heal* 2013;36:684–92.
22. Allen N, Sudlow C, Downey P, Peakman T, Danesh J, Elliott P, *et al.* UK Biobank: Current status

and what it means for epidemiology. *Heal Policy Technol* 2012;1:123–6.
23. Mclennan D, Barnes H, Noble M, Davies J, Garratt E. The English Indices of Deprivation 2010 - technical report. *Soc Policy* Published Online First: 2011. doi:http://dx.doi.org/http://www.communities.gov.uk/publications/corporate/statistics/indices2010technicalreport
24. Hull S a., Mathur R, Badrick E, Robson J, Boomla K. Recording ethnicity in primary care: Assessing the methods and impact. *Br J Gen Pract* 2011;61:e290-4.
25. Office for National Statistics. Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2014. 2015.http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-368259 (accessed 1 Nov 2015).
26. Delcourt C, Massin P, Rosilio M. Epidemiology of diabetic retinopathy: Expected vs reported prevalence of cases in the French population. *Diabetes Metab* 2009;35:431–8.
27. Lindenmeyer A, Sturt JA, Hipwell A, Stratton IM, Al-Athamneh N, Gadsby R, *et al.* Influence of primary care practices on patients' uptake of diabetic retinopathy screening: A qualitative case study. *Br J Gen Pract* 2014;64:484–92.
28. Strutton R, Du Chemin A, Stratton IM, Forster AS. System-level and patient-level explanations for non-attendance at diabetic retinopathy screening in Sutton and Merton (London, UK): a qualitative analysis of a service evaluation: Table 1. *BMJ Open* 2016;6:e010952.
29. Beeching NJ, Gill G V. Deprivation and Type 2 diabetes mellitus prevalence. *Diabet Med* 2000;17:813.
30. Doran T, Fullwood C, Gravelle H, Reeves D, Kontopantelis E, Hiroeh U, *et al.* Pay-for-Performance Programs in Family Practices in the United Kingdom. N. Engl. J. Med. 2006.http://www.nejm.org/doi/full/10.1056/NEJMsa055505 (accessed 27 Jul 2015).
31. Khunti K, Gadsby R, Millett C, Majeed a., Davies M. Quality of diabetes care in the UK: Comparison of published quality-of-care reports with results of the Quality and Outcomes Framework for Diabetes. *Diabet Med* 2007;24:1436–41.
32. Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69:4–14.
33. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60:e128-36.
34. Jick SS, Kaye JA, Vasilakis-Scaramozza C, Garcia Rodriguez LA, Ruigomez A, Meier CR, *et al.* Validity of the general practice research database. *Pharmacotherapy* 2003;23:686–9.
35. Konig M, Lamos EM, Stein SA, Davis SN. An insight into the recent diabetes trials: what is the best approach to prevent macrovascular and microvascular complications?. *Curr Diabetes Rev* 2013;9:371–81.
36. Turner R, Matthews D, Neil A, Mcelroy H. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *Br Med J* 1998;317:703–13.
37. ONS. Total Population (UK) Mid-2014 Estimate. 2014.http://ons.gov.uk/ons/taxonomy/index.html?nscl=Population (accessed 30 Jul 2015).
38. Public Health England; NHS Screening Programmes in England 2013/14. 2013.
39. Knight A, Lindfield R. The relationship between socio-economic status and access to eye health services in the UK: A systematic review. Public Health. 2015;129:94–102.

FIGURE LEGENDS

Figure 1. Age standardised prevalence and incidence of diabetes and diabetic retinopathy 2004-2014

Figure 2. Relative risk of diabetic retinopathy in patients with type 2 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes

Figure 3. Relative risk of diabetic retinopathy in patients with type 1 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes

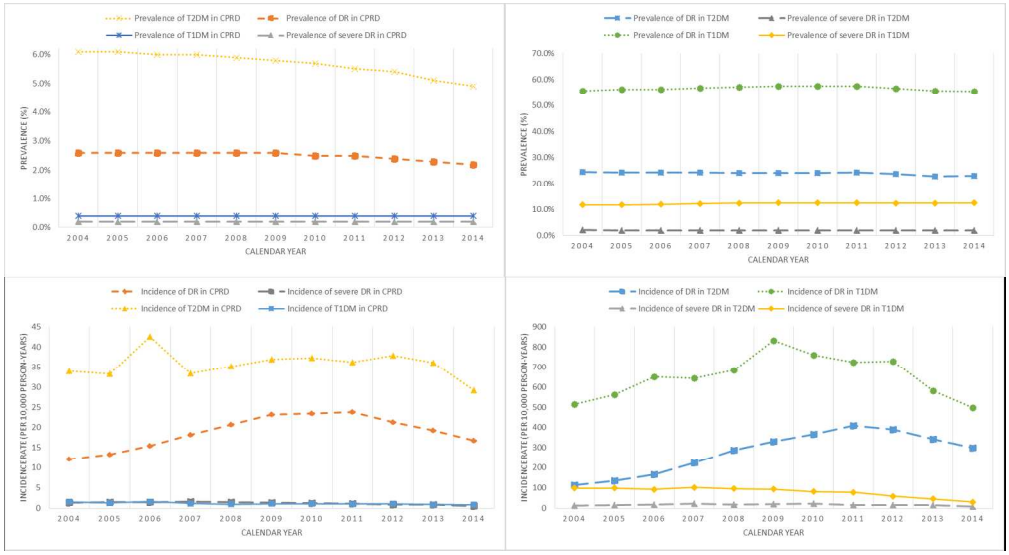

Figure 1. Age standardised prevalence and incidence of diabetes and diabetic retinopathy 2004-2014
(Insert Figure 1 here)
350x192mm (150 x 150 DPI)

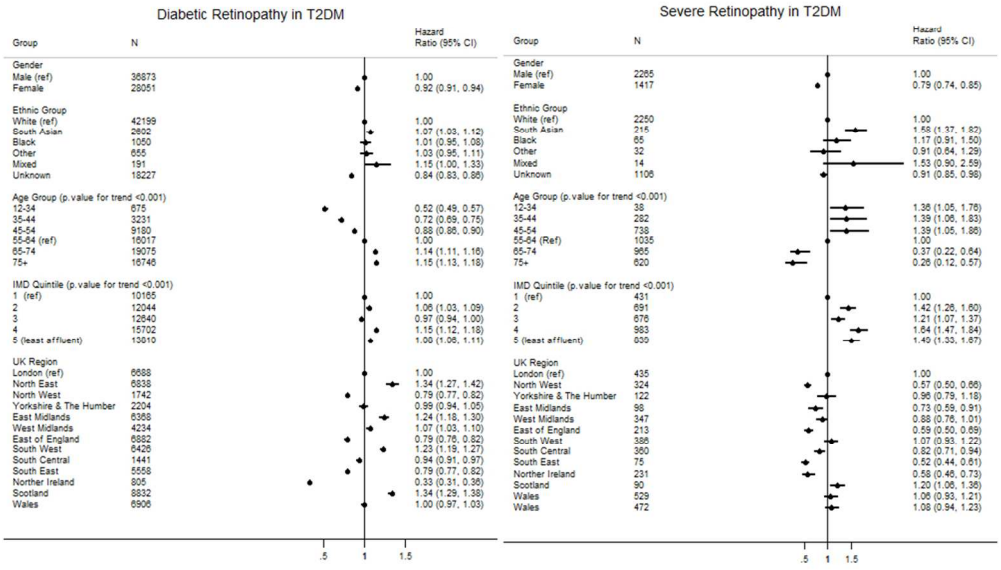

Figure 2. Relative risk of diabetic retinopathy in patients with type 2 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes
(Insert Figures 2 and 3 about
354x257mm (72 x 72 DPI)

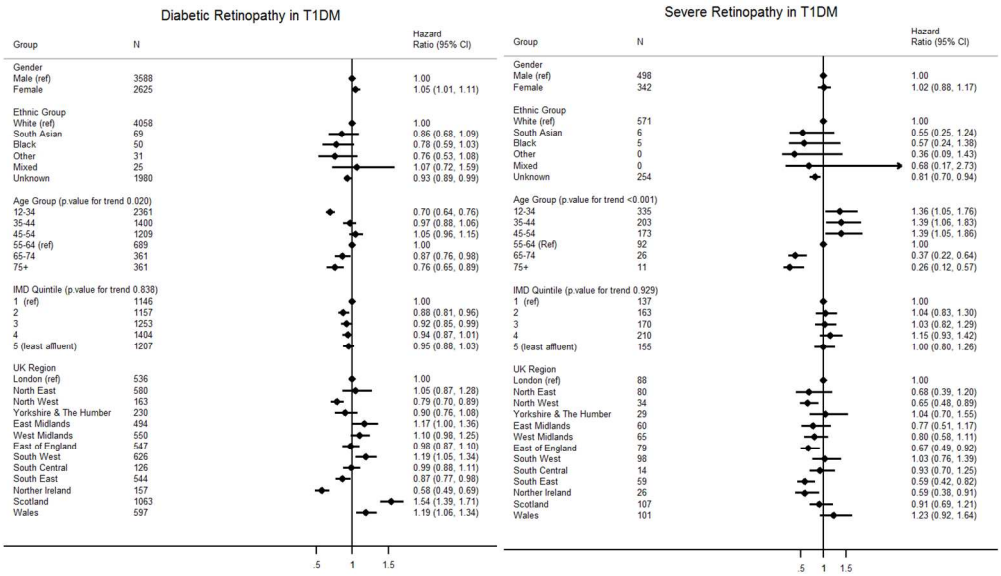

Figure 3. Relative risk of diabetic retinopathy in patients with type 1 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes
(Insert Figures 2 and 3 about
514x374mm (72 x 72 DPI)

Supplementary Materials

Tables

Figures

a. Population Flow Diagram

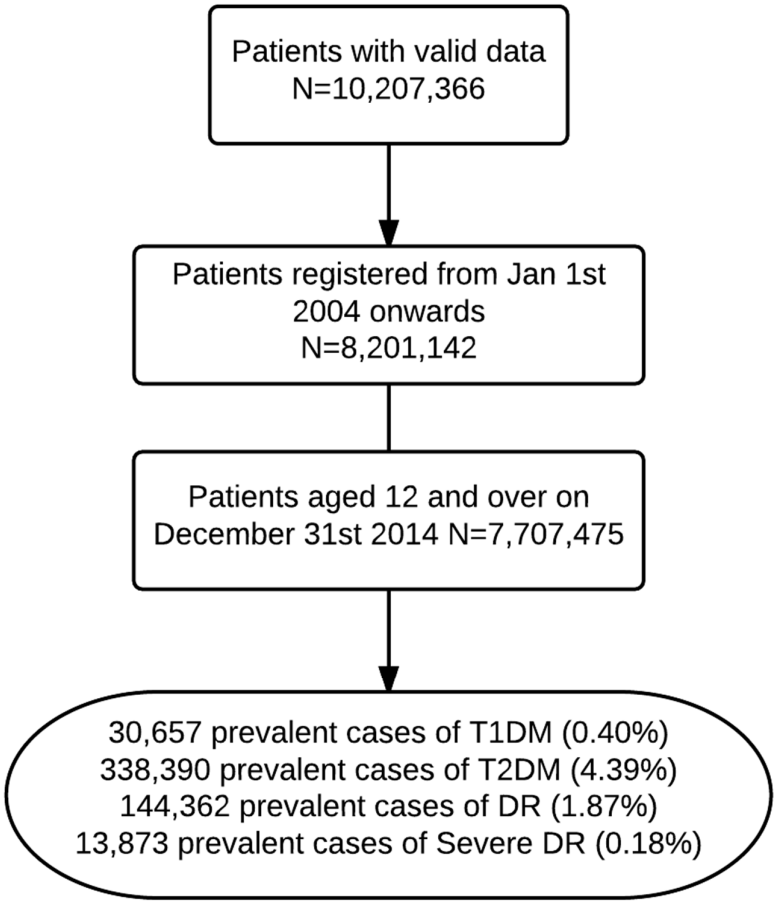

Figure 1. Derivation of study population from the CPRD

b. Results of the diabetes adjudication algorithms

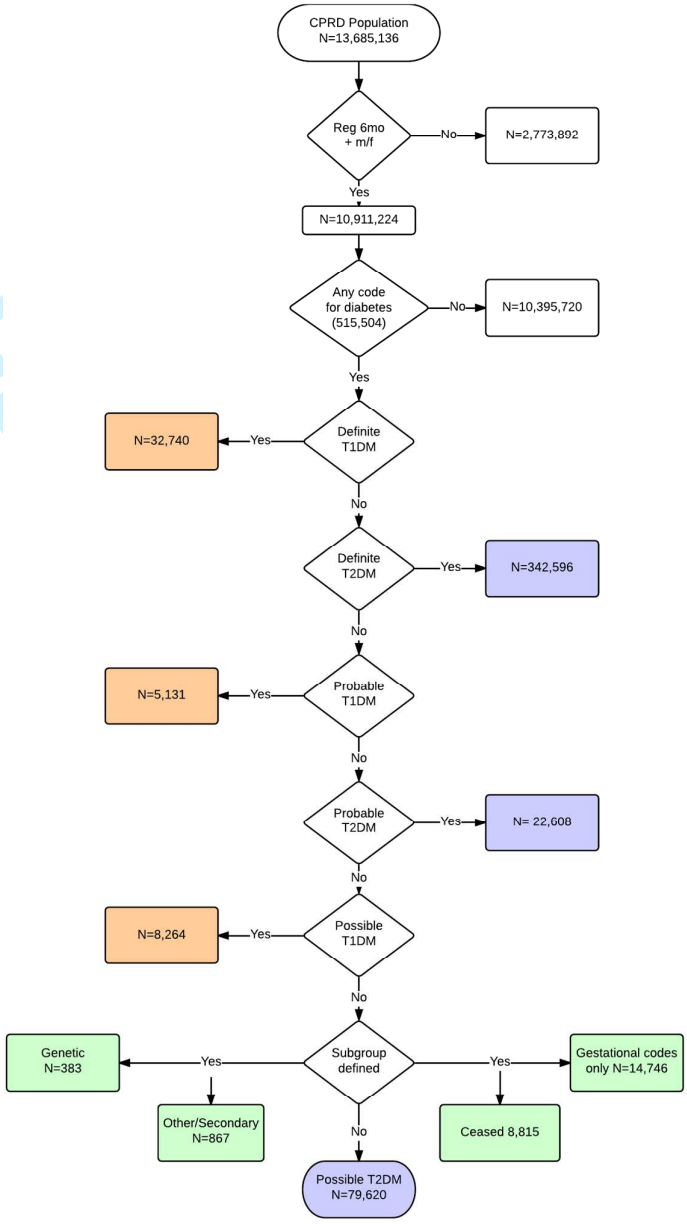

Figure 2. Results from Flowchart 1: Initial Sort and Classification

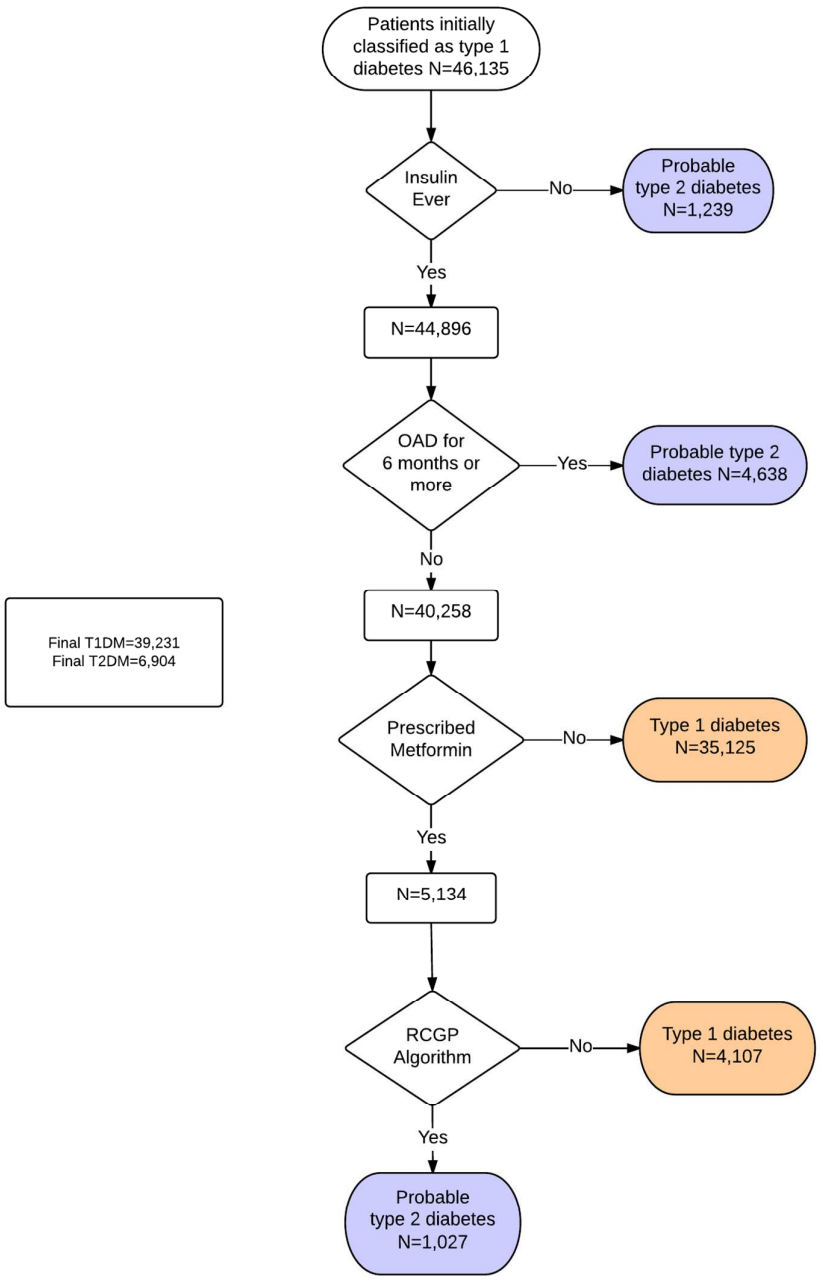

Figure 3. Results from Flowchart 2: Improving classification of type 1 diabetes

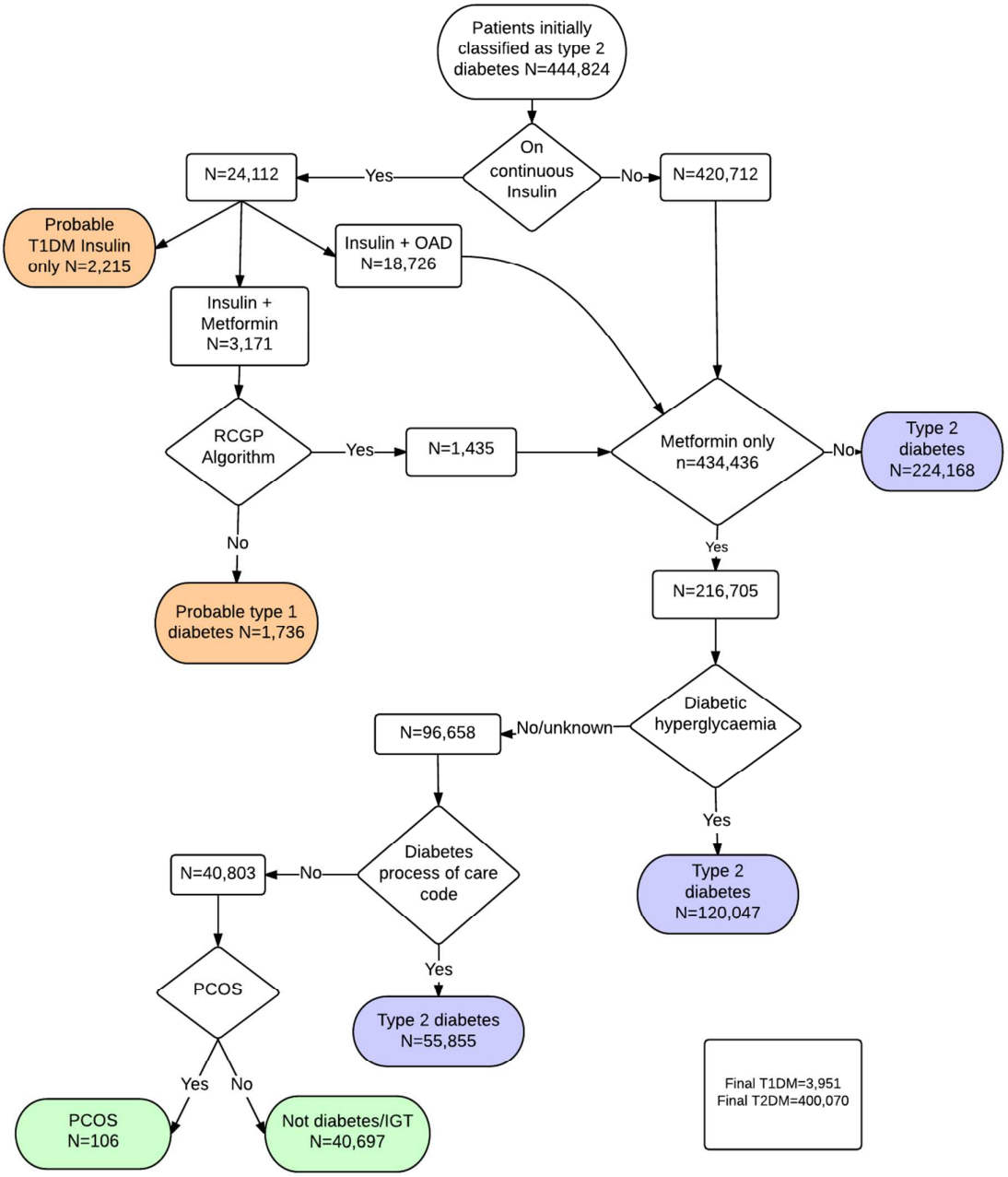

Figure 4. Results from Flowchart 3: Improving classification of type 2 diabetes

c. Codelists

Table 1. Search terms for Diabetic Retinopathy

Keywords for identifying diabetic retinopathy in the CPRD
RETINAL **and** or *SCR* or *ARTERIES* or *EXUDATE* or *MICROANEURYSMS* or *PHOTOGRAPHY* or *ABNORMALITY*
O/E **and** *RETINA* or *FUNDUS* or *PHOTOCOAGULATION* or *MACULAR* or *VITREOUS*
*LASER" **and** *RETINA*
RETINOPATHY or *FUNDOSCOPY* or *MACULOPATHY* or *RED REFLEX* or *SEEN BY OP* or *RETINAL SCR* or *RETINOSCOPY* or *SLIT LAMP* or *DIABETIC EYE* or *EYE FUNDUS* or *EXAMINATION OF RETINA* or *RETINA AND OTHER PARTS OF EYE OPERATIONS* or *VITRECTOMY*
Keywords excluded (to remove obstetric terms related to "fundus")
TERM SIZE or *WEEK SIZE* or *OBSTETRIC*

Table 2. Categorization of Read codes for Diabetes Mellitus

	Type 1 Diabetes	Type 2 Diabetes	Other
Definite	Type 1 DM: C10E Not contradicted/ceased/superseded	Type 2 DM: C10F Not contradicted/ceased/superseded	Gestational L180 Genetic C10c-C10D Other/Secondary C10G-J, L-N, C11y0 Insulin resistance: C10K, C1098, C10F8 Ceased: 21263, 212H
Probable	IDDM: C108 Adult onset: C1073 Gestational: L1805 Not contradicted/ceased/superseded	NIDDM: C109 Gestational: L1806 Gestational: L180X Not contradicted/ceased/superseded	
Possible	Diabetes mellitus, adult onset: C10z1 C10y0 C110 Not contradicted/ceased/superseded	Diabetes mellitus, adult onset: C10%, C112 (z), L180x Not contradicted/ceased/superseded	

Table 3. Read codes for Diabetes Mellitus

medcode	readcode	readterm	category
28622	2126300	Diabetes resolved	Diabetes ceased
18766	212H.00	Diabetes resolved	Diabetes ceased
711	C10..00	Diabetes mellitus	Vague codes
38986	C100.00	Diabetes mellitus with no mention of complication	Vague codes
24490	C100000	Diabetes mellitus, juvenile type, no mention of complication	Possible T1 codes
1038	C100011	Insulin dependent diabetes mellitus	Possible T1 codes
14803	C100100	Diabetes mellitus, adult onset, no mention of complication	Possible T2 codes
14889	C100111	Maturity onset diabetes	Possible T2 codes
506	C100112	Non-insulin dependent diabetes mellitus	Possible T2 codes
50972	C100z00	Diabetes mellitus NOS with no mention of complication	Vague codes
1682	C101.00	Diabetes mellitus with ketoacidosis	Vague codes
53200	C101000	Diabetes mellitus, juvenile type, with ketoacidosis	Possible T1 codes
54856	C101100	Diabetes mellitus, adult onset, with ketoacidosis	Vague codes
38617	C101y00	Other specified diabetes mellitus with ketoacidosis	Vague codes
42505	C101z00	Diabetes mellitus NOS with ketoacidosis	Vague codes
21482	C102.00	Diabetes mellitus with hyperosmolar coma	Vague codes
40023	C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma	Possible T1 codes
43139	C102100	Diabetes mellitus, adult onset, with hyperosmolar coma	Possible T2 codes
72345	C102z00	Diabetes mellitus NOS with hyperosmolar coma	Vague codes
15690	C103.00	Diabetes mellitus with ketoacidotic coma	Vague codes
42567	C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma	Possible T1 codes
68843	C103100	Diabetes mellitus, adult onset, with ketoacidotic coma	Possible T2 codes
59288	C103y00	Other specified diabetes mellitus with coma	Vague codes
65062	C103z00	Diabetes mellitus NOS with ketoacidotic coma	Vague codes
16502	C104.00	Diabetes mellitus with renal manifestation	Vague codes
2475	C104.11	Diabetic nephropathy	Vague codes
93922	C104000	Diabetes mellitus, juvenile type, with renal manifestation	Possible T1 codes
35105	C104100	Diabetes mellitus, adult onset, with renal manifestation	Possible T2 codes
13279	C104y00	Other specified diabetes mellitus with renal complications	Vague codes

medcode	readcode	readterm	category
35107	C104z00	Diabetes mellitis with nephropathy NOS	Vague codes
33254	C105.00	Diabetes mellitus with ophthalmic manifestation	Vague codes
69748	C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation	Possible T1 codes
41389	C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation	Possible T2 codes
47377	C105y00	Other specified diabetes mellitus with ophthalmic complicatn	Vague codes
34283	C105z00	Diabetes mellitus NOS with ophthalmic manifestation	Vague codes
16230	C106.00	Diabetes mellitus with neurological manifestation	Vague codes
59903	C106.11	Diabetic amyotrophy	Vague codes
7795	C106.12	Diabetes mellitus with neuropathy	Vague codes
16491	C106.13	Diabetes mellitus with polyneuropathy	Vague codes
67853	C106000	Diabetes mellitus, juvenile, + neurological manifestation	Possible T1 codes
39317	C106100	Diabetes mellitus, adult onset, + neurological manifestation	Possible T2 codes
61523	C106y00	Other specified diabetes mellitus with neurological comps	Vague codes
22573	C106z00	Diabetes mellitus NOS with neurological manifestation	Vague codes
35399	C107.00	Diabetes mellitus with peripheral circulatory disorder	Vague codes
32403	C107.11	Diabetes mellitus with gangrene	Vague codes
32556	C107.12	Diabetes with gangrene	Vague codes
70448	C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder	Possible T1 codes
63357	C107100	Diabetes mellitus, adult, + peripheral circulatory disorder	Possible T2 codes
33807	C107200	Diabetes mellitus, adult with gangrene	Possible T2 codes
69124	C107300	IDDM with peripheral circulatory disorder	Probable T1 codes
56803	C107400	NIDDM with peripheral circulatory disorder	Probable T2 codes
65025	C107z00	Diabetes mellitus NOS with peripheral circulatory disorder	Vague codes
1647	C108.00	Insulin dependent diabetes mellitus	Probable T1 codes
18505	C108.11	IDDM-Insulin dependent diabetes mellitus	Probable T1 codes

medcode	readcode	readterm	category
17858	C108.12	Type 1 diabetes mellitus	Probable T1 codes
24423	C108.13	Type I diabetes mellitus	Probable T1 codes
46963	C108000	Insulin-dependent diabetes mellitus with renal complications	Probable T1 codes
61344	C108011	Type I diabetes mellitus with renal complications	Probable T1 codes
21983	C108012	Type 1 diabetes mellitus with renal complications	Probable T1 codes
49276	C108100	Insulin-dependent diabetes mellitus with ophthalmic comps	Probable T1 codes
52283	C108200	Insulin-dependent diabetes mellitus with neurological comps	Probable T1 codes
49146	C108211	Type I diabetes mellitus with neurological complications	Probable T1 codes
61829	C108212	Type 1 diabetes mellitus with neurological complications	Probable T1 codes
52104	C108300	Insulin dependent diabetes mellitus with multiple complicatn	Probable T1 codes
26855	C108400	Unstable insulin dependant diabetes mellitus	Probable T1 codes
60107	C108411	Unstable type I diabetes mellitus	Probable T1 codes
97474	C108412	Unstable type 1 diabetes mellitus	Probable T1 codes
44443	C108500	Insulin dependent diabetes mellitus with ulcer	Probable T1 codes
51957	C108511	Type I diabetes mellitus with ulcer	Probable T1 codes
68390	C108512	Type 1 diabetes mellitus with ulcer	Probable T1 codes
60499	C108600	Insulin dependent diabetes mellitus with gangrene	Probable T1 codes
6509	C108700	Insulin dependent diabetes mellitus with retinopathy	Probable T1 codes
38161	C108711	Type I diabetes mellitus with retinopathy	Probable T1 codes
41049	C108712	Type 1 diabetes mellitus with retinopathy	Probable T1 codes
6791	C108800	Insulin dependant diabetes mellitus - poor control	Probable T1 codes
46850	C108811	Type I diabetes mellitus - poor control	Probable T1 codes
45914	C108812	Type 1 diabetes mellitus - poor control	Probable T1 codes
31310	C108900	Insulin dependant diabetes maturity onset	Probable T1 codes
63017	C108911	Type I diabetes mellitus maturity onset	Probable T1 codes
97446	C108912	Type 1 diabetes mellitus maturity onset	Probable T1 codes
56448	C108A00	Insulin-dependent diabetes without complication	Probable T1 codes
95992	C108A11	Type I diabetes mellitus without complication	Probable T1 codes

medcode	readcode	readterm	category
24694	C108B00	Insulin dependent diabetes mellitus with mononeuropathy	Probable T1 codes
99231	C108B11	Type I diabetes mellitus with mononeuropathy	Probable T1 codes
41716	C108C00	Insulin dependent diabetes mellitus with polyneuropathy	Probable T1 codes
57621	C108D00	Insulin dependent diabetes mellitus with nephropathy	Probable T1 codes
66872	C108D11	Type I diabetes mellitus with nephropathy	Probable T1 codes
44440	C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma	Probable T1 codes
42729	C108E11	Type I diabetes mellitus with hypoglycaemic coma	Probable T1 codes
70766	C108E12	Type 1 diabetes mellitus with hypoglycaemic coma	Probable T1 codes
44260	C108F00	Insulin dependent diabetes mellitus with diabetic cataract	Probable T1 codes
17545	C108F11	Type I diabetes mellitus with diabetic cataract	Probable T1 codes
64446	C108G00	Insulin dependent diab mell with peripheral angiopathy	Probable T1 codes
65616	C108H00	Insulin dependent diabetes mellitus with arthropathy	Probable T1 codes
62352	C108H11	Type I diabetes mellitus with arthropathy	Probable T1 codes
39809	C108J00	Insulin dependent diab mell with neuropathic arthropathy	Probable T1 codes
60208	C108J11	Type I diabetes mellitus with neuropathic arthropathy	Probable T1 codes
18230	C108J12	Type 1 diabetes mellitus with neuropathic arthropathy	Probable T1 codes
46290	C108y00	Other specified diabetes mellitus with multiple comps	Vague codes
64449	C108z00	Unspecified diabetes mellitus with multiple complications	Vague codes
4513	C109.00	Non-insulin dependent diabetes mellitus	Probable T2 codes
5884	C109.11	NIDDM - Non-insulin dependent diabetes mellitus	Probable T2 codes
17859	C109.12	Type 2 diabetes mellitus	Probable T2 codes
18219	C109.13	Type II diabetes mellitus	Probable T2 codes
52303	C109000	Non-insulin-dependent diabetes mellitus with renal comps	Probable T2 codes
50225	C109011	Type II diabetes mellitus with renal complications	Probable T2 codes
18209	C109012	Type 2 diabetes mellitus with renal complications	Probable T2 codes
50429	C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps	Probable T2 codes

medcode	readcode	readterm	category
59725	C109111	Type II diabetes mellitus with ophthalmic complications	Probable T2 codes
70316	C109112	Type 2 diabetes mellitus with ophthalmic complications	Probable T2 codes
55842	C109200	Non-insulin-dependent diabetes mellitus with neuro comps	Probable T2 codes
67905	C109211	Type II diabetes mellitus with neurological complications	Probable T2 codes
45919	C109212	Type 2 diabetes mellitus with neurological complications	Probable T2 codes
62146	C109300	Non-insulin-dependent diabetes mellitus with multiple comps	Probable T2 codes
34912	C109400	Non-insulin dependent diabetes mellitus with ulcer	Probable T2 codes
55075	C109411	Type II diabetes mellitus with ulcer	Probable T2 codes
65704	C109412	Type 2 diabetes mellitus with ulcer	Probable T2 codes
40401	C109500	Non-insulin dependent diabetes mellitus with gangrene	Probable T2 codes
62107	C109511	Type II diabetes mellitus with gangrene	Probable T2 codes
46150	C109512	Type 2 diabetes mellitus with gangrene	Probable T2 codes
17262	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	Probable T2 codes
58604	C109611	Type II diabetes mellitus with retinopathy	Probable T2 codes
42762	C109612	Type 2 diabetes mellitus with retinopathy	Probable T2 codes
8403	C109700	Non-insulin dependant diabetes mellitus - poor control	Probable T2 codes
24458	C109711	Type II diabetes mellitus - poor control	Probable T2 codes
45913	C109712	Type 2 diabetes mellitus - poor control	Probable T2 codes
39406	C109800	Reaven's syndrome	Not diabetes
29979	C109900	Non-insulin-dependent diabetes mellitus without complication	Probable T2 codes
72320	C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy	Probable T2 codes
50813	C109A11	Type II diabetes mellitus with mononeuropathy	Probable T2 codes
45467	C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy	Probable T2 codes
47409	C109B11	Type II diabetes mellitus with polyneuropathy	Probable T2 codes
59365	C109C00	Non-insulin dependent diabetes mellitus with nephropathy	Probable T2 codes

medcode	readcode	readterm	category
64571	C109C11	Type II diabetes mellitus with nephropathy	Probable T2 codes
24836	C109C12	Type 2 diabetes mellitus with nephropathy	Probable T2 codes
43785	C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma	Probable T2 codes
56268	C109D11	Type II diabetes mellitus with hypoglycaemic coma	Probable T2 codes
61071	C109D12	Type 2 diabetes mellitus with hypoglycaemic coma	Probable T2 codes
69278	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract	Probable T2 codes
48192	C109E11	Type II diabetes mellitus with diabetic cataract	Probable T2 codes
44779	C109E12	Type 2 diabetes mellitus with diabetic cataract	Probable T2 codes
54212	C109F00	Non-insulin-dependent d m with peripheral angiopath	Probable T2 codes
54899	C109F11	Type II diabetes mellitus with peripheral angiopathy	Probable T2 codes
60699	C109F12	Type 2 diabetes mellitus with peripheral angiopathy	Probable T2 codes
24693	C109G00	Non-insulin dependent diabetes mellitus with arthropathy	Probable T2 codes
18143	C109G11	Type II diabetes mellitus with arthropathy	Probable T2 codes
49869	C109G12	Type 2 diabetes mellitus with arthropathy	Probable T2 codes
40962	C109H00	Non-insulin dependent d m with neuropathic arthropathy	Probable T2 codes
47816	C109H11	Type II diabetes mellitus with neuropathic arthropathy	Probable T2 codes
66965	C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	Probable T2 codes
18278	C109J00	Insulin treated Type 2 diabetes mellitus	Probable T2 codes
37648	C109J11	Insulin treated non-insulin dependent diabetes mellitus	Probable T2 codes
18264	C109J12	Insulin treated Type II diabetes mellitus	Probable T2 codes
36633	C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	Probable T2 codes
52236	C10A.00	Malnutrition-related diabetes mellitus	Secondary / Other types
66675	C10A000	Malnutrition-related diabetes mellitus with coma	Secondary / Other types
33969	C10A100	Malnutrition-related diabetes mellitus with ketoacidosis	Secondary / Other types
100347	C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn	Secondary / Other types
11551	C10B.00	Diabetes mellitus induced by steroids	Secondary / Other types
26108	C10B000	Steroid induced diabetes mellitus without complication	Secondary / Other types

medcode	readcode	readterm	category
43453	C10C.00	Diabetes mellitus autosomal dominant	Genetic
46624	C10C.11	Maturity onset diabetes in youth	Genetic
98392	C10C.12	Maturity onset diabetes in youth type 1	Genetic
36695	C10D.00	Diabetes mellitus autosomal dominant type 2	Genetic
59991	C10D.11	Maturity onset diabetes in youth type 2	Genetic
1549	C10E.00	Type 1 diabetes mellitus	Definite T1 codes
12455	C10E.11	Type I diabetes mellitus	Definite T1 codes
51261	C10E.12	Insulin dependent diabetes mellitus	Definite T1 codes
47582	C10E000	Type 1 diabetes mellitus with renal complications	Definite T1 codes
47649	C10E100	Type 1 diabetes mellitus with ophthalmic complications	Definite T1 codes
99311	C10E111	Type I diabetes mellitus with ophthalmic complications	Definite T1 codes
98071	C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps	Definite T1 codes
42831	C10E200	Type 1 diabetes mellitus with neurological complications	Definite T1 codes
47650	C10E300	Type 1 diabetes mellitus with multiple complications	Definite T1 codes
91942	C10E311	Type I diabetes mellitus with multiple complications	Definite T1 codes
45276	C10E312	Insulin dependent diabetes mellitus with multiple complicat	Definite T1 codes
43921	C10E400	Unstable type 1 diabetes mellitus	Definite T1 codes
49949	C10E411	Unstable type I diabetes mellitus	Definite T1 codes
54600	C10E412	Unstable insulin dependent diabetes mellitus	Definite T1 codes
18683	C10E500	Type 1 diabetes mellitus with ulcer	Definite T1 codes
93878	C10E511	Type I diabetes mellitus with ulcer	Definite T1 codes
98704	C10E512	Insulin dependent diabetes mellitus with ulcer	Definite T1 codes
69993	C10E600	Type 1 diabetes mellitus with gangrene	Definite T1 codes
18387	C10E700	Type 1 diabetes mellitus with retinopathy	Definite T1 codes
95343	C10E711	Type I diabetes mellitus with retinopathy	Definite T1 codes
93875	C10E712	Insulin dependent diabetes mellitus with retinopathy	Definite T1 codes
35288	C10E800	Type 1 diabetes mellitus - poor control	Definite T1 codes
72702	C10E812	Insulin dependent diabetes mellitus - poor control	Definite T1 codes
40682	C10E900	Type 1 diabetes mellitus maturity onset	Definite T1 codes
96235	C10E911	Type I diabetes mellitus maturity onset	Definite T1 codes

medcode	readcode	readterm	category
97849	C10E912	Insulin dependent diabetes maturity onset	Definite T1 codes
69676	C10EA00	Type 1 diabetes mellitus without complication	Definite T1 codes
62613	C10EA11	Type I diabetes mellitus without complication	Definite T1 codes
99719	C10EA12	Insulin-dependent diabetes without complication	Definite T1 codes
68105	C10EB00	Type 1 diabetes mellitus with mononeuropathy	Definite T1 codes
46301	C10EC00	Type 1 diabetes mellitus with polyneuropathy	Definite T1 codes
91943	C10EC11	Type I diabetes mellitus with polyneuropathy	Definite T1 codes
101311	C10EC12	Insulin dependent diabetes mellitus with polyneuropathy	Definite T1 codes
10418	C10ED00	Type 1 diabetes mellitus with nephropathy	Definite T1 codes
39070	C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma	Definite T1 codes
99716	C10EE12	Insulin dependent diabetes mellitus with hypoglycaemic coma	Definite T1 codes
49554	C10EF00	Type 1 diabetes mellitus with diabetic cataract	Definite T1 codes
100770	C10EF12	Insulin dependent diabetes mellitus with diabetic cataract	Definite T1 codes
93468	C10EG00	Type 1 diabetes mellitus with peripheral angiopathy	Definite T1 codes
18642	C10EH00	Type 1 diabetes mellitus with arthropathy	Definite T1 codes
54008	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy	Definite T1 codes
30323	C10EK00	Type 1 diabetes mellitus with persistent proteinuria	Definite T1 codes
30294	C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	Definite T1 codes
10692	C10EM00	Type 1 diabetes mellitus with ketoacidosis	Definite T1 codes
62209	C10EM11	Type I diabetes mellitus with ketoacidosis	Definite T1 codes
40837	C10EN00	Type 1 diabetes mellitus with ketoacidotic coma	Definite T1 codes
66145	C10EN11	Type I diabetes mellitus with ketoacidotic coma	Definite T1 codes
22871	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	Definite T1 codes
97894	C10EP11	Type I diabetes mellitus with exudative maculopathy	Definite T1 codes
55239	C10EQ00	Type 1 diabetes mellitus with gastroparesis	Definite T1 codes
95636	C10ER00	Latent autoimmune diabetes mellitus in adult	Secondary / Other types
758	C10F.00	Type 2 diabetes mellitus	Definite T2 codes
22884	C10F.11	Type II diabetes mellitus	Definite T2 codes
18777	C10F000	Type 2 diabetes mellitus with renal complications	Definite T2 codes

medcode	readcode	readterm	category
57278	C10F011	Type II diabetes mellitus with renal complications	Definite T2 codes
47321	C10F100	Type 2 diabetes mellitus with ophthalmic complications	Definite T2 codes
100964	C10F111	Type II diabetes mellitus with ophthalmic complications	Definite T2 codes
34268	C10F200	Type 2 diabetes mellitus with neurological complications	Definite T2 codes
98616	C10F211	Type II diabetes mellitus with neurological complications	Definite T2 codes
65267	C10F300	Type 2 diabetes mellitus with multiple complications	Definite T2 codes
43227	C10F311	Type II diabetes mellitus with multiple complications	Definite T2 codes
49074	C10F400	Type 2 diabetes mellitus with ulcer	Definite T2 codes
91646	C10F411	Type II diabetes mellitus with ulcer	Definite T2 codes
12736	C10F500	Type 2 diabetes mellitus with gangrene	Definite T2 codes
18496	C10F600	Type 2 diabetes mellitus with retinopathy	Definite T2 codes
49655	C10F611	Type II diabetes mellitus with retinopathy	Definite T2 codes
25627	C10F700	Type 2 diabetes mellitus - poor control	Definite T2 codes
47315	C10F711	Type II diabetes mellitus - poor control	Definite T2 codes
54773	C10F800	Reaven's syndrome	Not diabetes
39481	C10F811	Metabolic syndrome X	Not diabetes
47954	C10F900	Type 2 diabetes mellitus without complication	Definite T2 codes
53392	C10F911	Type II diabetes mellitus without complication	Definite T2 codes
62674	C10FA00	Type 2 diabetes mellitus with mononeuropathy	Definite T2 codes
95351	C10FA11	Type II diabetes mellitus with mononeuropathy	Definite T2 codes
18425	C10FB00	Type 2 diabetes mellitus with polyneuropathy	Definite T2 codes
50527	C10FB11	Type II diabetes mellitus with polyneuropathy	Definite T2 codes
12640	C10FC00	Type 2 diabetes mellitus with nephropathy	Definite T2 codes
46917	C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma	Definite T2 codes
98723	C10FD11	Type II diabetes mellitus with hypoglycaemic coma	Definite T2 codes
44982	C10FE00	Type 2 diabetes mellitus with diabetic cataract	Definite T2 codes
93727	C10FE11	Type II diabetes mellitus with diabetic cataract	Definite T2 codes
37806	C10FF00	Type 2 diabetes mellitus with peripheral angiopathy	Definite T2 codes
59253	C10FG00	Type 2 diabetes mellitus with arthropathy	Definite T2 codes
35385	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy	Definite T2 codes
1407	C10FJ00	Insulin treated Type 2 diabetes mellitus	Definite T2 codes
64668	C10FJ11	Insulin treated Type II diabetes mellitus	Definite T2 codes

medcode	readcode	readterm	category
34450	C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	Definite T2 codes
26054	C10FL00	Type 2 diabetes mellitus with persistent proteinuria	Definite T2 codes
60796	C10FL11	Type II diabetes mellitus with persistent proteinuria	Definite T2 codes
18390	C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	Definite T2 codes
85991	C10FM11	Type II diabetes mellitus with persistent microalbuminuria	Definite T2 codes
32627	C10FN00	Type 2 diabetes mellitus with ketoacidosis	Definite T2 codes
51756	C10FP00	Type 2 diabetes mellitus with ketoacidotic coma	Definite T2 codes
25591	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	Definite T2 codes
63690	C10FR00	Type 2 diabetes mellitus with gastroparesis	Definite T2 codes
95539	C10FS00	Maternally inherited diabetes mellitus	Genetic
51697	C10G.00	Secondary pancreatic diabetes mellitus	Secondary / Other types
96506	C10G000	Secondary pancreatic diabetes mellitus without complication	Secondary / Other types
61122	C10H.00	Diabetes mellitus induced by non-steroid drugs	Secondary / Other types
67212	C10H000	DM induced by non-steroid drugs without complication	Secondary / Other types
68517	C10J.00	Insulin autoimmune syndrome	Secondary / Other types
37957	C10K.00	Type A insulin resistance	Not diabetes
56885	C10K000	Type A insulin resistance without complication	Not diabetes
43857	C10M.00	Lipoatrophic diabetes mellitus	Secondary / Other types
22487	C10N.00	Secondary diabetes mellitus	Secondary / Other types
94383	C10N000	Secondary diabetes mellitus without complication	Secondary / Other types
93380	C10N100	Cystic fibrosis related diabetes mellitus	Secondary / Other types
33343	C10y.00	Diabetes mellitus with other specified manifestation	Vague codes
63371	C10y100	Diabetes mellitus, adult, + other specified manifestation	Probable T2 codes
10098	C10yy00	Other specified diabetes mellitus with other spec comps	Vague codes
70821	C10yz00	Diabetes mellitus NOS with other specified manifestation	Vague codes
45491	C10z.00	Diabetes mellitus with unspecified complication	Vague codes
68792	C10z000	Diabetes mellitus, juvenile type, + unspecified complication	Possible T1 codes

medcode	readcode	readterm	category
63762	C10z100	Diabetes mellitus, adult onset, + unspecified complication	Probable T2 codes
64283	C10zy00	Other specified diabetes mellitus with unspecified comps	Vague codes
64357	C10zz00	Diabetes mellitus NOS with unspecified complication	Vague codes
2472	C110.00	Hypoglycaemic coma	Possible T1 codes
53630	C110.11	Insulin coma	Possible T1 codes
61520	C110000	Iatrogenic hyperinsulinism	Secondary / Other types
72882	C110100	Self-induced hyperinsulinism	Probable T1 codes
51371	C110z00	Hypoglycaemic coma NOS	Possible T1 codes
1410	C112.00	Hypoglycaemia unspecified	Possible T2 codes
4563	C112000	Reactive hypoglycaemia NOS	Possible T2 codes
24405	C112100	Spontaneous hypoglycaemia NOS	Possible T2 codes
20368	C112z00	Hypoglycaemia unspecified NOS	Possible T2 codes
11359	L180.00	Diabetes mellitus during pregnancy/childbirth/puerperium	Probable Gestational diabetes
67635	L180000	Diabetes mellitus - unspec whether in pregnancy/puerperium	Probable Gestational diabetes
34639	L180100	Diabetes mellitus during pregnancy - baby delivered	Probable Gestational diabetes
49559	L180300	Diabetes mellitus during pregnancy - baby not yet delivered	Probable Gestational diabetes
96823	L180400	Diabetes mellitus in pueperium - baby previously delivered	Probable T1 codes
50960	L180500	Pre-existing diabetes mellitus, insulin-dependent	Probable T1 codes
50609	L180600	Pre-existing diabetes mellitus, non-insulin-dependent	Probable T2 codes
10278	L180800	Diabetes mellitus arising in pregnancy	Probable Gestational diabetes
8446	L180811	Gestational diabetes mellitus	Probable Gestational diabetes
2664	L180900	Gestational diabetes mellitus	Probable Gestational diabetes
55431	L180X00	Pre-existing diabetes mellitus, unspecified	Vague codes
64384	L180z00	Diabetes mellitus in pregnancy/childbirth/puerperium NOS	Probable Gestational diabetes

Table 4. Read codes for Diabetic Retinopathy diagnosis and screening

medcode	readcode	readterm	DR category
52041	2BBl.00	O/E - left eye stable treated prolif diabetic retinopathy	DR
52630	2BBo.00	O/E - sight threatening diabetic retinopathy	DR
19533	2BBY.00	O/E - referable retinopathy	DR
3837	F420400	Diabetic maculopathy	DR
47328	2BBk.00	O/E - right eye stable treated prolif diabetic retinopathy	DR
101881	2BBr.00	Impaired vision due to diabetic retinopathy	DR
3914	2BB9.00	O/E - retinal pigmentation	DR
9339	F421.00	Other background retinopathy	DR
10882	F421400	Exudative retinopathy	DR
48751	2BB3.00	O/E - retinal A-V nipping	DR
42762	C109612	Type 2 diabetes mellitus with retinopathy	DR
35659	2BB7.00	O/E - retinal vascular prolif.	DR
38161	C108711	Type I diabetes mellitus with retinopathy	DR
72424	7270B00	Vitrectomy using anterior approach	DR
9835	2BBL.00	O/E - diabetic maculopathy present both eyes	DR
39457	F421C00	Other intraretinal microvascular abnormality	DR
55026	7270B11	Anterior vitrectomy	DR
11053	F421800	Retinal microaneurysms NOS	DR
18387	C10E700	Type 1 diabetes mellitus with retinopathy	DR
4514	7270011	Anterior vitrectomy	DR
13102	2BBW.00	O/E - right eye diabetic maculopathy	DR
13108	2BBX.00	O/E - left eye diabetic maculopathy	DR
36119	F421111	Arteroscleroticretinopathy	DR
93875	C10E712	Insulin dependent diabetes mellitus with retinopathy	DR
8595	F42y600	Retinal exudate or deposit	DR
102242	2BBs.00	Retinal arteries silverwire	DR
17916	F422011	Retinopathy of prematurity	DR
22871	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	DR
1411	3128100	Fundoscopy abnormal	DR
11626	F420z00	Diabetic retinopathy NOS	DR
34455	F421112	Atheroscleritic retinopathy	DR
66964	F426500	Pseudoretinitis pigmentosa	DR
2254	F424100	Central serous retinopathy	DR
36867	2BBa.00	O/E- non-referable retinopathy	DR
11129	2BBQ.00	O/E - left eye background diabetic retinopathy	DR
88368	7270411	Vitrectomy using pars plana approach	DR
6509	C108700	Insulin dependent diabetes mellitus with retinopathy	DR
45876	F421200	Renal retinopathy	DR
8742	2BB5.00	O/E - retinal haemorrhages	DR
17262	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	DR
13107	2BBn.00	O/E - left eye clinically significant macular oedema	DR
104263	F425900	Maculopathy	DR

58604	C109611	Type II diabetes mellitus with retinopathy	DR
41049	C108712	Type 1 diabetes mellitus with retinopathy	DR
1323	F420.00	Diabetic retinopathy	DR
40982	F421z00	Other background retinopathy NOS	DR
50656	2BBc.00	O/E - No retinal laser photocoagulation scars	DR
36855	2BBG.00	Retinal abnormality - non-diabetes	DR
3822	2BB8.00	O/E - vitreous haemorrhages	DR
49655	C10F611	Type II diabetes mellitus with retinopathy	DR
11433	2BBP.00	O/E - right eye background diabetic retinopathy	DR
17293	727..00	Retina and other parts of eye operations	DR
69662	F421G00	Venostasis retinopathy	DR
7069	F420000	Background diabetic retinopathy	DR
1438	F421000	Unspecified background retinopathy	DR
97894	C10EP11	Type I diabetes mellitus with exudative maculopathy	DR
13106	2BB6.00	O/E - retinal exudates	DR
22967	2BBF.00	Retinal abnormality - diabetes related	DR
25888	2BBm.00	O/E - right eye clinically significant macular oedema	DR
25591	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	DR
18496	C10F600	Type 2 diabetes mellitus with retinopathy	DR
31829	F433100	Solar retinopathy	DR
41229	F421100	Atherosclerotic retinopathy	DR
19532	2BB4.00	O/E - retinal microaneurysms	DR
95343	C10E711	Type I diabetes mellitus with retinopathy	DR
11858	7270400	Pars plana vitrectomy	DR
6702	F421300	Hypertensive retinopathy	DR
45145	2BB2.00	O/E - retinal vessel narrowing	DR
27022	5B42.00	Laser therapy - retinal lesion	Severe DR
86068	7272800	Panretinal laser photocoagulation to lesion of retina	Severe DR
13097	2BBT.00	O/E - right eye proliferative diabetic retinopathy	Severe DR
100979	7272900	Focal laser photocoagulation of retina	Severe DR
11874	F422100	Proliferative retinopathy due to sickle cell disease	Severe DR
96926	FyuF700	[X]Other proliferative retinopathy	Severe DR
6836	7271100	Laser photocoagulation of retina for detachment	Severe DR
11912	5B4..11	Retinal laser therapy	Severe DR
30477	F420700	High risk proliferative diabetic retinopathy	Severe DR
9318	7272300	Laser destruction of lesion of retina	Severe DR
36035	F422y00	Other specified other proliferative retinopathy	Severe DR
18775	2BBO.00	O/E - Laser photocoagulation scars	Severe DR
10099	F420300	Advanced diabetic maculopathy	Severe DR
2986	F420200	Preproliferative diabetic retinopathy	Severe DR
13103	2BBS.00	O/E - left eye preproliferative diabetic retinopathy	Severe DR
13099	2BBR.00	O/E - right eye preproliferative diabetic retinopathy	Severe DR
46068	7272500	Panretinal laser photocoagulation to lesion of retina NEC	Severe DR
10755	F420600	Non proliferative diabetic retinopathy	Severe DR

13101	2BBV.00	O/E - left eye proliferative diabetic retinopathy	Severe DR
38096	F422z00	Proliferative retinopathy NOS	Severe DR
3286	F420100	Proliferative diabetic retinopathy	Severe DR
65463	F420800	High risk non proliferative diabetic retinopathy	Severe DR
7890	F422.00	Other proliferative retinopathy	Severe DR
881	3128	Fundoscopy	Screening
19535	2BBA.00	Examination of retina	Screening
10701	8HBD.00	Retinopathy follow up	Screening
25116	2BBZ.00	O/E - retinal inspection NOS	Screening
92317	2BBf.00	O/E - left retina partially assessable	Screening
18311	68A7.00	Diabetic retinopathy screening	Screening
106269	9m0..00	Diabetic retinopathy screening administrative status	Screening
33681	2BB..00	O/E - retinal inspection	Screening
17871	312E.00	Direct fundoscopy following mydriatic	Screening
17198	2BB..11	O/E - retina	Screening
19531	3128.11	Retinoscopy	Screening
13196	66AD.00	Fundoscopy - diabetic check	Screening
36619	312F.00	Camera fundoscopy	Screening
19534	3128300	Camera fundoscopy	Screening
11891	68A8.00	Digital retinal screening	Screening
9974	9N1v.00	Seen in diabetic eye clinic	Screening
70163	2BBe.00	O/E - right retina partially assessable	Screening
8140	9N2V.00	Seen by optometrist	Screening
66273	2BBg.00	O/E - right retina fully assessable	Screening
61021	68AB.00	Diabetic digital retinopathy screening offered	Screening
13105	58C1.00	Retinal photography	Screening
13098	3128Z00	Fundoscopy NOS	Screening
30111	3129	Eye fundus photography	Screening
20991	312A.00	Slit lamp examination	Screening
12528	9NNC.00	Under care of retinal screener	Screening
18662	8HBH.00	Diabetic retinopathy 6 month review	Screening
12636	9N2f.00	Seen by retinal screener	Screening
9934	9N2e.00	Seen by ophthalmologist	Screening
11018	8HBG.00	Diabetic retinopathy 12 month review	Screening
22966	3128400	Indirect fundoscopy following mydriatic	Screening
6108	9N2U.00	Seen by optician	Screening
64070	312G.00	Indirect fundoscopy following mydriatic	Screening
95916	2BBh.00	O/E - left retina fully assessable	Screening

Table 5.Read codes for Ethnicity (Table reproduced from http://www.clininf.eu/ethnicity.html)

Grouping of the 9S and 9i ethnic codes to the '16+1' format and the five category classifications			
Five category	**16 category framework**	**9i… Ethnic category hierarchy**	**9S.. Ethnic group hierarchy**
1. White	1. British or Mixed British	**9i0** British or mixed British	**9S1** White, **9S10** White British, **9S14** Other white British ethnic grp
	2. Irish	**9i1** Irish	**9S11** White Irish, **9SA9** Irish NMO, **9SI** Irish traveller
	3. Other White	**9i2** Other White	**9S12** Other white ethnic group
		9i20 English	
		9i21 Scottish	**9S13** White Scottish
		9i22 Welsh, **9i26** Cypriot part unsp, **9i27** Greek, **9i28** Greek Cypriot, **9i29** Turkish, **9i2A** Turkish Cypriot, **9i2B** Italian, **9i2C** Irish Traveller, **9i2D** Traveller, **9i2E** Gypsy/Romany, **9i2F** Polish, **9i2H**Commonwealth of (Russian), **9i2J** Kosovan, **9i2K** Albanian Serbian, **9i2P** Oth repub Yugoslav, **9i2R** Oth White/unsp/Mix Eur,**9i2S** Oth mixed White, **9i2T** Other White or White unspecified.	
2. Mixed	4. White + Black Caribbean	**9i3** White & Black Caribbean	**9SB5** Black Caribbean and White
	5. White + Black African	**9i4** White and Black African	**9SB6** Black African and White
	6. White + Asian	**9i5** White & Asian	**9SB2** Other ethnic, Asian/White orig
	7. Other mixed	**9i6** Other Mixed	**9SB** Other ethnic, mixed origin , **9SB3** Other ethnic, mixed white orig, **9SB4** Other ethnic, other mixed

			orig,**9S52** Other Black - Black/Asian orig.
		9i60 Black & Asian, **9i61** Black & Chinese	
		9i62 Black and White	**9SB1** Other ethnic, Black/White orig, **9S51** Other Black – Black/White orig
		9i63 Chinese & White, **9i64** Asian & Chinese	
3. Asian or Asian British	8. Indian or British Indian	**9i7** Indian/British Indians	**9S6** Indian
	9. Pakistani or British Pakistani	**9i8** Pakistani/Brit Pakists	**9S7** Pakistani
	10. Bangladeshi or British Bangladeshi	**9i9** Bangladeshi/Brit Bangl	**9S8** Bangladeshi
	11. Other Asian	**9iA** Other Asian	**9SH** Other Asian ethnic group, **9SA8** Other Asian NMO, **9SA7** Indian sub-continent NMO
		9iA3 East African Asian	**9SA6** E Afric Asian/Indo-Carib NMO
		9iA4 Sri Lankan, **9iA5** Tamil, **9iA6** Sinhalese, **9iA7** Carib Asian,**9iA8** Briti Asian, **9iA9** Mixed Asian	
4. Other Black	12. Caribbean	**9iB** Caribbean	**9S2** Black Caribbean
	13. African	**9iC** African	**9S3** Black African, **9S44**Black - other African country,**9SA5** Other African countries NMO
	14 Other Black	**9iD** Other Black	**9S4** Black, other, non-mixed origin, **9S42** Black Caribbean/W.I./ Guyana, **9S43** Black N African/Arab/Ira

			nian, **9S45** Black E Afric Asia/Indo-Caribb, **9SG** Other black ethnic group, **9S47** Bla ck - other Asian, **9S48** Blac k Black - other, **9S5** Black - other, mixed, **9SA3** Car ibbean I./W.I./Guyana NMO
		9iD0 Somali, **9iD1** Nigerian	
		9iD2 Black British	**9S41** Black British
5. Other ethnic groups	15. Chinese	**9iE** Chinese	**9S9** Chinese
	16. Other	**9iF** Other	**9SJ** Other ethnic group, **9SA**Othe r ethnic non-mixed NMO, **9SA2** Brit. ethnic minor. unsp NMO, **9SAA**Gre ek/Greek Cypriot NMO,**9SAB** Turk ish/Turkish Cypriot NMO **9SAC** Other European NMO,**9SAD** Oth er ethnic NEC NMO
		9iF0 Vietnamese	**9SC** Vietnamese
		9iF1 Japanese, **9iF2** Filipino, **9iF3** Malaysian, **9iF9** A rab	
		9iFA North African	**9SA4** N African Arab/Iranian NMO
		9iFB ME ex Isr/Iran/Arab, **9iFD** Iranian, **9iFE** Kurdish, **9iFG** Lati n American, **9iFH** South/Central American, **9iFJ** Multi-ethnic islands: Mauritian or Seychellois or Maldivian or St Helena, **9iFK** Any other - ethn categ	

6. Not stated	17. (16+1) Not stated	**9iG** Ethn cat not stated	**9S** Ethnic groups census,**9SD** Ethnic group - patient refused, **9SE** Ethnic group not recorded, **9SZ** Ethnic groups census NOS

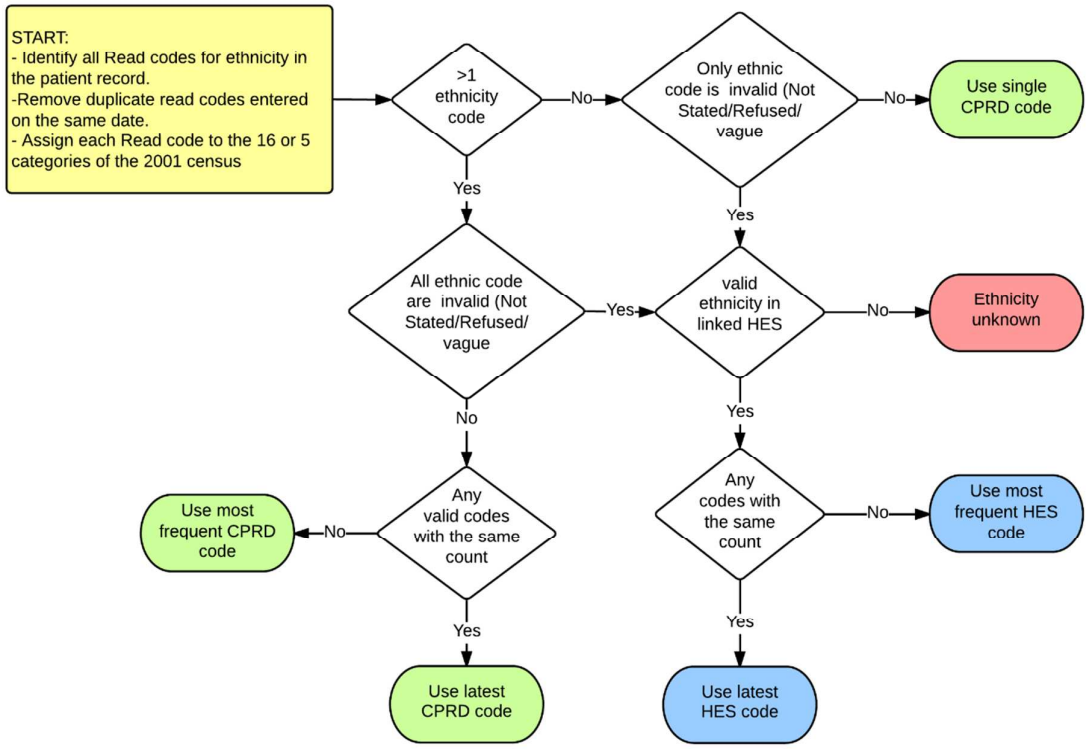

Figure 5. Classification of Ethnicity in the CPRD (From Mathur et al. Journal of Public Health, 2013)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4-5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	

Results			page
Participants6	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table1,2
		(b) Indicate number of participants with missing data for each variable of interest	Table1,2
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Fig 2. Fig 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2, Fig 2, Fig 3
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

BMJ Open

Population trends in the ten-year incidence and prevalence of diabetic retinopathy in the UK: a cohort study in the Clinical Practice Research Datalink 2004-2014

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TITLE PAGE

Title: Population trends in the ten-year incidence and prevalence of diabetic retinopathy in the UK: a cohort study in the Clinical Practice Research Datalink 2004-2014

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Running Head: Population trends in in the incidence and prevalence diabetic retinopathy in the UK

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ABSTRACT

Objectives: To describe trends in the incidence and prevalence of diabetic retinopathy (DR) in the UK by diabetes type, age, sex, ethnicity, deprivation, region, and calendar year.

Design: Cohort study utilizing the Clinical Practice Research Datalink (CPRD).

Setting: UK Primary Care.

Participants: 7.7 million patients ≥ 12 contributing to the CPRD from 2004-2014.

Primary and secondary outcome measures: Age standardised prevalence and incidence of diabetes, DR and severe DR (requiring photocoagulation) by calendar year and population subgroup. Relative risk of developing DR and severe DR by population subgroup.

Results: The prevalence of DR was 48.4% in the population T1DM (14,846/30,657) and 28.3% (95,807/338,390) in the population with T2DM. Prevalence of DR remained stable in people with T2DM and decreased in people with T1DM. Screening for DR increased over time for patients with T2DM and remained static for patients with T1DM Incidence of DR increased in parallel with the incidence of T2DM in both diabetic populations. Amongst patients with T2DM, relative risk of DR varied significantly by region, was increased for older age groups and in men compared to women, with risk of severe DR increased in South Asian groups and more deprived groups. Relative risk of DR for patients with T1DM varied by age and region, but not by gender, ethnic group, or deprivation.

Conclusions: This is the largest study to date examining the burden of DR in the UK. Regional disparities in incidence may relate to differences in screening delivery and disease ascertainment. Evidence that deprivation and ethnicity are associated with a higher risk of severe DR highlights a significant potential health inequality. Findings from this study will have implications for professionals working in the diabetes and sight loss sectors, particularly to inform approaches for diagnosis of retinopathy and campaigning to better tackle the disease for at risk groups.

ARTICLE SUMMARY

Strengths and limitations of this study

- This study constitutes the largest ever sample size to examine trends in the burden of diabetes and diabetic retinopathy in the UK which allowed for sufficient power to detect relationships between population subgroups, which is often unfeasible in smaller studies where population sizes do not allow for such granular comparisons.

- Since recording of screening of diabetic retinopathy was incentivised under QOF from 2004-2014 and QOF indicators are known to be well recorded by GPs and so we anticipate that screening and identification of DR will have been recorded with a high degree of accuracy during the study period.

- This study relied on coded diagnoses of diabetes and retinopathy as we did not have access to data from other sources such as retinal photography or practitioner letters, which could have been used to validate the diagnoses.

FUNDING STATEMENT

Funding was provided by the RNIB for the salary of RM for the completion of this project. Funders were not involved in the study design, data collection, or analysis. Funders were involved in generating the research question and gave comments on the final manuscript. KB holds a Sir Henry Dale fellowship jointly funded by the Wellcome Trust and the Royal Society (107731/Z/15/Z). LS is supported by a Wellcome Trust Senior Research Fellowship in Clinical Science [098504/Z/12/Z].

COMPETING INTERESTS

none declared

INTRODUCTION

Diabetic retinopathy (DR) is the most common form of eye disease amongst individuals with diabetes mellitus. In the UK, within 20 years of diabetes diagnosis nearly all people with type 1 and almost two thirds of people with type 2 diabetes (60%) have some degree of retinopathy.(1,2) Diabetic retinopathy is the leading cause of visual impairment and blindness in the UK, amongst people of working age; Compared with the general population, risks of cataract and of glaucoma are doubled amongst individuals with established diabetic retinopathy.(3)

Diabetic retinopathy is a progressive disease directly attributable to diabetes, which affects the blood vessels of the retina. The blood vessels can leak, become blocked, or proliferate excessively.(4,5) If untreated, this can lead to retinal damage and visual impairment(6).

Differences in the risk of diabetes by gender, ethnic group, and deprivation have been established both in the UK and worldwide.(7–11) In the UK, the risk of developing type 2 diabetes is elevated approximately twofold in South Asian and African Caribbean communities compared to the White British population.(12–14) Ethnic differences in diabetes are mirrored by ethnic differences in diabetic retinopathy both in the UK and globally.(15,16) In the USA, several studies have reported differences between white, black, Hispanic, and Mexican American populations.(17–20) For example, the National Health and Nutrition Examination Survey reported the prevalence of diabetic retinopathy to be 36% higher in black and 84% higher in Mexican American populations relative to the white population with diabetes.(21) UK studies have demonstrated higher prevalence of diabetic retinopathy amongst individuals of South Asian ethnicity relative to white.(16,22) Socioeconomic deprivation has also been found to be associated with diabetic retinopathy, with both UK and international studies reporting higher prevalence amongst more deprived groups.(23,24)

In order to prevent, delay and better manage diabetic retinopathy, annual screening using digital photography is recommended for all people with diabetes aged 12 and over in the UK. Introduced in 2004, uptake of the screening program has increased steadily, achieving full national coverage in 2008 (25). Implementation of screening varies across each of the four devolved nations of the UK; Typically, all people with diabetes aged 12 and over are invited for a screening appointment via letter or phone call, which can take place in general practices, hospitals, at specialist diabetes clinics, mobile clinics, or at the high street opticians. Retinal photography to assess grade of retinopathy is completed. If the DR is considered to be sight threatening, the individual is referred to hospital eye

services for treatment, otherwise the results are sent back to the GP for continuing diabetes care.(26,27)

Despite extensive literature detailing the prevalence and incidence of diabetes in the UK, population-wide measures of incidence and prevalence of diabetic retinopathy in a UK context have not been determined. Previous UK focussed research on retinopathy has largely been limited to estimates based on regional screening programmes or small general practices samples.(28–32) Having a more complete understanding of the burden of disease due to diabetic retinopathy across the diverse UK population will help improve future service planning and provision of preventive and therapeutic care. The aim of this study was to generate nationally representative estimates of the incidence and prevalence of diabetic retinopathy in the United Kingdom between 2004 and 2014 using the Clinical Practice Research Datalink (CPRD), and to examine trends in the prevalence and relative risk of retinopathy by diabetes type, age, sex, ethnicity, socio-economic deprivation and region.

METHODS

Data Sources

The CPRD is an electronic health database which currently contains longitudinal primary care records for approximately 13.5 million patients from 601 general practices across the UK (covering 7% of the UK population), of whom 5.5 million are currently active.(33) The CPRD contains anonymised patient level information on demographics, lifestyle data, clinical diagnoses, prescriptions, and preventive care. The database was established in 1987, and continuous observational data has been collected in most practices for over six years yielding over 30 million patient years of observation. Data undergo regular quality checks and practices are deemed to be "up to standard" if their data are deemed to be of research level quality.(33) The Clinical Practice Research Datalink has been found to be representative of the UK population with respect to gender, age and ethnic group. (33,34)

Identification of diabetic retinopathy

Within the CPRD, diagnoses and symptoms are coded using the Read clinical hierarchy, which is the coding standard used across UK primary care.(35) Clinical terms to identify diagnoses of diabetic retinopathy were agreed upon via consultation between the research team and clinicians. All diagnoses of diabetic retinopathy were identified by searching for Read clinical terms in the CPRD.

Diabetic retinopathy was classified as severe if the codes pertained to laser therapy, advanced retinopathy, or proliferative retinopathy.

Onset of diabetic retinopathy was defined as the first ever diagnostic Read code entered onto the patient record. Patients with a diagnosis for severe retinopathy at any time were included in a sub-analysis of patients with advanced disease, with onset defined as the earliest ever code of severe DR on the patient record.

Screening for diabetic retinopathy was identified using a set of clinical terms which indicated that a screening event had occurred. Codes indicating that an individual had been invited to or referred for screening were not included. A summary of the clinical terms used to identify diabetic retinopathy and screening can be found in the supplementary material.

Identification of diabetes mellitus

For the purposes of this study, classification of patients into categories of type 1 diabetes or type 2 diabetes was determined using algorithms developed by the UK Biobank study for use in electronic health records.(36) The algorithms initially classify patients according to the presence of diagnostic Read codes for type 1 or type 2 diabetes. The diagnoses are then confirmed if supporting information such as prescriptions of antidiabetic medications, raised blood glucose, and diabetes process of care measures are present. All individuals identified as having type 1 or type 2 diabetes after successfully passing through the adjudication algorithm were included in the final analysis.

Covariate definition

Age was grouped into ten-year age-bands. Deprivation was classified using the Index of Multiple Deprivation (IMD) and divided into quintiles.(37) Each patient in the study was assigned a deprivation score relating to the deprivation value of their general practice. Information on ethnic group was derived from the CPRD record where available and updated using ethnicity recorded in linked Hospital Episode Statistics data if missing in CPRD. Conflicts between the two data sources were resolved using a defined and previously validated algorithm.(38) Ethnicity was grouped into the five categories of the 2011 census, namely, White, South Asian, Black African/Caribbean, Mixed, and Other. Patients with missing ethnicity, or with codes which were unusable were collapsed into a category of unknown ethnicity (See supplementary material for algorithm and Read codes). Duration of diabetes at onset of diabetic retinopathy (expressed in years) was calculated by subtracting the date of the first diagnostic code for diabetes from the date of the first diagnostic code for diabetic

retinopathy. Age at diabetes onset (expressed in years) was calculated by subtracting the date of birth from the date of diabetes onset.

Statistical *Methods*

A population based cohort study was conducted to examine the prevalence and incidence of diabetic retinopathy in all patients aged 12 years and over registered with the CPRD between January 2004 and December 2014. The prevalence and incidence of diabetes and diabetic retinopathy and severe diabetic retinopathy was examined separately for individuals with type 1 diabetes and type 2 diabetes. The age standardised prevalence of screening in each year was also examined for individuals with type 1 and type 2 diabetes.

All prevalence and incidence estimates were standardised against the mid-2014 UK population estimates from the Office for National Statistics.(39) The overall age standardised prevalence of diabetic retinopathy stratified by diabetes status, gender, ethnic group, deprivation quintile, and region was calculated for the entire study population. For the study of prevalence over time, the outcome was defined as all individuals with a relevant diagnostic code at the midpoint of each calendar year from January 2004 to December 2014. Point prevalence was calculated by dividing the number of individuals with diabetic retinopathy, severe diabetic retinopathy by the number of patients in the CPRD aged 12 years and over on July 1st of each year. The proportion of patients receiving diabetic retinopathy screening in each year was determined by dividing the number of patients with a code for screening in each calendar year by the number of patients in the CPRD as a whole, and with type 1 or type 2 diabetes, aged 12 and over on July 1st of each year.

For the study of disease incidence, the outcome was first diagnosis of diabetic retinopathy or severe diabetic retinopathy between January 2004 and December 2014. Individuals with a first diagnosis of retinopathy prior to 2004 were excluded from the analysis. Incidence was calculated by dividing the number of newly diagnosed patients aged 12 and over by the number of person-years of follow-up of all eligible patients aged 12 and over contributing to the CPRD for each calendar year. Age standardised incidence rates of diabetic retinopathy and severe diabetic retinopathy per 10,000 person years of follow-up time were calculated for all patients in the CPRD for 2014, the final year of the study.

Cox proportional-hazards regression was used to evaluate the risk of diabetic retinopathy in all patients between January 2004 and December 2014. Hazard Ratios for the relative risk of diabetic

retinopathy and severe diabetic retinopathy, mutually adjusted for age, gender, deprivation, ethnic group, region, and duration of diabetes, were calculated separately for individuals with type 1 and type 2 diabetes. The start of follow-up was defined as the latest of practice "up to standard date" (up to standard indicating the practice data meets the range of quality criteria as defined and applied by CPRD) or 12 months after the patients' current registration date. Follow-up time ended at the earliest date of; first diagnosis of diabetic retinopathy, transferring out of the practice, latest data collection, death, or December 31st 2014. Stata statistical software version 13 was used for all analyses.(40)

RESULTS

From the entire CPRD population of 13.7 million patients, 7,707,475 patients registered with the CPRD between 2004 and 2014 aged 12 and over were eligible for inclusion in the study (see appendix figure 1). Amongst all patients aged 12 and over, 338,390 patients with type 2 diabetes and 30,657 patients with type 1 diabetes were identified using the diabetes classification algorithms (see appendix figures 2-5 for full details).

Table 1. Demographic characteristics of the CPRD population registered between 2004-2014

Population	All CPRD Patients		T1DM Patients		T2DM Patients	
	N	%	N	%	N	%
Total (12+)	7,707,475	100.0%	30,657	100.0%	338,390	100.0%
Gender						
Men	3,790,664	49.2%	17,761	57.9%	187,141	55.3%
Women	3,916,811	50.8%	12,896	42.1%	151,249	44.7%
Ethnic Group						
White	4,006,927	52.0%	19,810	64.6%	205,168	60.6%
South Asian	223,090	2.9%	453	1.5%	15,840	4.7%
Black	142,070	1.8%	373	1.2%	7,186	2.1%
Other	109,402	1.4%	254	0.8%	3,891	1.2%
Mixed	50,363	0.7%	152	0.5%	1,095	0.3%
Unknown	3,175,623	41.2%	9,615	31.4%	105,210	31.1%
IMD Quintile						
1 (most affluent)	1,338,388	17.4%	5,280	17.2%	52,280	15.5%
2	1,496,051	19.4%	5,934	19.4%	61,008	18.0%
3	1,621,330	21.0%	6,517	21.3%	71,982	21.3%
4	1,723,122	22.4%	6,910	22.5%	79,130	23.4%
5 (least affluent)	1,470,726	19.1%	5,833	19.0%	72,094	21.3%
Region						
North East	121,334	1.6%	516	1.7%	5,465	1.6%
North West	803,853	10.4%	3,226	10.5%	40,255	11.9%
Yorkshire & The Humber	269,265	3.5%	1,050	3.4%	10,888	3.2%
East Midlands	296,884	3.9%	1,182	3.9%	12,489	3.7%
West Midlands	654,656	8.5%	2,451	8.0%	30,710	9.1%
East of England	752,786	9.8%	3,041	9.9%	29,139	8.6%
South West	651,327	8.5%	2,601	8.5%	30,330	9.0%
South Central	853,405	11.1%	3,242	10.6%	33,416	9.9%
London	1,017,747	13.2%	3,150	10.3%	39,281	11.6%
South East	792,775	10.3%	3,123	10.2%	33,399	9.9%
Northern Ireland	199,509	2.6%	937	3.1%	9,322	2.8%
Scotland	711,397	9.2%	3,601	11.7%	31,387	9.3%
Wales	582,537	7.6%	2,537	8.3%	32,309	9.5%
Retinopathy screen 2004-2014	710,445	8.7%	24,828	79.3%	279,495	82.6%
Retinopathy screen in last 15 months	336,960	4.1%	15,788	50.4%	180,268	53.3%
Diabetic Retinopathy	144,362	1.9%	14,846	48.4%	95,807	28.3%
Severe Diabetic Retinopathy	9,085	0.1%	2,148	7.0%	4,651	1.4%
Age at diabetes diagnosis (in years, mean, SD)			26	(18)	60	(14)
Mean duration of diabetes at DR onset (years, SD)			14.7	(12.2)	5.9	(6.9)
Mean duration of diabetes at Severe DR onset (years, SD)			20.9	(12.7)	10.4	(8.7)

*All columns refer to number and %, unless otherwise specified

Overall Prevalence of diabetic retinopathy

Over the ten-year study period, 79.3% of individuals with type 1 diabetes and 82.6% of individuals with type 2 diabetes had evidence of ever having had a diabetic retinopathy screen completed, with over 50% having had their latest screen in the 15 months prior to the end of their follow-up period.

A total of 144,362 prevalent cases of diabetic retinopathy were identified between 2004 and 2014, giving a crude 10-year period prevalence of 1.9% in the entire CPRD population, 48.4% in the population with type 1 diabetes, and 28.3% in the population with type 2 diabetes. A total of 9,085 prevalent cases of severe diabetic retinopathy were identified during the study period. The crude 10-year period prevalence of severe diabetic retinopathy was 0.1% in the CPRD population, 7.0% in the population with type 1 diabetes and 1.4% in the population with type 2 diabetes (Table 1).

Mean duration of diabetes at time of DR onset ranged from 6 years for people with type 2 diabetes to 15 years for people with type 1 diabetes, with duration approximately 5 years longer for onset of severe diabetic retinopathy.

Age standardised prevalence and incidence of diabetic retinopathy and screening over time

In the whole CPRD population, the age standardised prevalence of diabetic retinopathy decreased over time from 2.6% to 2.2% while the age standardised prevalence of severe diabetic retinopathy remained stable at 0.1%. The incidence of diabetic retinopathy increased from 12.1 events per 10,000 years in 2004 to a peak of 23.82 events per 10,000 person years in 2011 before declining again (annual increase of 0.7 events per 10,000 person years, p=0.062). The incidence of severe diabetic retinopathy remained stable at 1 event per 10,000 person years (no trend over time, p=0.265).

The age standardised proportion of patients having received a diabetic retinopathy screen in each calendar increased over the ten-year study period for patients with type 2 diabetes from 40.3% in 2004 to 63.9% in 2014 (annual increase of 2.3%, p<0.001) and oscillated between 59 and 67% for patients with type 1 diabetes over the study period (no trend over time, p=0.291).

Amongst patients with type 2 diabetes, the prevalence of diabetic retinopathy reduced from 24.6% in 2004 to 23.1% in 2014. The age standardised incidence of diabetic retinopathy increased in parallel with the incidence of type 2 diabetes, increasing from 113.2 events per 10,000 person-years in 2004 to 408.6 events per 10,000 person-years in 2011 and declining thereafter (annual increase of 26 events per 10,000 person-years, CI95% 13.2-39.3, p=0.001). The age standardised prevalence of severe diabetic retinopathy increased from 0.3% in 2004 to 0.9% in 2014 (annual increase of 0.06%

per year, p<0.001). The age standardised incidence of severe diabetic retinopathy increased from 5.2 events per 10,000 person years in 2004 to 10.2 events pre 10,000 person years in 2014 (annual increase of 0.6 events per 10,000 person-years, CI95% 0.01-1.16, p=0.046) (Figure 1).

Amongst patients with type 1 diabetes the age standardised prevalence of diabetic retinopathy remained stable at 55% (no trend over time p=0.917). The age standardised incidence of diabetic retinopathy increased from 514.7 events per 10,000 person-years in 2004 to 832 events per 10,000 person-years in 2009 and declined thereafter (annual increase of 55.6 events per 10,000 person-years from 2004-2009, CI95% 29.6-81.7, p=0.004) The prevalence of severe diabetic retinopathy increased from 3.5% in 2004 to 8.0% in 2014 (annual increase of 0.05%, CI95% 0.04%-0.05%, p<0.001). The incidence of severe diabetic retinopathy decreased non-significantly from 48 events per 10,000 person-years in 2004 to 25.4 events per 10,000 years in 2014 (no trend over time, p=0.459).

(Insert Figure 1 here)

Age standardised prevalence of diabetic retinopathy in 2014

In 2014, the final year of the study period, 73,658 prevalent cases of diabetic retinopathy were identified, giving an age-standardised point prevalence of 2.2% (CI95% 2.18% to 2.21%) in the entire CPRD population, 54.8% (CI95% 53.6% to 56.1%) in the population with type 1 diabetes and 22.7% (CI95% 22.0% to 23.8%) in the population with type 2 diabetes (Table 2).

Amongst patients with type 2 diabetes, the age-standardised prevalence of diabetic retinopathy diabetic retinopathy was higher amongst men and those of non-White ethnicity and varied substantially by geographic region. Age-standardised prevalence of diabetic retinopathy increased with age and with deprivation until quintile 4. The age standardised prevalence of severe diabetic retinopathy was higher for men, and those of South Asian and mixed ethnicity. Prevalence increased with age and varied by geographic region, but not by deprivation.

Amongst patients with type 1 diabetes, the prevalence of diabetic retinopathy and severe diabetic retinopathy was comparable between men and women and between deprivation quintiles. Prevalence of diabetic retinopathy was highest in the White ethnic group compared to all other ethnic groups, while prevalence of severe diabetic retinopathy was highest in the Black group.

Prevalence of both diabetic retinopathy and severe retinopathy varied substantially by geographic region.

Table 2. Age standardised prevalence of Diabetic Retinopathy in the CPRD 2014

		Diabetic Retinopathy						Severe Diabetic Retinopathy					
		T2DM Population			T1DM Population			T2DM Population			T1DM Population		
	2014 Denominator (12+)	**160,418**			13,848			160,418			13,848		
		N	%	p.val	N	%	p.val	N	%	p.val	N	%	p.val
Overall	*Prevalence (CI95)*	***49,166***	***22.7 (22.0-23.8)***		***7,583***	***54.8 (53.6-56.1)***		***1,933***	***0.9 (0.8-1.0)***		***1,117***	***8.1 (7.6-8.6)***	
Gender	Men	28,299	23.5	<0.001	4,393	54.5	0.916	1,206	0.9	<0.001	638	7.9	0.546
	Women	20,867	21.9		3,190	55.3		727	0.8		479	8.4	
Age Group	12-34	246	14.3	<0.001	1,522	32.9	<0.001	9	0.5	<0.001	125	2.7	<0.001
	35-44	1,307	20.4		1,381	58.5		49	0.8		209	8.9	
	45-54	5,039	24.2		1,906	65.4		209	1		321	11.0	
	55-64	10,107	28.6		1,376	70.8		437	1.2		222	11.4	
	65-74	14,837	32.1		888	70.4		620	1.3		162	12.9	
	75+	17,630	35.3		510	68.6		609	1.2		78	10.5	
Ethnic Group	White	30,253	23.6	<0.001	5,028	55.3	<0.001	1,105	0.8	<0.001	778	8.5	0.001
	South Asian	2,545	25.2		94	45.2		141	1.1		*	2.5	
	Black	1,190	25.4		59	45.8		75	0.8		10	10.3	
	Other	605	29.3		47	46.8		21	0.8		*	4.4	
	Mixed	156	19.8		22	42.2		16	1.8		*	4.3	
	Unknown	14,417	20.8		2,333	55.1		575	1.0		317	7.5	
IMD Quintile	1 (most affluent)	7,354	20.3	<0.001	1,501	55.1	0.010	276	1.0	0.435	226	8.4	0.114
	2	9,780	23.4		1,558	54.8		430	0.8		244	8.6	
	3	9,910	23.1		1,541	55.9		340	0.8		218	7.7	
	4	12,144	25.9		1,688	55.9		452	0.9		248	8.2	
	5 (least affluent)	9,456	20.6		1,233	51.8		398	0.9		174	7.6	
Region	North East	580	26.9	<0.001	73	57.9	<0.001	16	0.7	<0.001	12	9.2	<0.001
	North West	4,846	19.8		677	49.1		175	0.9		102	7.5	
	Yorkshire & Humber	398	20.4		76	50.2		11	0.8		14	8.4	
	East Midlands	218	44.4		17	68.1		*	0.6		6	24.4	
	West Midlands	4,310	22.1		555	55.0		177	0.8		94	9.4	
	East of England	2,563	19.8		494	53.6		119	0.8		66	7.1	
	South West	4,397	26.3		584	56.2		175	1.1		104	9.9	
	South Central	5,685	23.9		945	54.2		219	0.8		149	8.3	
	London	6,427	23.8		709	50.3		290	0.9		96	7.0	
	South East	4,635	17.4		773	49.4		157	0.6		103	6.5	
	Northern Ireland	813	10.6		240	39.7		77	0.7		37	627	
	Scotland	7,930	31.9		1,478	66.7		261	1.1		175	8.3	
	Wales	6,634	23.2		962	58.9		254	1.1		159	9.7	

*All figures standardised against the UK Mid-2014 population, p.values from chi-squared test for unordered categorical variables, from test for trend for ordered categorical variables (age group and IMD quintile). Table values under 5 are suppressed.

Relative risk of retinopathy in patients with Type 2 diabetes

Median follow-up time for patients with type 2 diabetes was 9.1 years (IQR 5.4-10.9 years). Within this population, fully adjusted hazard ratios from Cox-proportional hazards regression showed that the risk of developing both diabetic retinopathy and severe diabetic retinopathy was reduced in women compared to men (HR 0.93, CI95% 0.92-0.95 for DR and HR 0.80, CI95% 0.72-0.89 for Severe DR).

Relative to those aged 55-64, the risk of developing diabetic retinopathy was reduced in the youngest and oldest age groups. In the analysis of severe diabetic retinopathy, risk was increased in those aged 35-44 and 45-54 relative to those aged 55-64 and reduced in all older age groups.

Each 5-year increase in the duration of diabetes at baseline was associated with a 17% increase in the risk of diabetic retinopathy (CI95% 1.16-1.18) and a 42% increase in the risk of severe diabetic retinopathy (CI95% 1.39-1.45) after adjustment for all other factors.

Risk of diabetic retinopathy was equivalent between ethnic groups in the main analysis, and raised for the South Asian group relative to the White group in the analysis of severe diabetic retinopathy (HR 1.25 CI95% 1.00-1.56).

No clear relationship between deprivation and retinopathy was clear in analysis of all diabetic retinopathy. The risk severe diabetic retinopathy was raised in the 2nd most affluent group relative to the most affluent group only (HR 1.37 CI95% 1.16-1.63) Figure 2).

Risk of diabetic retinopathy varied substantially by geographic region, with differences attenuated for severe retinopathy. In comparison to London (the reference region), risk of retinopathy was reduced in Northern Ireland and the East of England, and increased in most other regions of the UK.

Relative risk of retinopathy in patients with Type 1 diabetes

Median follow-up time for patients with type 1 diabetes was 7.1 years (IQR 4.0-10.9 years). Within this population, fully adjusted hazard ratios from Cox-proportional hazards regression showed no evidence for differences in the risk of developing diabetic retinopathy or severe diabetic retinopathy by gender, ethnic group, or deprivation.

Relative to those aged 55-64, the risk of developing diabetic retinopathy was reduced in the both older age groups. In the analysis of severe diabetic retinopathy, risk decreased as age increased.

Each 5-year increase in the duration of diabetes at baseline was associated with a 10% increase in the risk of diabetic retinopathy (CI95% 1.09-1.11) and a 26% increase in the risk of severe diabetic retinopathy (CI95% 1.21-1.31) after adjustment for all other factors. Regional differences in the risk of retinopathy and severe retinopathy for patients with type 1 diabetes mirrored those found in the analysis of patients with type 2 diabetes (Figure 3).

(Insert Figures 2 and 3 about here)

DISCUSSION

Main findings

The study has shown that while the age standardised prevalence of diabetic retinopathy has remained stable over time for patients with type 1 and type 2 diabetes, the prevalence of severe diabetic retinopathy has increased three-fold over the ten-year study period. In contrast, while the incidence of diabetic retinopathy amongst people with type 1 and type 2 diabetes has increased to a peak and subsequently decreased, in parallel to the incidence of type 2 diabetes, the incidence of severe diabetic retinopathy has increased for patients with type 2 diabetes and halved for patients with type 1 diabetes. The proportion of patients receiving a diabetic retinopathy screen in each calendar increased steadily over the ten-year study period for patients with type 2 diabetes to 64% in 2014 and remained stable over time for patients with type 2 diabetes.

The study has further demonstrated that, for individuals with type 2 diabetes, the relative risk of developing diabetic retinopathy varies by region, age group and gender, while the relative risk of developing severe retinopathy varies also by ethnicity.

The overall prevalence of diabetic retinopathy found in our CPRD population is comparable to that of contemporaneous studies. A 2015 study of the Welsh National Diabetic Retinopathy Screening Service has reported that the prevalence of diabetic retinopathy is 56% in those with type 1 diabetes and 30.3% in those with type 2 diabetes.(30) These figures tally closely with the respective ten-year prevalence figures of 48.4% for patients with type 1 diabetes and 28.3% for patients with type 2 diabetes from our study overall, and also for the estimates specific to Wales reported herein (58.9% and 23.2% respectively). Similarities extend to severe diabetic retinopathy also; the same study reports prevalences of 11.2% in those with type 1 diabetes and 2.9% in those with type 2 diabetes. Our study has found the prevalence to be 10.3% and 2.4% respectively. A recent review of diabetic

retinopathy studies in western countries has reported the prevalence of diabetic retinopathy in to be 28.7% for all people with diabetes, further lending credence to our findings.(41)

The overall incidence of retinopathy increased to a peak partway through the study before decreasing again. Increases in the incidence of retinopathy are likely to be related to increasing incidence of type 2 diabetes and increased ascertainment of retinopathy through nationwide screening programs, which increased in coverage over the duration of the study period. Annual incidence figures obtained in our study are largely in line with incidence figures reported in the Liverpool Diabetic Eye Study, which examined incidence amongst patients with type 2 diabetes.(31)

A key finding of the study was large regional variations in the relative incidence of retinopathy, after accounting for age, gender, deprivation, and ethnicity. Regional differences in incidence may relate to regional differences in the organization and delivery of screening programs, and subsequent ascertainment of disease. It has been suggested that uptake of screening, and as a result, opportunities for diagnosis, may be lower in rural versus urban areas, due to decreased accessibility of screening services.(32) Qualitative research elucidating the influence of practice levels factors on attendance at screening has also identified challenges in identifying diabetic retinopathy including communication with screening services, communication with patients, integration of screening services with other aspects of clinical care, and ethnically diverse patient populations.(26,42)

The increased risk of severe diabetic retinopathy for South Asian individuals with type 2 diabetes relative to the White group mirrors ethnic differences in diabetes prevalence, and may be due to the same underlying genetic and biological factors which predispose South Asian groups to insulin resistance, as well as cultural factors such as diet.(43,44) Acculturation to western lifestyles amongst migrants is also associated with an increase in risk of developing non-communicable diseases, as migrant populations shift towards more sedentary and urbanized lifestyles.(43,45) Similarly, increased risk of severe diabetic retinopathy in the more deprived quintiles relative to the least deprived quintile is consistent with existing literature around socio-economic disparities in diabetes.(32,46)

Turning to patients with type 1 diabetes, the stability of the prevalence of retinopathy was to be expected as the prevalence and incidence of type 1 diabetes is not subject to large increases resulting from an increasingly obesogenic environment, as is the case with the current epidemic of type 2 diabetes.

The differences in prevalence by gender and ethnic group found here confirm those of recent smaller UK based studies. In 2012, Sivaprasad et al. reported reduced odds of prevalent retinopathy in women compared to men (OR 0.93 CI95% 0.90-0.97) and raised odds in South Asian and Black African/Caribbean groups compared to White (South Asian OR 1.10 CI95% 1.02-1.18, Black OR 1.79, CI95% 1.70-1.89) amongst individuals with diabetes in the UK. (47)

Strengths

This study made use of high levels of ethnicity recording and linkage with deprivation data provided by the ONS to describe patterns by ethnicity and Index of Multiple Deprivation. This study constitutes the largest ever sample size to examine trends in the burden of diabetes and diabetic retinopathy in the UK. This allowed for sufficient power to detect relationships between populations stratified by gender, ethnic group, geographic region and deprivation, which is often unfeasible in smaller studies where population sizes do not allow for such granular comparisons. At the time of publication, this is the only national study to examine ethnicity and deprivation in relation to the prevalence and incidence of diabetic retinopathy.

Since 2004 it has been a requirement of the UK Quality and Outcomes Framework (QOF) that patients with diabetes should be screened annually for diabetic retinopathy, and that screening should be recorded by general practitioners in patient records. QOF indicators are known to have been well recorded by GPs and so we anticipate results of screening will have been recorded with a high degree of accuracy during the study period.(48,49)

The advantage of routine electronic health databases is that they are regularly updated and can be used to provide timely information on the demographic makeup of the general population and on areas of growing healthcare need.

The CPRD has been used extensively for observational studies examining a wide range of health conditions and the data held within have been widely validated.(33) The data in the CPRD are prospectively collected and, as a result, the data are not subject to recall bias (the presence of a disease outcome affects the reporting of exposure status) or observer bias (the knowledge of the patient's disease status influences ascertainment or recording of exposure).

Limitations

The primary purpose of the clinical data held in the CPRD is for patient care, rather than research. By its nature it only includes information gathered at consultation and is thus routinely collected rather than researcher-led. As a result, the completeness and accuracy of data are subject to temporal changes in coding practices, health priorities and population need. Anything not reported to the general practitioner is necessarily not recorded. The absence of a code does not necessarily mean that an individual is free from that condition, but could also be interpreted as being unknown.

Information of ethnicity was missing for 30% of patients with diabetes, which may have resulted in an underestimate of the ethnic differences in incidence and prevalence estimates of diabetic retinopathy. In addition to incomplete data, a further potential problem with routine electronic health records is incorrect coding stemming from errors in the way data is entered. A wide range of studies have found the validity of diagnoses and process of care measures in CPRD to be high.(50–52) Combined with the fact that the CPRD data are subject to ongoing internal quality checks and that concerns with data quality are fed back to the general practices, researchers can be reassured that errors which do occur in the database are kept to a minimum.

This study relied solely on the coded diagnoses of diabetes, retinopathy, eye disease, and visual impairment. We did not have access to data from other sources such as retinal photography or practitioner letters, which could have been used to validate the diagnoses.

The use of multiple testing across a range of population subgroups meant that some of the observed associations may have arisen due to chance.

Clinical trials have established duration of diabetes, hyperglycaemia, and hypertension as key risk factors in the development of diabetic retinopathy.(53,54) Further work examining the role of pharmacological treatment and risk factor management will be essential in elucidating patterns of diabetic retinopathy further, particularly as the UK population ages and the burden of diabetes grows.

Policy Implications

According to the Office for National Statistics, the size of the UK population at the midpoint of 2014 was 64.6 million people.(55) Given that the CPRD is representative of the UK population structure, we estimate that the absolute number of people with any form of diabetic retinopathy in the UK is approximately 1.5 million and that the absolute number of people with severe diabetic retinopathy

is around 140,000. Increases in prevalence of DR are likely to be related to increasing prevalence of T2DM and potentially increased ascertainment through national screening programs.

Findings from the 2013-2014 Screening Programmes in England Report highlighted the success of diabetic retinopathy screening programmes in reducing the burden of diabetic retinopathy in the UK, to the point where, it is now, no longer the leading cause of blindness amongst working age people in the UK.(56) In 2014, attendance at diabetic retinopathy screening was removed from the Quality and Outcomes Framework, meaning that this important indicator will no longer be collected to such a high accuracy for all diabetic patients. Not only will this impact on future research into retinopathy, it is likely to have serious negative implications on service planning for diabetic patients unless the indicator is reinstated. Whether the proportion of patients receiving screening decreases from the figures reported in this study after 2014, and the impact this will have on future ascertainment and management of diabetic retinopathy will need to be explored.

Findings from this study will have implications for professionals working in the diabetes and sight loss sectors, particularly to inform approaches for diagnosis of retinopathy and campaigning to better tackle the disease for at risk groups. Evidence that deprivation may be associated with a higher risk of retinopathy, when viewed alongside previous evidence of lower retinopathy screening uptake amongst deprived groups, highlights a significant potential health inequality.(57) The national diabetic retinopathy screening programme and other stakeholders need to target and improve access to screening and support around self-management of diabetes for people living in deprived areas to avoid increasing inequalities.

Author Contribution

HL and EE provided the original remit for the study. The study was conceived and supervised by ID. ID and RM designed the study. RM extracted the data, conducted the statistical analysis and drafted the manuscript. EE HL LS KB NS contributed to interpretation of the findings, further drafts and approved the final manuscript. ID is guarantor.

Ethical approval

The pre-specified study protocol was approved by the Independent Scientific Advisory Committee for MHRA Database Research (ISAC). Approval was also received from the London School of Hygiene and Tropical Medicine ethics committee.

Data Sharing Statement

The data were obtained from the Clinical Practice Research Datalink (CPRD). CPRD is a research service that provides primary care and linked data for public health research. CPRD data governance and our own license to use CPRD data do not allow us to distribute or make available patient data directly to other parties. Researchers can apply for data access at www.cprd.com, and must have their study protocol approved by the Independent Scientific Advisory Committee for MHRA database research (details at www.cprd.com/isac).

REFERENCES

1. Diabetes UK. Key statistics on diabetes. 2010.
2. Diabetes UK. Eyes (Retinopathy). 2015.https://www.diabetes.org.uk/Guide-to-diabetes/Complications/Retinopathy/
3. Stratton IM, Adler AI, Neil HA, Matthews DR, Manley SE, Cull CA, *et al.* Association of glycaemia with macrovascular and microvascular complications of type 2 diabetes (UKPDS 35): prospective observational study. *BMJ* 2000;321:405–12.
4. Engerman RL. Pathogenesis of diabetic retinopathy. Diabetes. 1989;38:1203–6.
5. Harney F. Diabetic retinopathy. *Medicine (Baltimore)* 2006;34:95–8.
6. Cheung N, Mitchell P, Wong TY. Diabetic retinopathy. *Lancet* 2010;376:124–36.
7. Cappuccio FP, Barbato A, Kerry S. Hypertension, diabetes and cardiovascular risk in ethnic minorities in the UK. Br. J. Diabetes Vasc. Dis. 2003;3:286–93.
8. Bakker LE, Sleddering MA, Schoones JW, Meinders AE, Jazet IM. Pathogenesis of type 2 diabetes in South Asians. *Eur J Endocrinol* 2013;169:R99–114.
9. Tillin. T, Hughes AD, Whincup P, Forouhi NG, Godsland IF, Sattar N, *et al.* Excess diabetes in ethnic minorities-incidence and predictors. *Diabetologia* 2011;Conference:47th Annual Meeting of the European Association fo.
10. Agyemang C, Kunst AE, Bhopal R, Anujuo K, Zaninotto P, Nazroo J, *et al.* Diabetes prevalence in populations of South Asian Indian and African origins: a comparison of England and the Netherlands. *Epidemiology* 2011;22:563–7.
11. McKeigue PM, Shah B, Marmot MG, P.M. M, B. S, M.G. M. Relation of central obesity and insulin resistance with high diabetes prevalence and cardiovascular risk in South Asians. *Lancet* 1991;337:382–6.
12. Bhopal RS. A four-stage model explaining the higher risk of Type 2 diabetes mellitus in South Asians compared with European populations. *Diabet Med* 2013;30:35–42.
13. Tillin T, Hughes AD, Godsland IF, Whincup P, Forouhi NG, Welsh P, *et al.* Insulin Resistance and Truncal Obesity as Important Determinants of the Greater Incidence of Diabetes in Indian Asians and African Caribbeans Compared With Europeans: The Southall and Brent Revisited (SABRE) cohort. *Diabetes Care* Published Online First: 2012. doi:dc12-0544 [pii]10.2337/dc12-0544
14. Davis TME. Ethnic diversity in Type 2 diabetes. *Diabet Med* 2008;25:52–6.
15. Sivaprasad S, Gupta B, Crosby-Nwaobi R, Evans J. Prevalence of Diabetic Retinopathy in Various Ethnic Groups: A Worldwide Perspective. *Surv Ophthalmol* 2012;57:347–70.
16. Gupta R, Misra A. Epidemiology of Microvascular Complications of Diabetes in South Asians and Comparison with Other Ethnicities. *J Diabetes* 2016;:n/a-n/a.
17. Haffner SM, Fong D, Stern MP, Pugh JA, Hazuda HP, Patterson JK, *et al.* Diabetic retinopathy in Mexican Americans and non-Hispanic Whites. *Diabetes* 1988;37:878–84.
18. Zhang X, Saaddine JB, Chou C-F, Cotch MF, Cheng YJ, Geiss LS, *et al.* Prevalence of diabetic retinopathy in the United States, 2005-2008. *Jama* 2010;304:649–56.
19. Kempen JH, O'Colmain BJ, Leske MC, Haffner SM, Klein R, Moss SE, *et al.* The prevalence of diabetic retinopathy among adults in the United States. *Arch Ophthalmol* 2004;122:552–63.
20. Ting DSW, Cheung GCM, Wong TY. Diabetic retinopathy: global prevalence, major risk factors, screening practices and public health challenges: a review. *Clin Experiment Ophthalmol* 2015;:n/a-n/a.
21. Harris MI, Klein R, Cowie CC, Rowland M, Byrd-Holt DD. Is the risk of diabetic retinopathy greater in non-Hispanic blacks and Mexican Americans than in non-Hispanic whites with type 2 diabetes? A U.S. population study. *Diabetes Care* 1998;21:1230–5.
22. Raymond NT, Varadhan L, Reynold DR, Bush K, Sankaranarayanan S, Bellary S, *et al.* Higher prevalence of retinopathy in diabetic patients of South Asian ethnicity compared with white Europeans in the community: a cross-sectional study. *Diabetes Care* 2009;32:410–5.

23. Low L, Law JP, Hodson J, McAlpine R, O'Colmain U, MacEwen C. Impact of socioeconomic deprivation on the development of diabetic retinopathy: a population-based, cross-sectional and longitudinal study over 12 years. *BMJ Open* 2015;5:e007290.
24. Lane M, Mathewson PA, Sharma HE, Palmer H, Shah P, Nightingale P, *et al.* Social deprivation as a risk factor for late presentation of proliferative diabetic retinopathy. *Clin Ophthalmol* 2015;9:347–52.
25. Harris M, Lead C, Warehouse V, Docks T. The NHS Diabetic Eye Screening Programme: New Common Pathway. 2012;:5–6.
26. Lindenmeyer A, Sturt JA, Hipwell A, Stratton IM, Al-Athamneh N, Gadsby R, *et al.* Influence of primary care practices on patients' uptake of diabetic retinopathy screening: A qualitative case study. *Br J Gen Pract* 2014;64:484–92.
27. Broadbent D. Diabetic retinopathy: fundamentals for primary care. *Diabetes Prim Care* 2013;12:201–10.
28. Kostev K, Rathmann W. Diabetic retinopathy at diagnosis of type 2 diabetes in the UK: A database analysis. *Diabetologia* 2013;56:109–11.
29. Looker HC, Cromie D. Diabetic retinopathy at diagnosis of type 2 diabetes in Scotland. Diabetes. 2011;60:A183.
30. Thomas RL, Dunstan FD, Luzio SD, Chowdhury SR, North R V., Hale SL, *et al.* Prevalence of diabetic retinopathy within a national diabetic retinopathy screening service. *Br J Ophthalmol* 2015;99:64–8.
31. 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;361:195–200.
32. Leese GP, Boyle P, Zhiqiang F, Emslie-Smith A, Ellis JD. Screening uptake in a well-established diabetic retinopathy screening program the role of geographical access and deprivation. *Diabetes Care* 2008;31:2131–5.
33. Herrett E, Gallagher AM, Bhaskaran K, Forbes H, Mathur R, van Staa T, *et al.* Data Resource Profile: Clinical Practice Research Datalink (CPRD). *Int J Epidemiol* Published Online First: 6 June 2015. doi:10.1093/ije/dyv098
34. Mathur R, Bhaskaran K, Chaturvedi N, Leon DA, vanStaa T, Grundy E, *et al.* Completeness and usability of ethnicity data in UK-based primary care and hospital databases. *J Public Heal* 2013;36:684–92.
35. Chisholm J. The Read clinical classification. *BMJ* 1990;300:1092.
36. Allen N, Sudlow C, Downey P, Peakman T, Danesh J, Elliott P, *et al.* UK Biobank: Current status and what it means for epidemiology. *Heal Policy Technol* 2012;1:123–6.
37. Mclennan D, Barnes H, Noble M, Davies J, Garratt E. The English Indices of Deprivation 2010 - technical report. *Soc Policy* Published Online First: 2011. doi:http://dx.doi.org/http://www.communities.gov.uk/publications/corporate/statistics/indices2010technicalreport
38. Hull S a., Mathur R, Badrick E, Robson J, Boomla K. Recording ethnicity in primary care: Assessing the methods and impact. *Br J Gen Pract* 2011;61:e290-4.
39. Office for National Statistics. Population Estimates for UK, England and Wales, Scotland and Northern Ireland, Mid-2014. 2015.http://www.ons.gov.uk/ons/publications/re-reference-tables.html?edition=tcm%3A77-368259 (accessed 1 Nov 2015).
40. StataCorp. Stata Statistical Software: Release 13. 2013.
41. Delcourt C, Massin P, Rosilio M. Epidemiology of diabetic retinopathy: Expected vs reported prevalence of cases in the French population. *Diabetes Metab* 2009;35:431–8.
42. Strutton R, Du Chemin A, Stratton IM, Forster AS. System-level and patient-level explanations for non-attendance at diabetic retinopathy screening in Sutton and Merton (London, UK): a qualitative analysis of a service evaluation: Table 1. *BMJ Open* 2016;6:e010952.
43. Garduño-Diaz SD, Khokhar S. Prevalence, risk factors and complications associated with type

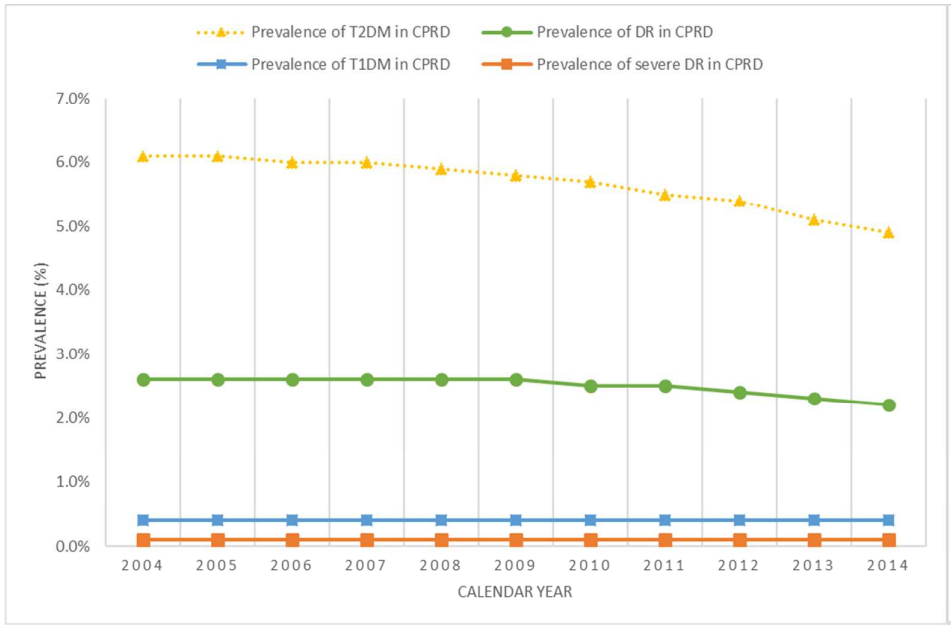
2 diabetes in migrant South Asians. Diabetes. Metab. Res. Rev. 2012;28:6–24.
44. Gholap N, Davies M, Patel K, Sattar N, Khunti K. Type 2 diabetes and cardiovascular disease in South Asians. *Prim Care Diabetes* 2011;5:45–56.
45. S.L. I, K.M. M, C.L. F, A.M. K. Prevalence and correlates of cardiovascular risk factors in South Asians: population-based data from two California surveys. Ethn. Dis. 2006;16:886–93.
46. Beeching NJ, Gill G V. Deprivation and Type 2 diabetes mellitus prevalence. *Diabet Med* 2000;17:813.
47. Ethnic variations in the prevalence of diabetic retinopathy in people with diabetes attending screening in the United Kingdom (DRIVE UK). *PLoS One* 2012;7. doi:http://dx.doi.org/10.1371/journal.pone.0032182
48. Doran T, Fullwood C, Gravelle H, Reeves D, Kontopantelis E, Hiroeh U, *et al.* Pay-for-Performance Programs in Family Practices in the United Kingdom. N. Engl. J. Med. 2006.http://www.nejm.org/doi/full/10.1056/NEJMsa055505 (accessed 27 Jul 2015).
49. Khunti K, Gadsby R, Millett C, Majeed a., Davies M. Quality of diabetes care in the UK: Comparison of published quality-of-care reports with results of the Quality and Outcomes Framework for Diabetes. *Diabet Med* 2007;24:1436–41.
50. Herrett E, Thomas SL, Schoonen WM, Smeeth L, Hall AJ. Validation and validity of diagnoses in the General Practice Research Database: a systematic review. *Br J Clin Pharmacol* 2010;69:4–14.
51. Khan NF, Harrison SE, Rose PW. Validity of diagnostic coding within the General Practice Research Database: a systematic review. *Br J Gen Pract* 2010;60:e128-36.
52. Jick SS, Kaye JA, Vasilakis-Scaramozza C, Garcia Rodriguez LA, Ruigomez A, Meier CR, *et al.* Validity of the general practice research database. *Pharmacotherapy* 2003;23:686–9.
53. Konig M, Lamos EM, Stein SA, Davis SN. An insight into the recent diabetes trials: what is the best approach to prevent macrovascular and microvascular complications?. *Curr Diabetes Rev* 2013;9:371–81.
54. Turner R, Matthews D, Neil A, Mcelroy H. Tight blood pressure control and risk of macrovascular and microvascular complications in type 2 diabetes: UKPDS 38. *Br Med J* 1998;317:703–13.
55. ONS. Total Population (UK) Mid-2014 Estimate. 2014.http://ons.gov.uk/ons/taxonomy/index.html?nscl=Population (accessed 30 Jul 2015).
56. Public Health England; NHS Screening Programmes in England 2013/14. 2013.
57. Knight A, Lindfield R. The relationship between socio-economic status and access to eye health services in the UK: A systematic review. Public Health. 2015;129:94–102.

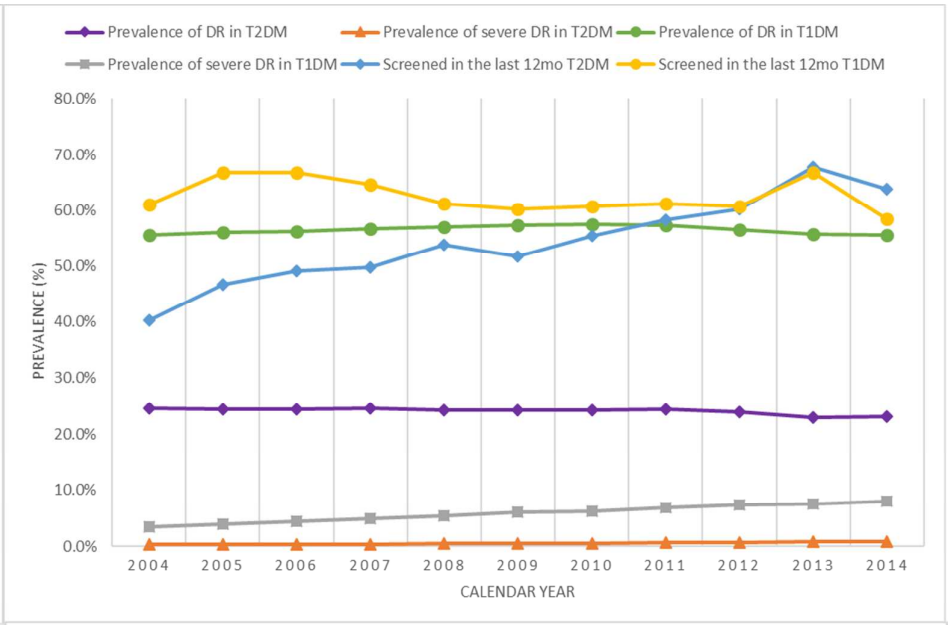
FIGURE LEGENDS

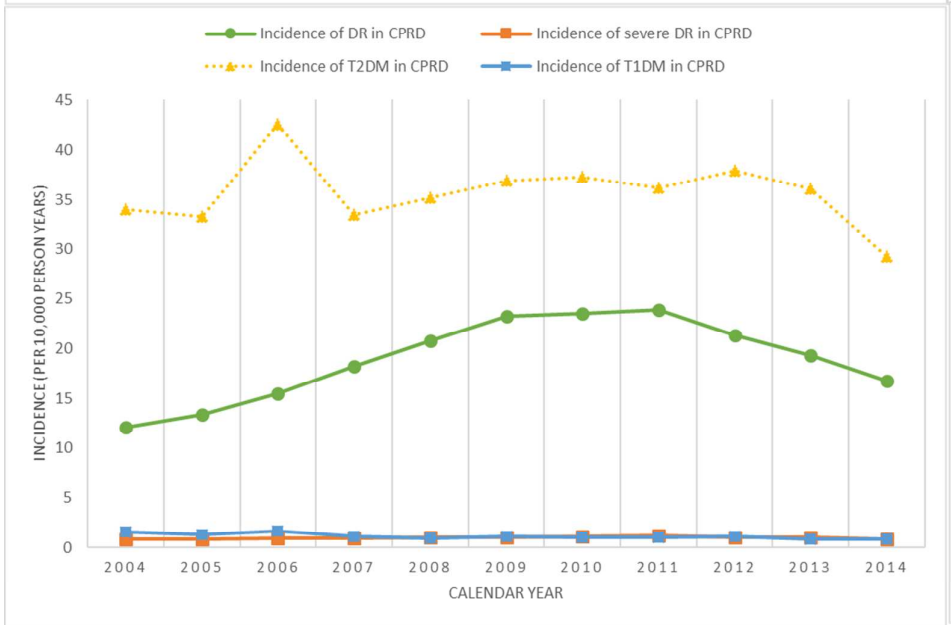
Figure 1. Age standardised prevalence and incidence of diabetes, screening and diabetic retinopathy 2004-2014

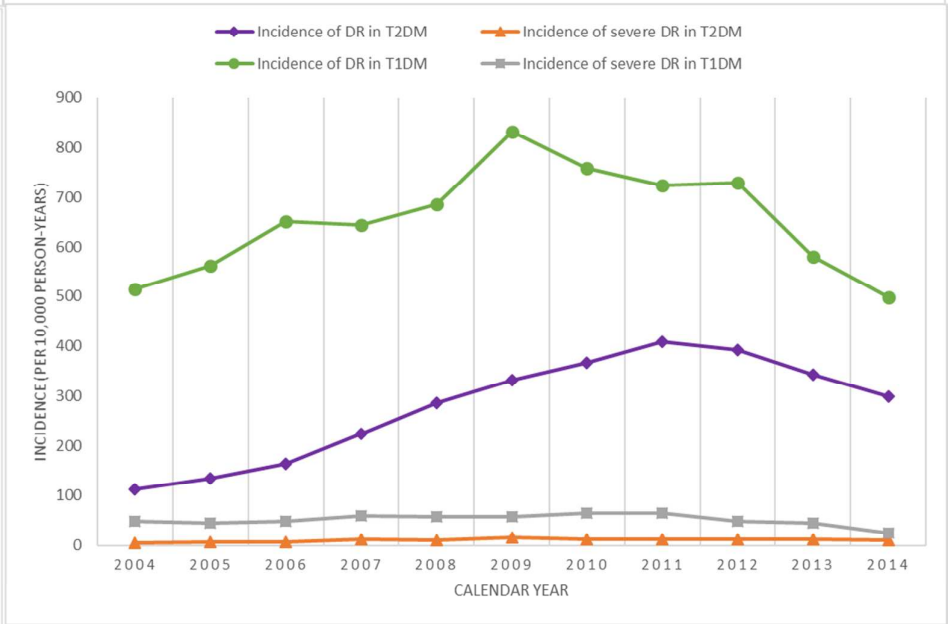
Figure 2. Relative risk of diabetic retinopathy in patients with type 2 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes

Figure 3. Relative risk of diabetic retinopathy in patients with type 1 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes









*Proportion of patients screened for DR not cumulative, patients can contribute in multiple years

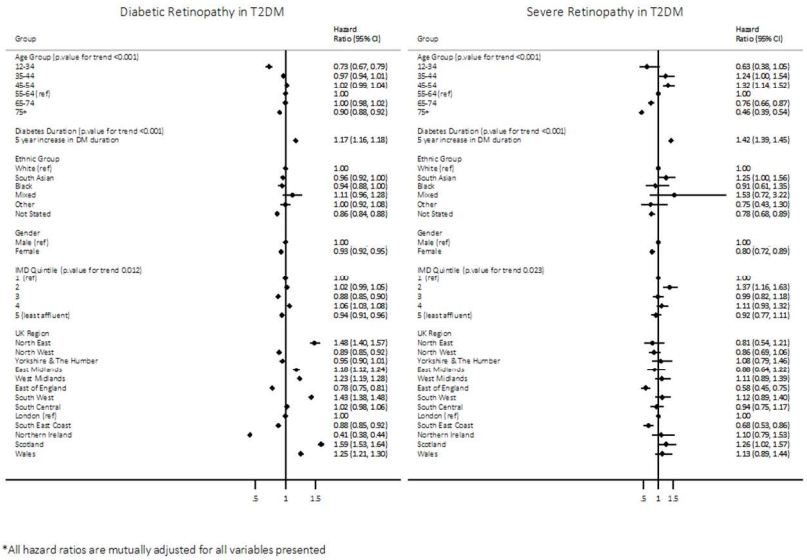
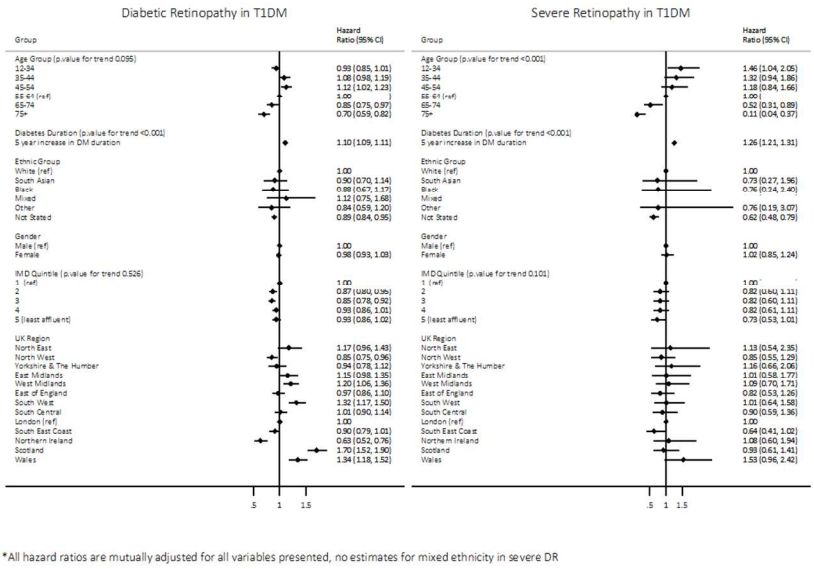


Figure 2. Relative risk of diabetic retinopathy in patients with type 2 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes
(Insert Figures 2 and 3 about



*All hazard ratios are mutually adjusted for all variables presented, no estimates for mixed ethnicity in severe DR

Figure 3. Relative risk of diabetic retinopathy in patients with type 1 diabetes by gender, ethnic group, age group, deprivation, region, and duration of diabetes
(Insert Figures 2 and 3 about

Supplementary Materials

Tables

Figures

a. Population Flow Diagram

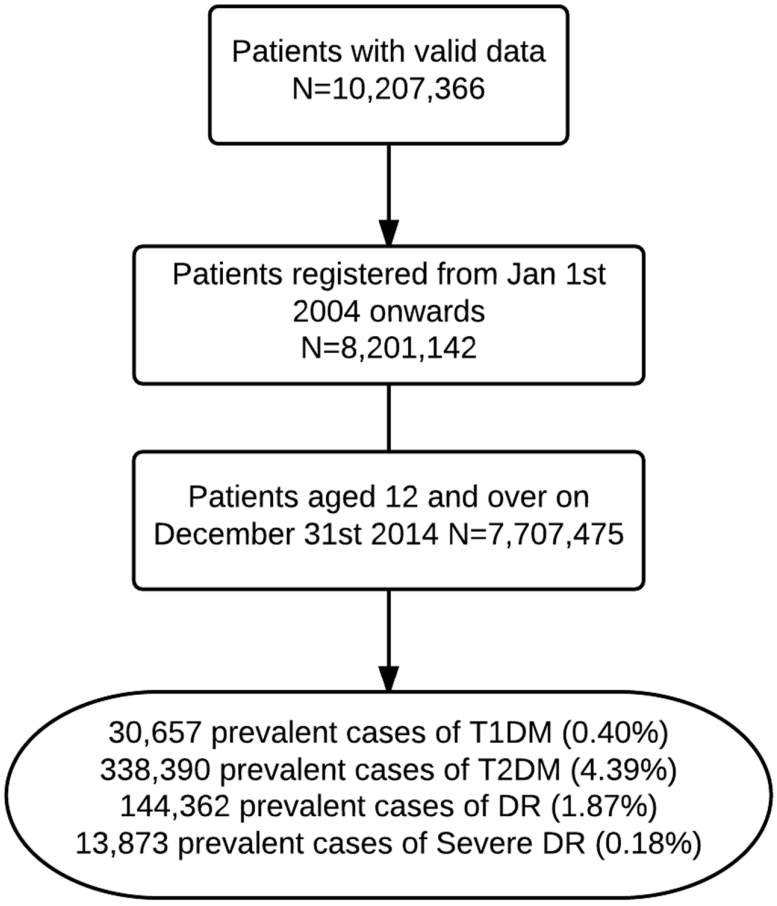


Figure 1. Derivation of study population from the CPRD

b. Results of the diabetes adjudication algorithms

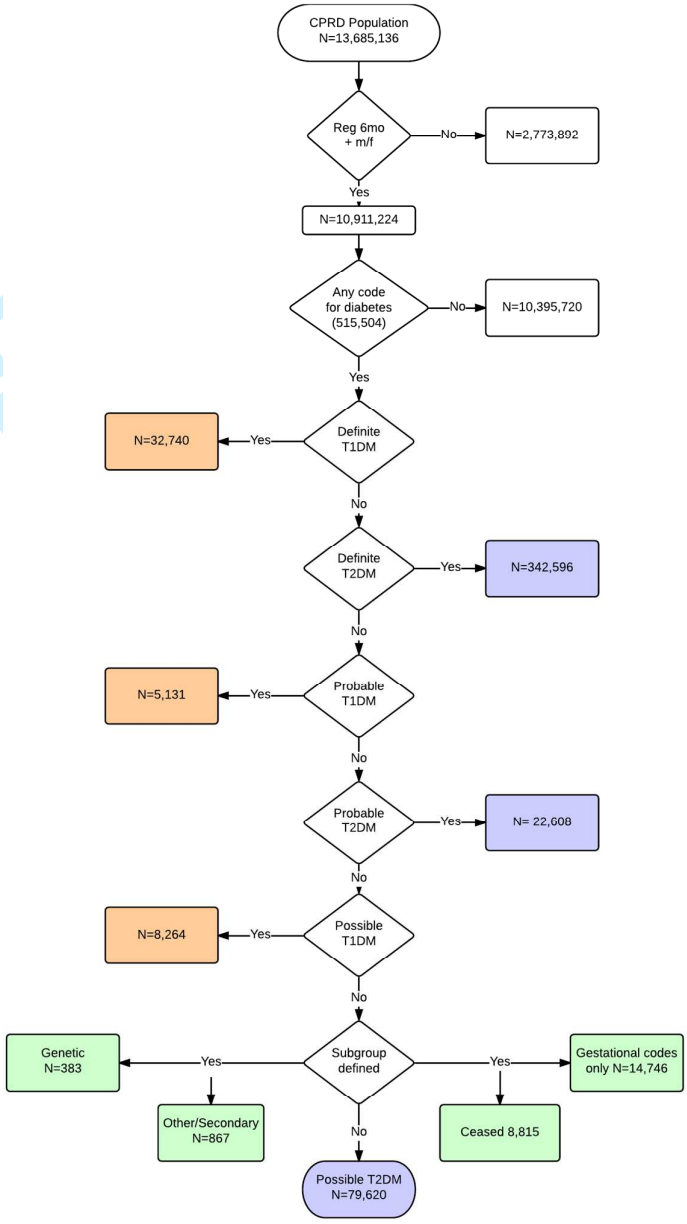


Figure 2. Results from Flowchart 1: Initial Sort and Classification

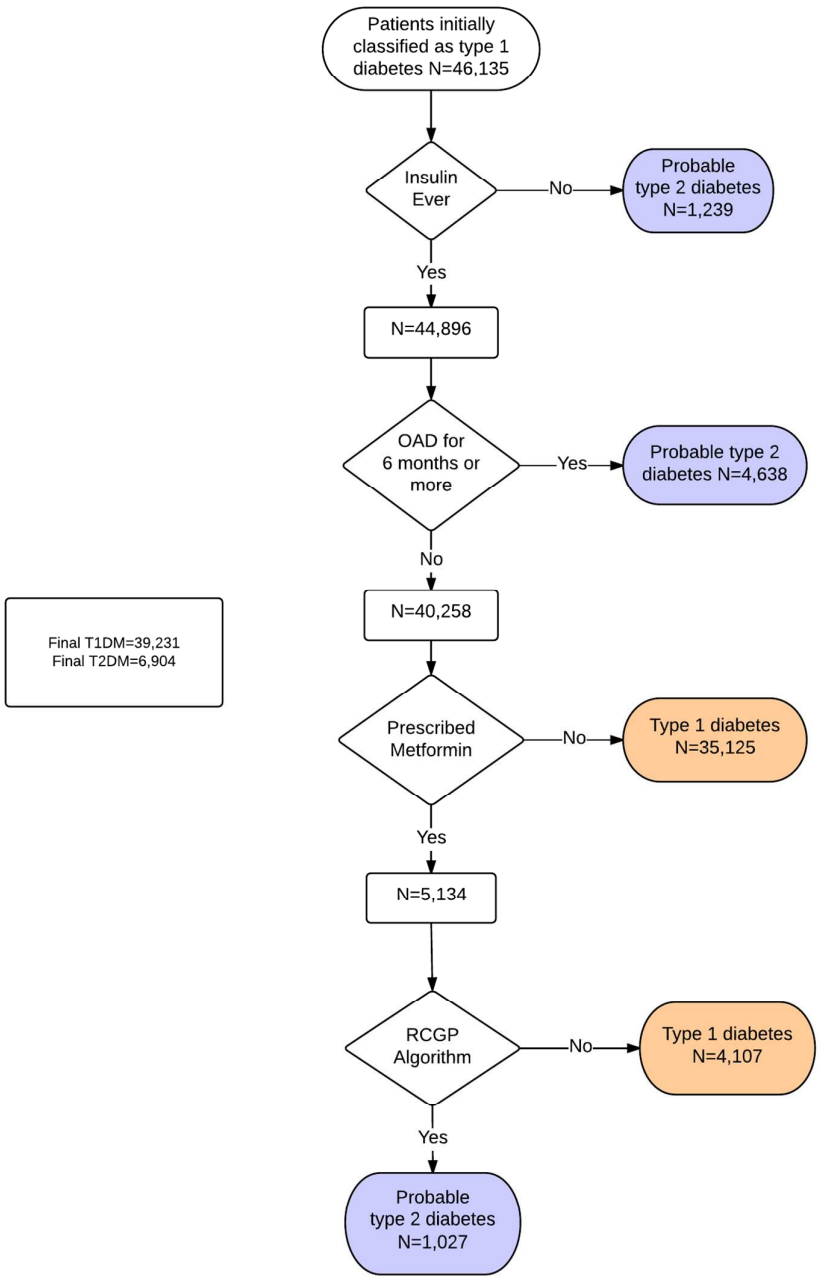


Figure 3. Results from Flowchart 2: Improving classification of type 1 diabetes

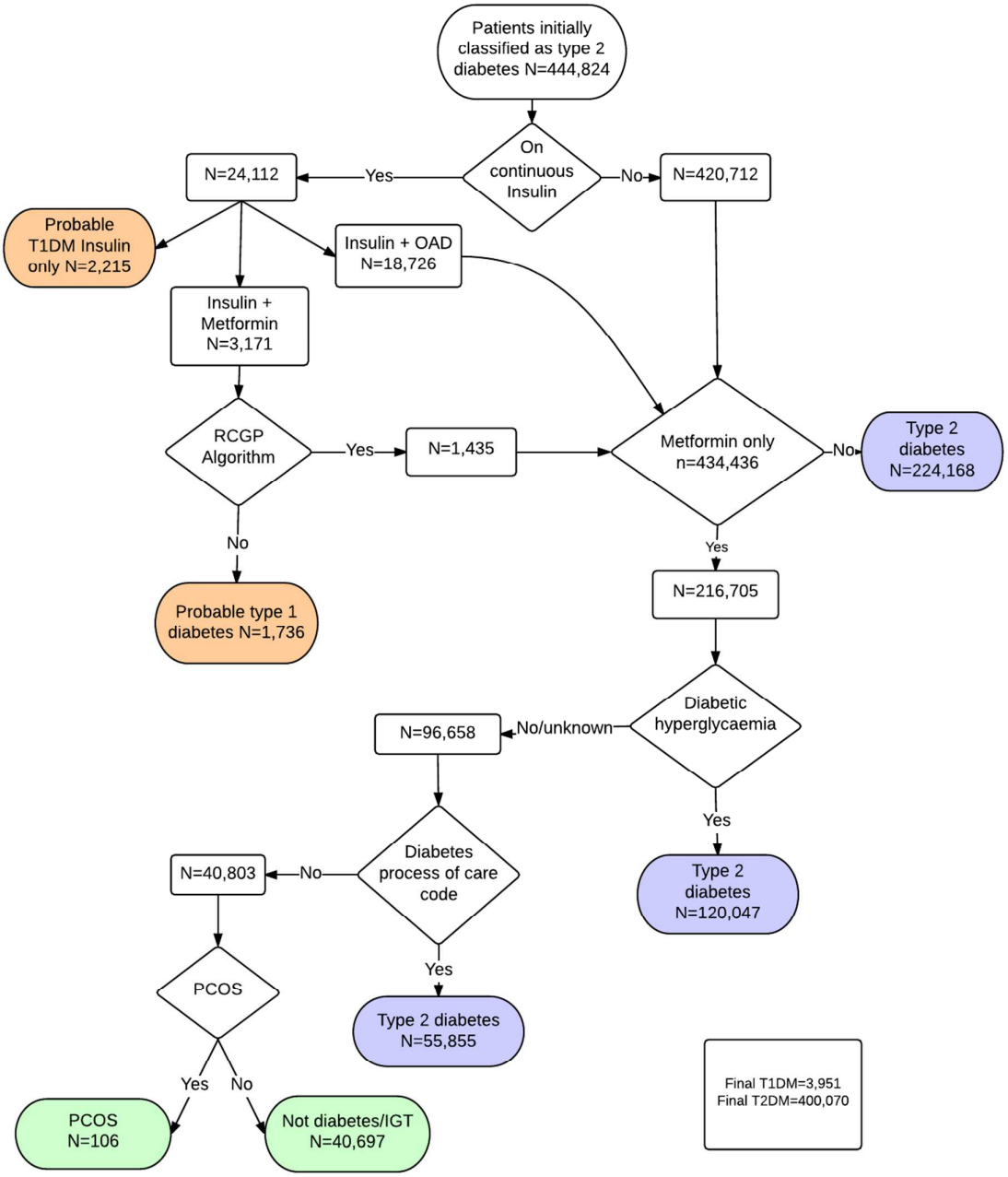


Figure 4. Results from Flowchart 3: Improving classification of type 2 diabetes

c. Codelists

Table 1. Search terms for Diabetic Retinopathy

Keywords for identifying diabetic retinopathy in the CPRD
RETINAL **and** or *SCR* or *ARTERIES* or *EXUDATE* or *MICROANEURYSMS* or *PHOTOGRAPHY* or *ABNORMALITY*
O/E **and** *RETINA* or *FUNDUS* or *PHOTOCOAGULATION* or *MACULAR* or *VITREOUS*
*LASER" **and** *RETINA*
RETINOPATHY or *FUNDOSCOPY* or *MACULOPATHY* or *RED REFLEX* or *SEEN BY OP* or *RETINAL SCR* or *RETINOSCOPY* or *SLIT LAMP* or *DIABETIC EYE* or *EYE FUNDUS* or *EXAMINATION OF RETINA* or *RETINA AND OTHER PARTS OF EYE OPERATIONS* or *VITRECTOMY*
Keywords excluded (to remove obstetric terms related to "fundus")
TERM SIZE or *WEEK SIZE* or *OBSTETRIC*

Table 2. Categorization of Read codes for Diabetes Mellitus

	Type 1 Diabetes	Type 2 Diabetes	Other
Definite	Type 1 DM: C10E Not contradicted/ceased/superseded	Type 2 DM: C10F Not contradicted/ceased/superseded	Gestational L180 Genetic C10c-C10D Other/Secondary C10G-J, L-N, C11y0 Insulin resistance: C10K, C1098, C10F8 Ceased: 21263, 212H
Probable	IDDM: C108 Adult onset: C1073 Gestational: L1805 Not contradicted/ceased/superseded	NIDDM: C109 Gestational: L1806 Gestational: L180X Not contradicted/ceased/superseded	
Possible	Diabetes mellitus, adult onset: C10z1 C10y0 C110 Not contradicted/ceased/superseded	Diabetes mellitus, adult onset: C10%, C112 (z), L180x Not contradicted/ceased/superseded	

Table 3. Read codes for Diabetes Mellitus

medcode	readcode	readterm	category
28622	2126300	Diabetes resolved	Diabetes ceased
18766	212H.00	Diabetes resolved	Diabetes ceased
711	C10..00	Diabetes mellitus	Vague codes
38986	C100.00	Diabetes mellitus with no mention of complication	Vague codes
24490	C100000	Diabetes mellitus, juvenile type, no mention of complication	Possible T1 codes
1038	C100011	Insulin dependent diabetes mellitus	Possible T1 codes
14803	C100100	Diabetes mellitus, adult onset, no mention of complication	Possible T2 codes
14889	C100111	Maturity onset diabetes	Possible T2 codes
506	C100112	Non-insulin dependent diabetes mellitus	Possible T2 codes
50972	C100z00	Diabetes mellitus NOS with no mention of complication	Vague codes
1682	C101.00	Diabetes mellitus with ketoacidosis	Vague codes
53200	C101000	Diabetes mellitus, juvenile type, with ketoacidosis	Possible T1 codes
54856	C101100	Diabetes mellitus, adult onset, with ketoacidosis	Vague codes
38617	C101y00	Other specified diabetes mellitus with ketoacidosis	Vague codes
42505	C101z00	Diabetes mellitus NOS with ketoacidosis	Vague codes
21482	C102.00	Diabetes mellitus with hyperosmolar coma	Vague codes
40023	C102000	Diabetes mellitus, juvenile type, with hyperosmolar coma	Possible T1 codes
43139	C102100	Diabetes mellitus, adult onset, with hyperosmolar coma	Possible T2 codes
72345	C102z00	Diabetes mellitus NOS with hyperosmolar coma	Vague codes
15690	C103.00	Diabetes mellitus with ketoacidotic coma	Vague codes
42567	C103000	Diabetes mellitus, juvenile type, with ketoacidotic coma	Possible T1 codes
68843	C103100	Diabetes mellitus, adult onset, with ketoacidotic coma	Possible T2 codes
59288	C103y00	Other specified diabetes mellitus with coma	Vague codes
65062	C103z00	Diabetes mellitus NOS with ketoacidotic coma	Vague codes
16502	C104.00	Diabetes mellitus with renal manifestation	Vague codes
2475	C104.11	Diabetic nephropathy	Vague codes
93922	C104000	Diabetes mellitus, juvenile type, with renal manifestation	Possible T1 codes
35105	C104100	Diabetes mellitus, adult onset, with renal manifestation	Possible T2 codes
13279	C104y00	Other specified diabetes mellitus with renal complications	Vague codes

medcode	readcode	readterm	category
35107	C104z00	Diabetes mellitis with nephropathy NOS	Vague codes
33254	C105.00	Diabetes mellitus with ophthalmic manifestation	Vague codes
69748	C105000	Diabetes mellitus, juvenile type, + ophthalmic manifestation	Possible T1 codes
41389	C105100	Diabetes mellitus, adult onset, + ophthalmic manifestation	Possible T2 codes
47377	C105y00	Other specified diabetes mellitus with ophthalmic complicatn	Vague codes
34283	C105z00	Diabetes mellitus NOS with ophthalmic manifestation	Vague codes
16230	C106.00	Diabetes mellitus with neurological manifestation	Vague codes
59903	C106.11	Diabetic amyotrophy	Vague codes
7795	C106.12	Diabetes mellitus with neuropathy	Vague codes
16491	C106.13	Diabetes mellitus with polyneuropathy	Vague codes
67853	C106000	Diabetes mellitus, juvenile, + neurological manifestation	Possible T1 codes
39317	C106100	Diabetes mellitus, adult onset, + neurological manifestation	Possible T2 codes
61523	C106y00	Other specified diabetes mellitus with neurological comps	Vague codes
22573	C106z00	Diabetes mellitus NOS with neurological manifestation	Vague codes
35399	C107.00	Diabetes mellitus with peripheral circulatory disorder	Vague codes
32403	C107.11	Diabetes mellitus with gangrene	Vague codes
32556	C107.12	Diabetes with gangrene	Vague codes
70448	C107000	Diabetes mellitus, juvenile +peripheral circulatory disorder	Possible T1 codes
63357	C107100	Diabetes mellitus, adult, + peripheral circulatory disorder	Possible T2 codes
33807	C107200	Diabetes mellitus, adult with gangrene	Possible T2 codes
69124	C107300	IDDM with peripheral circulatory disorder	Probable T1 codes
56803	C107400	NIDDM with peripheral circulatory disorder	Probable T2 codes
65025	C107z00	Diabetes mellitus NOS with peripheral circulatory disorder	Vague codes
1647	C108.00	Insulin dependent diabetes mellitus	Probable T1 codes
18505	C108.11	IDDM-Insulin dependent diabetes mellitus	Probable T1 codes

medcode	readcode	readterm	category
17858	C108.12	Type 1 diabetes mellitus	Probable T1 codes
24423	C108.13	Type I diabetes mellitus	Probable T1 codes
46963	C108000	Insulin-dependent diabetes mellitus with renal complications	Probable T1 codes
61344	C108011	Type I diabetes mellitus with renal complications	Probable T1 codes
21983	C108012	Type 1 diabetes mellitus with renal complications	Probable T1 codes
49276	C108100	Insulin-dependent diabetes mellitus with ophthalmic comps	Probable T1 codes
52283	C108200	Insulin-dependent diabetes mellitus with neurological comps	Probable T1 codes
49146	C108211	Type I diabetes mellitus with neurological complications	Probable T1 codes
61829	C108212	Type 1 diabetes mellitus with neurological complications	Probable T1 codes
52104	C108300	Insulin dependent diabetes mellitus with multiple complicatn	Probable T1 codes
26855	C108400	Unstable insulin dependant diabetes mellitus	Probable T1 codes
60107	C108411	Unstable type I diabetes mellitus	Probable T1 codes
97474	C108412	Unstable type 1 diabetes mellitus	Probable T1 codes
44443	C108500	Insulin dependent diabetes mellitus with ulcer	Probable T1 codes
51957	C108511	Type I diabetes mellitus with ulcer	Probable T1 codes
68390	C108512	Type 1 diabetes mellitus with ulcer	Probable T1 codes
60499	C108600	Insulin dependent diabetes mellitus with gangrene	Probable T1 codes
6509	C108700	Insulin dependent diabetes mellitus with retinopathy	Probable T1 codes
38161	C108711	Type I diabetes mellitus with retinopathy	Probable T1 codes
41049	C108712	Type 1 diabetes mellitus with retinopathy	Probable T1 codes
6791	C108800	Insulin dependant diabetes mellitus - poor control	Probable T1 codes
46850	C108811	Type I diabetes mellitus - poor control	Probable T1 codes
45914	C108812	Type 1 diabetes mellitus - poor control	Probable T1 codes
31310	C108900	Insulin dependant diabetes maturity onset	Probable T1 codes
63017	C108911	Type I diabetes mellitus maturity onset	Probable T1 codes
97446	C108912	Type 1 diabetes mellitus maturity onset	Probable T1 codes
56448	C108A00	Insulin-dependent diabetes without complication	Probable T1 codes
95992	C108A11	Type I diabetes mellitus without complication	Probable T1 codes

medcode	readcode	readterm	category
24694	C108B00	Insulin dependent diabetes mellitus with mononeuropathy	Probable T1 codes
99231	C108B11	Type I diabetes mellitus with mononeuropathy	Probable T1 codes
41716	C108C00	Insulin dependent diabetes mellitus with polyneuropathy	Probable T1 codes
57621	C108D00	Insulin dependent diabetes mellitus with nephropathy	Probable T1 codes
66872	C108D11	Type I diabetes mellitus with nephropathy	Probable T1 codes
44440	C108E00	Insulin dependent diabetes mellitus with hypoglycaemic coma	Probable T1 codes
42729	C108E11	Type I diabetes mellitus with hypoglycaemic coma	Probable T1 codes
70766	C108E12	Type 1 diabetes mellitus with hypoglycaemic coma	Probable T1 codes
44260	C108F00	Insulin dependent diabetes mellitus with diabetic cataract	Probable T1 codes
17545	C108F11	Type I diabetes mellitus with diabetic cataract	Probable T1 codes
64446	C108G00	Insulin dependent diab mell with peripheral angiopathy	Probable T1 codes
65616	C108H00	Insulin dependent diabetes mellitus with arthropathy	Probable T1 codes
62352	C108H11	Type I diabetes mellitus with arthropathy	Probable T1 codes
39809	C108J00	Insulin dependent diab mell with neuropathic arthropathy	Probable T1 codes
60208	C108J11	Type I diabetes mellitus with neuropathic arthropathy	Probable T1 codes
18230	C108J12	Type 1 diabetes mellitus with neuropathic arthropathy	Probable T1 codes
46290	C108y00	Other specified diabetes mellitus with multiple comps	Vague codes
64449	C108z00	Unspecified diabetes mellitus with multiple complications	Vague codes
4513	C109.00	Non-insulin dependent diabetes mellitus	Probable T2 codes
5884	C109.11	NIDDM - Non-insulin dependent diabetes mellitus	Probable T2 codes
17859	C109.12	Type 2 diabetes mellitus	Probable T2 codes
18219	C109.13	Type II diabetes mellitus	Probable T2 codes
52303	C109000	Non-insulin-dependent diabetes mellitus with renal comps	Probable T2 codes
50225	C109011	Type II diabetes mellitus with renal complications	Probable T2 codes
18209	C109012	Type 2 diabetes mellitus with renal complications	Probable T2 codes
50429	C109100	Non-insulin-dependent diabetes mellitus with ophthalm comps	Probable T2 codes

medcode	readcode	readterm	category
59725	C109111	Type II diabetes mellitus with ophthalmic complications	Probable T2 codes
70316	C109112	Type 2 diabetes mellitus with ophthalmic complications	Probable T2 codes
55842	C109200	Non-insulin-dependent diabetes mellitus with neuro comps	Probable T2 codes
67905	C109211	Type II diabetes mellitus with neurological complications	Probable T2 codes
45919	C109212	Type 2 diabetes mellitus with neurological complications	Probable T2 codes
62146	C109300	Non-insulin-dependent diabetes mellitus with multiple comps	Probable T2 codes
34912	C109400	Non-insulin dependent diabetes mellitus with ulcer	Probable T2 codes
55075	C109411	Type II diabetes mellitus with ulcer	Probable T2 codes
65704	C109412	Type 2 diabetes mellitus with ulcer	Probable T2 codes
40401	C109500	Non-insulin dependent diabetes mellitus with gangrene	Probable T2 codes
62107	C109511	Type II diabetes mellitus with gangrene	Probable T2 codes
46150	C109512	Type 2 diabetes mellitus with gangrene	Probable T2 codes
17262	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	Probable T2 codes
58604	C109611	Type II diabetes mellitus with retinopathy	Probable T2 codes
42762	C109612	Type 2 diabetes mellitus with retinopathy	Probable T2 codes
8403	C109700	Non-insulin dependant diabetes mellitus - poor control	Probable T2 codes
24458	C109711	Type II diabetes mellitus - poor control	Probable T2 codes
45913	C109712	Type 2 diabetes mellitus - poor control	Probable T2 codes
39406	C109800	Reaven's syndrome	Not diabetes
29979	C109900	Non-insulin-dependent diabetes mellitus without complication	Probable T2 codes
72320	C109A00	Non-insulin dependent diabetes mellitus with mononeuropathy	Probable T2 codes
50813	C109A11	Type II diabetes mellitus with mononeuropathy	Probable T2 codes
45467	C109B00	Non-insulin dependent diabetes mellitus with polyneuropathy	Probable T2 codes
47409	C109B11	Type II diabetes mellitus with polyneuropathy	Probable T2 codes
59365	C109C00	Non-insulin dependent diabetes mellitus with nephropathy	Probable T2 codes

medcode	readcode	readterm	category
64571	C109C11	Type II diabetes mellitus with nephropathy	Probable T2 codes
24836	C109C12	Type 2 diabetes mellitus with nephropathy	Probable T2 codes
43785	C109D00	Non-insulin dependent diabetes mellitus with hypoglyca coma	Probable T2 codes
56268	C109D11	Type II diabetes mellitus with hypoglycaemic coma	Probable T2 codes
61071	C109D12	Type 2 diabetes mellitus with hypoglycaemic coma	Probable T2 codes
69278	C109E00	Non-insulin depend diabetes mellitus with diabetic cataract	Probable T2 codes
48192	C109E11	Type II diabetes mellitus with diabetic cataract	Probable T2 codes
44779	C109E12	Type 2 diabetes mellitus with diabetic cataract	Probable T2 codes
54212	C109F00	Non-insulin-dependent d m with peripheral angiopath	Probable T2 codes
54899	C109F11	Type II diabetes mellitus with peripheral angiopathy	Probable T2 codes
60699	C109F12	Type 2 diabetes mellitus with peripheral angiopathy	Probable T2 codes
24693	C109G00	Non-insulin dependent diabetes mellitus with arthropathy	Probable T2 codes
18143	C109G11	Type II diabetes mellitus with arthropathy	Probable T2 codes
49869	C109G12	Type 2 diabetes mellitus with arthropathy	Probable T2 codes
40962	C109H00	Non-insulin dependent d m with neuropathic arthropathy	Probable T2 codes
47816	C109H11	Type II diabetes mellitus with neuropathic arthropathy	Probable T2 codes
66965	C109H12	Type 2 diabetes mellitus with neuropathic arthropathy	Probable T2 codes
18278	C109J00	Insulin treated Type 2 diabetes mellitus	Probable T2 codes
37648	C109J11	Insulin treated non-insulin dependent diabetes mellitus	Probable T2 codes
18264	C109J12	Insulin treated Type II diabetes mellitus	Probable T2 codes
36633	C109K00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	Probable T2 codes
52236	C10A.00	Malnutrition-related diabetes mellitus	Secondary / Other types
66675	C10A000	Malnutrition-related diabetes mellitus with coma	Secondary / Other types
33969	C10A100	Malnutrition-related diabetes mellitus with ketoacidosis	Secondary / Other types
100347	C10A500	Malnutritn-relat diabetes melitus wth periph circul complctn	Secondary / Other types
11551	C10B.00	Diabetes mellitus induced by steroids	Secondary / Other types
26108	C10B000	Steroid induced diabetes mellitus without complication	Secondary / Other types

medcode	readcode	readterm	category
43453	C10C.00	Diabetes mellitus autosomal dominant	Genetic
46624	C10C.11	Maturity onset diabetes in youth	Genetic
98392	C10C.12	Maturity onset diabetes in youth type 1	Genetic
36695	C10D.00	Diabetes mellitus autosomal dominant type 2	Genetic
59991	C10D.11	Maturity onset diabetes in youth type 2	Genetic
1549	C10E.00	Type 1 diabetes mellitus	Definite T1 codes
12455	C10E.11	Type I diabetes mellitus	Definite T1 codes
51261	C10E.12	Insulin dependent diabetes mellitus	Definite T1 codes
47582	C10E000	Type 1 diabetes mellitus with renal complications	Definite T1 codes
47649	C10E100	Type 1 diabetes mellitus with ophthalmic complications	Definite T1 codes
99311	C10E111	Type I diabetes mellitus with ophthalmic complications	Definite T1 codes
98071	C10E112	Insulin-dependent diabetes mellitus with ophthalmic comps	Definite T1 codes
42831	C10E200	Type 1 diabetes mellitus with neurological complications	Definite T1 codes
47650	C10E300	Type 1 diabetes mellitus with multiple complications	Definite T1 codes
91942	C10E311	Type I diabetes mellitus with multiple complications	Definite T1 codes
45276	C10E312	Insulin dependent diabetes mellitus with multiple complicat	Definite T1 codes
43921	C10E400	Unstable type 1 diabetes mellitus	Definite T1 codes
49949	C10E411	Unstable type I diabetes mellitus	Definite T1 codes
54600	C10E412	Unstable insulin dependent diabetes mellitus	Definite T1 codes
18683	C10E500	Type 1 diabetes mellitus with ulcer	Definite T1 codes
93878	C10E511	Type I diabetes mellitus with ulcer	Definite T1 codes
98704	C10E512	Insulin dependent diabetes mellitus with ulcer	Definite T1 codes
69993	C10E600	Type 1 diabetes mellitus with gangrene	Definite T1 codes
18387	C10E700	Type 1 diabetes mellitus with retinopathy	Definite T1 codes
95343	C10E711	Type I diabetes mellitus with retinopathy	Definite T1 codes
93875	C10E712	Insulin dependent diabetes mellitus with retinopathy	Definite T1 codes
35288	C10E800	Type 1 diabetes mellitus - poor control	Definite T1 codes
72702	C10E812	Insulin dependent diabetes mellitus - poor control	Definite T1 codes
40682	C10E900	Type 1 diabetes mellitus maturity onset	Definite T1 codes
96235	C10E911	Type I diabetes mellitus maturity onset	Definite T1 codes

medcode	readcode	readterm	category
97849	C10E912	Insulin dependent diabetes maturity onset	Definite T1 codes
69676	C10EA00	Type 1 diabetes mellitus without complication	Definite T1 codes
62613	C10EA11	Type I diabetes mellitus without complication	Definite T1 codes
99719	C10EA12	Insulin-dependent diabetes without complication	Definite T1 codes
68105	C10EB00	Type 1 diabetes mellitus with mononeuropathy	Definite T1 codes
46301	C10EC00	Type 1 diabetes mellitus with polyneuropathy	Definite T1 codes
91943	C10EC11	Type I diabetes mellitus with polyneuropathy	Definite T1 codes
101311	C10EC12	Insulin dependent diabetes mellitus with polyneuropathy	Definite T1 codes
10418	C10ED00	Type 1 diabetes mellitus with nephropathy	Definite T1 codes
39070	C10EE00	Type 1 diabetes mellitus with hypoglycaemic coma	Definite T1 codes
99716	C10EE12	Insulin dependent diabetes mellitus with hypoglycaemic coma	Definite T1 codes
49554	C10EF00	Type 1 diabetes mellitus with diabetic cataract	Definite T1 codes
100770	C10EF12	Insulin dependent diabetes mellitus with diabetic cataract	Definite T1 codes
93468	C10EG00	Type 1 diabetes mellitus with peripheral angiopathy	Definite T1 codes
18642	C10EH00	Type 1 diabetes mellitus with arthropathy	Definite T1 codes
54008	C10EJ00	Type 1 diabetes mellitus with neuropathic arthropathy	Definite T1 codes
30323	C10EK00	Type 1 diabetes mellitus with persistent proteinuria	Definite T1 codes
30294	C10EL00	Type 1 diabetes mellitus with persistent microalbuminuria	Definite T1 codes
10692	C10EM00	Type 1 diabetes mellitus with ketoacidosis	Definite T1 codes
62209	C10EM11	Type I diabetes mellitus with ketoacidosis	Definite T1 codes
40837	C10EN00	Type 1 diabetes mellitus with ketoacidotic coma	Definite T1 codes
66145	C10EN11	Type I diabetes mellitus with ketoacidotic coma	Definite T1 codes
22871	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	Definite T1 codes
97894	C10EP11	Type I diabetes mellitus with exudative maculopathy	Definite T1 codes
55239	C10EQ00	Type 1 diabetes mellitus with gastroparesis	Definite T1 codes
95636	C10ER00	Latent autoimmune diabetes mellitus in adult	Secondary / Other types
758	C10F.00	Type 2 diabetes mellitus	Definite T2 codes
22884	C10F.11	Type II diabetes mellitus	Definite T2 codes
18777	C10F000	Type 2 diabetes mellitus with renal complications	Definite T2 codes

medcode	readcode	readterm	category
57278	C10F011	Type II diabetes mellitus with renal complications	Definite T2 codes
47321	C10F100	Type 2 diabetes mellitus with ophthalmic complications	Definite T2 codes
100964	C10F111	Type II diabetes mellitus with ophthalmic complications	Definite T2 codes
34268	C10F200	Type 2 diabetes mellitus with neurological complications	Definite T2 codes
98616	C10F211	Type II diabetes mellitus with neurological complications	Definite T2 codes
65267	C10F300	Type 2 diabetes mellitus with multiple complications	Definite T2 codes
43227	C10F311	Type II diabetes mellitus with multiple complications	Definite T2 codes
49074	C10F400	Type 2 diabetes mellitus with ulcer	Definite T2 codes
91646	C10F411	Type II diabetes mellitus with ulcer	Definite T2 codes
12736	C10F500	Type 2 diabetes mellitus with gangrene	Definite T2 codes
18496	C10F600	Type 2 diabetes mellitus with retinopathy	Definite T2 codes
49655	C10F611	Type II diabetes mellitus with retinopathy	Definite T2 codes
25627	C10F700	Type 2 diabetes mellitus - poor control	Definite T2 codes
47315	C10F711	Type II diabetes mellitus - poor control	Definite T2 codes
54773	C10F800	Reaven's syndrome	Not diabetes
39481	C10F811	Metabolic syndrome X	Not diabetes
47954	C10F900	Type 2 diabetes mellitus without complication	Definite T2 codes
53392	C10F911	Type II diabetes mellitus without complication	Definite T2 codes
62674	C10FA00	Type 2 diabetes mellitus with mononeuropathy	Definite T2 codes
95351	C10FA11	Type II diabetes mellitus with mononeuropathy	Definite T2 codes
18425	C10FB00	Type 2 diabetes mellitus with polyneuropathy	Definite T2 codes
50527	C10FB11	Type II diabetes mellitus with polyneuropathy	Definite T2 codes
12640	C10FC00	Type 2 diabetes mellitus with nephropathy	Definite T2 codes
46917	C10FD00	Type 2 diabetes mellitus with hypoglycaemic coma	Definite T2 codes
98723	C10FD11	Type II diabetes mellitus with hypoglycaemic coma	Definite T2 codes
44982	C10FE00	Type 2 diabetes mellitus with diabetic cataract	Definite T2 codes
93727	C10FE11	Type II diabetes mellitus with diabetic cataract	Definite T2 codes
37806	C10FF00	Type 2 diabetes mellitus with peripheral angiopathy	Definite T2 codes
59253	C10FG00	Type 2 diabetes mellitus with arthropathy	Definite T2 codes
35385	C10FH00	Type 2 diabetes mellitus with neuropathic arthropathy	Definite T2 codes
1407	C10FJ00	Insulin treated Type 2 diabetes mellitus	Definite T2 codes
64668	C10FJ11	Insulin treated Type II diabetes mellitus	Definite T2 codes

medcode	readcode	readterm	category
34450	C10FK00	Hyperosmolar non-ketotic state in type 2 diabetes mellitus	Definite T2 codes
26054	C10FL00	Type 2 diabetes mellitus with persistent proteinuria	Definite T2 codes
60796	C10FL11	Type II diabetes mellitus with persistent proteinuria	Definite T2 codes
18390	C10FM00	Type 2 diabetes mellitus with persistent microalbuminuria	Definite T2 codes
85991	C10FM11	Type II diabetes mellitus with persistent microalbuminuria	Definite T2 codes
32627	C10FN00	Type 2 diabetes mellitus with ketoacidosis	Definite T2 codes
51756	C10FP00	Type 2 diabetes mellitus with ketoacidotic coma	Definite T2 codes
25591	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	Definite T2 codes
63690	C10FR00	Type 2 diabetes mellitus with gastroparesis	Definite T2 codes
95539	C10FS00	Maternally inherited diabetes mellitus	Genetic
51697	C10G.00	Secondary pancreatic diabetes mellitus	Secondary / Other types
96506	C10G000	Secondary pancreatic diabetes mellitus without complication	Secondary / Other types
61122	C10H.00	Diabetes mellitus induced by non-steroid drugs	Secondary / Other types
67212	C10H000	DM induced by non-steroid drugs without complication	Secondary / Other types
68517	C10J.00	Insulin autoimmune syndrome	Secondary / Other types
37957	C10K.00	Type A insulin resistance	Not diabetes
56885	C10K000	Type A insulin resistance without complication	Not diabetes
43857	C10M.00	Lipoatrophic diabetes mellitus	Secondary / Other types
22487	C10N.00	Secondary diabetes mellitus	Secondary / Other types
94383	C10N000	Secondary diabetes mellitus without complication	Secondary / Other types
93380	C10N100	Cystic fibrosis related diabetes mellitus	Secondary / Other types
33343	C10y.00	Diabetes mellitus with other specified manifestation	Vague codes
63371	C10y100	Diabetes mellitus, adult, + other specified manifestation	Probable T2 codes
10098	C10yy00	Other specified diabetes mellitus with other spec comps	Vague codes
70821	C10yz00	Diabetes mellitus NOS with other specified manifestation	Vague codes
45491	C10z.00	Diabetes mellitus with unspecified complication	Vague codes
68792	C10z000	Diabetes mellitus, juvenile type, + unspecified complication	Possible T1 codes

medcode	readcode	readterm	category
63762	C10z100	Diabetes mellitus, adult onset, + unspecified complication	Probable T2 codes
64283	C10zy00	Other specified diabetes mellitus with unspecified comps	Vague codes
64357	C10zz00	Diabetes mellitus NOS with unspecified complication	Vague codes
2472	C110.00	Hypoglycaemic coma	Possible T1 codes
53630	C110.11	Insulin coma	Possible T1 codes
61520	C110000	Iatrogenic hyperinsulinism	Secondary / Other types
72882	C110100	Self-induced hyperinsulinism	Probable T1 codes
51371	C110z00	Hypoglycaemic coma NOS	Possible T1 codes
1410	C112.00	Hypoglycaemia unspecified	Possible T2 codes
4563	C112000	Reactive hypoglycaemia NOS	Possible T2 codes
24405	C112100	Spontaneous hypoglycaemia NOS	Possible T2 codes
20368	C112z00	Hypoglycaemia unspecified NOS	Possible T2 codes
11359	L180.00	Diabetes mellitus during pregnancy/childbirth/puerperium	Probable Gestational diabetes
67635	L180000	Diabetes mellitus - unspec whether in pregnancy/puerperium	Probable Gestational diabetes
34639	L180100	Diabetes mellitus during pregnancy - baby delivered	Probable Gestational diabetes
49559	L180300	Diabetes mellitus during pregnancy - baby not yet delivered	Probable Gestational diabetes
96823	L180400	Diabetes mellitus in pueperium - baby previously delivered	Probable T1 codes
50960	L180500	Pre-existing diabetes mellitus, insulin-dependent	Probable T1 codes
50609	L180600	Pre-existing diabetes mellitus, non-insulin-dependent	Probable T2 codes
10278	L180800	Diabetes mellitus arising in pregnancy	Probable Gestational diabetes
8446	L180811	Gestational diabetes mellitus	Probable Gestational diabetes
2664	L180900	Gestational diabetes mellitus	Probable Gestational diabetes
55431	L180X00	Pre-existing diabetes mellitus, unspecified	Vague codes
64384	L180z00	Diabetes mellitus in pregnancy/childbirth/puerperium NOS	Probable Gestational diabetes

Table 4. Read codes for Diabetic Retinopathy diagnosis and screening

medcode	readcode	readterm	DR category
52041	2BBl.00	O/E - left eye stable treated prolif diabetic retinopathy	DR
52630	2BBo.00	O/E - sight threatening diabetic retinopathy	DR
19533	2BBY.00	O/E - referable retinopathy	DR
3837	F420400	Diabetic maculopathy	DR
47328	2BBk.00	O/E - right eye stable treated prolif diabetic retinopathy	DR
101881	2BBr.00	Impaired vision due to diabetic retinopathy	DR
3914	2BB9.00	O/E - retinal pigmentation	DR
9339	F421.00	Other background retinopathy	DR
10882	F421400	Exudative retinopathy	DR
48751	2BB3.00	O/E - retinal A-V nipping	DR
42762	C109612	Type 2 diabetes mellitus with retinopathy	DR
35659	2BB7.00	O/E - retinal vascular prolif.	DR
38161	C108711	Type I diabetes mellitus with retinopathy	DR
72424	7270B00	Vitrectomy using anterior approach	DR
9835	2BBL.00	O/E - diabetic maculopathy present both eyes	DR
39457	F421C00	Other intraretinal microvascular abnormality	DR
55026	7270B11	Anterior vitrectomy	DR
11053	F421800	Retinal microaneurysms NOS	DR
18387	C10E700	Type 1 diabetes mellitus with retinopathy	DR
4514	7270011	Anterior vitrectomy	DR
13102	2BBW.00	O/E - right eye diabetic maculopathy	DR
13108	2BBX.00	O/E - left eye diabetic maculopathy	DR
36119	F421111	Arteroscleroticretinopathy	DR
93875	C10E712	Insulin dependent diabetes mellitus with retinopathy	DR
8595	F42y600	Retinal exudate or deposit	DR
102242	2BBs.00	Retinal arteries silverwire	DR
17916	F422011	Retinopathy of prematurity	DR
22871	C10EP00	Type 1 diabetes mellitus with exudative maculopathy	DR
1411	3128100	Fundoscopy abnormal	DR
11626	F420z00	Diabetic retinopathy NOS	DR
34455	F421112	Atheroscleritic retinopathy	DR
66964	F426500	Pseudoretinitis pigmentosa	DR
2254	F424100	Central serous retinopathy	DR
36867	2BBa.00	O/E- non-referable retinopathy	DR
11129	2BBQ.00	O/E - left eye background diabetic retinopathy	DR
88368	7270411	Vitrectomy using pars plana approach	DR
6509	C108700	Insulin dependent diabetes mellitus with retinopathy	DR
45876	F421200	Renal retinopathy	DR
8742	2BB5.00	O/E - retinal haemorrhages	DR
17262	C109600	Non-insulin-dependent diabetes mellitus with retinopathy	DR
13107	2BBn.00	O/E - left eye clinically significant macular oedema	DR
104263	F425900	Maculopathy	DR

58604	C109611	Type II diabetes mellitus with retinopathy	DR
41049	C108712	Type 1 diabetes mellitus with retinopathy	DR
1323	F420.00	Diabetic retinopathy	DR
40982	F421z00	Other background retinopathy NOS	DR
50656	2BBc.00	O/E - No retinal laser photocoagulation scars	DR
36855	2BBG.00	Retinal abnormality - non-diabetes	DR
3822	2BB8.00	O/E - vitreous haemorrhages	DR
49655	C10F611	Type II diabetes mellitus with retinopathy	DR
11433	2BBP.00	O/E - right eye background diabetic retinopathy	DR
17293	727..00	Retina and other parts of eye operations	DR
69662	F421G00	Venostasis retinopathy	DR
7069	F420000	Background diabetic retinopathy	DR
1438	F421000	Unspecified background retinopathy	DR
97894	C10EP11	Type I diabetes mellitus with exudative maculopathy	DR
13106	2BB6.00	O/E - retinal exudates	DR
22967	2BBF.00	Retinal abnormality - diabetes related	DR
25888	2BBm.00	O/E - right eye clinically significant macular oedema	DR
25591	C10FQ00	Type 2 diabetes mellitus with exudative maculopathy	DR
18496	C10F600	Type 2 diabetes mellitus with retinopathy	DR
31829	F433100	Solar retinopathy	DR
41229	F421100	Atherosclerotic retinopathy	DR
19532	2BB4.00	O/E - retinal microaneurysms	DR
95343	C10E711	Type I diabetes mellitus with retinopathy	DR
11858	7270400	Pars plana vitrectomy	DR
6702	F421300	Hypertensive retinopathy	DR
45145	2BB2.00	O/E - retinal vessel narrowing	DR
2986	F420200	Preproliferative diabetic retinopathy	DR
13103	2BBS.00	O/E - left eye preproliferative diabetic retinopathy	DR
13099	2BBR.00	O/E - right eye preproliferative diabetic retinopathy	DR
10755	F420600	Non proliferative diabetic retinopathy	DR
65463	F420800	High risk non proliferative diabetic retinopathy	DR
27022	5B42.00	Laser therapy - retinal lesion	Severe DR
86068	7272800	Panretinal laser photocoagulation to lesion of retina	Severe DR
13097	2BBT.00	O/E - right eye proliferative diabetic retinopathy	Severe DR
100979	7272900	Focal laser photocoagulation of retina	Severe DR
11874	F422100	Proliferative retinopathy due to sickle cell disease	Severe DR
96926	FyuF700	[X]Other proliferative retinopathy	Severe DR
6836	7271100	Laser photocoagulation of retina for detachment	Severe DR
11912	5B4..11	Retinal laser therapy	Severe DR
30477	F420700	High risk proliferative diabetic retinopathy	Severe DR
9318	7272300	Laser destruction of lesion of retina	Severe DR
36035	F422y00	Other specified other proliferative retinopathy	Severe DR
18775	2BBO.00	O/E - Laser photocoagulation scars	Severe DR
10099	F420300	Advanced diabetic maculopathy	Severe DR
46068	7272500	Panretinal laser photocoagulation to lesion of retina	Severe DR

		NEC	
13101	2BBV.00	O/E - left eye proliferative diabetic retinopathy	Severe DR
38096	F422z00	Proliferative retinopathy NOS	Severe DR
3286	F420100	Proliferative diabetic retinopathy	Severe DR
7890	F422.00	Other proliferative retinopathy	Severe DR
881	3128	Fundoscopy	Screening
19535	2BBA.00	Examination of retina	Screening
10701	8HBD.00	Retinopathy follow up	Screening
25116	2BBZ.00	O/E - retinal inspection NOS	Screening
92317	2BBf.00	O/E - left retina partially assessable	Screening
18311	68A7.00	Diabetic retinopathy screening	Screening
106269	9m0..00	Diabetic retinopathy screening administrative status	Screening
33681	2BB..00	O/E - retinal inspection	Screening
17871	312E.00	Direct fundoscopy following mydriatic	Screening
17198	2BB..11	O/E - retina	Screening
19531	3128.11	Retinoscopy	Screening
13196	66AD.00	Fundoscopy - diabetic check	Screening
36619	312F.00	Camera fundoscopy	Screening
19534	3128300	Camera fundoscopy	Screening
11891	68A8.00	Digital retinal screening	Screening
9974	9N1v.00	Seen in diabetic eye clinic	Screening
70163	2BBe.00	O/E - right retina partially assessable	Screening
8140	9N2V.00	Seen by optometrist	Screening
66273	2BBg.00	O/E - right retina fully assessable	Screening
61021	68AB.00	Diabetic digital retinopathy screening offered	Screening
13105	58C1.00	Retinal photography	Screening
13098	3128Z00	Fundoscopy NOS	Screening
30111	3129	Eye fundus photography	Screening
20991	312A.00	Slit lamp examination	Screening
12528	9NNC.00	Under care of retinal screener	Screening
18662	8HBH.00	Diabetic retinopathy 6 month review	Screening
12636	9N2f.00	Seen by retinal screener	Screening
9934	9N2e.00	Seen by ophthalmologist	Screening
11018	8HBG.00	Diabetic retinopathy 12 month review	Screening
22966	3128400	Indirect fundoscopy following mydriatic	Screening
6108	9N2U.00	Seen by optician	Screening
64070	312G.00	Indirect fundoscopy following mydriatic	Screening
95916	2BBh.00	O/E - left retina fully assessable	Screening

Table 5.Read codes for Ethnicity (Table reproduced from http://www.clininf.eu/ethnicity.html)

Grouping of the 9S and 9i ethnic codes to the '16+1' format and the five category classifications			
Five category	**16 category framework**	**9i… Ethnic category hierarchy**	**9S.. Ethnic group hierarchy**
1. White	1. British or Mixed British	**9i0** British or mixed British	**9S1** White, **9S10** White British, **9S14** Other white British ethnic grp
	2. Irish	**9i1** Irish	**9S11** White Irish, **9SA9** Irish NMO, **9SI** Irish traveller
	3. Other White	**9i2** Other White	**9S12** Other white ethnic group
		9i20 English	
		9i21 Scottish	**9S13** White Scottish
		9i22 Welsh, **9i26** Cypriot part unsp, **9i27** Greek, **9i28** Greek Cypriot, **9i29** Turkish, **9i2A** Turkish Cypriot, **9i2B** Italian, **9i2C** Irish Traveller, **9i2D** Traveller, **9i2E** Gypsy/Romany, **9i2F** Polish, **9i2H**Commonwealth of (Russian), **9i2J** Kosovan, **9i2K** Albanian Serbian, **9i2P** Oth repub Yugoslav, **9i2R** Oth White/unsp/Mix Eur,**9i2S** Oth mixed White, **9i2T** Other White or White unspecified.	
2. Mixed	4. White + Black Caribbean	**9i3** White & Black Caribbean	**9SB5** Black Caribbean and White
	5. White + Black African	**9i4** White and Black African	**9SB6** Black African and White
	6. White + Asian	**9i5** White & Asian	**9SB2** Other ethnic, Asian/White orig
	7. Other mixed	**9i6** Other Mixed	**9SB** Other ethnic, mixed origin , **9SB3** Other ethnic, mixed white orig, **9SB4** Other ethnic, other mixed

			orig,**9S52** Other Black - Black/Asian orig.
		9i60 Black & Asian, **9i61** Black & Chinese	
		9i62 Black and White	**9SB1** Other ethnic, Black/White orig, **9S51** Other Black – Black/White orig
		9i63 Chinese & White, **9i64** Asian & Chinese	
3. Asian or Asian British	8. Indian or British Indian	**9i7** Indian/British Indians	**9S6** Indian
	9. Pakistani or British Pakistani	**9i8** Pakistani/Brit Pakists	**9S7** Pakistani
	10. Bangladeshi or British Bangladeshi	**9i9** Bangladeshi/Brit Bangl	**9S8** Bangladeshi
	11. Other Asian	**9iA** Other Asian	**9SH** Other Asian ethnic group, **9SA8** Oth er Asian NMO, **9SA7** Indi an sub-continent NMO
		9iA3 East African Asian	**9SA6** E Afric Asian/Indo-Carib NMO
		9iA4 Sri Lankan, **9iA5** Tamil, **9iA6** Sinhalese, **9iA7** Carib Asian,**9iA8** Briti Asian, **9iA9** Mixed Asian	
4. Other Black	12. Caribbean	**9iB** Caribbean	**9S2** Black Caribbean
	13. African	**9iC** African	**9S3** Black African, **9S44**Bla ck - other African country,**9SA5** Ot her African countries NMO
	14 Other Black	**9iD** Other Black	**9S4** Black, other, non-mixed origin, **9S42** Black Caribbean/W.I./ Guyana, **9S43** Black N African/Arab/Ira

			nian, **9S45** Black E Afric Asia/Indo-Caribb, **9SG** Other black ethnic group, **9S47** Bla ck - other Asian, **9S48** Blac k Black - other, **9S5** Black - other, mixed, **9SA3** Car ibbean I./W.I./Guyana NMO
		9iD0 Somali, **9iD1** Nigerian	
		9iD2 Black British	**9S41** Black British
5. Other ethnic groups	15. Chinese	**9iE** Chinese	**9S9** Chinese
	16. Other	**9iF** Other	**9SJ** Other ethnic group, **9SA**Othe r ethnic non-mixed NMO, **9SA2** Brit. ethnic minor. unsp NMO, **9SAA**Gre ek/Greek Cypriot NMO,**9SAB** Turk ish/Turkish Cypriot NMO **9SAC** Other European NMO,**9SAD** Oth er ethnic NEC NMO
		9iF0 Vietnamese	**9SC** Vietnamese
		9iF1 Japanese, **9iF2** Filipino, **9iF3** Malaysian, **9iF9** A rab	
		9iFA North African	**9SA4** N African Arab/Iranian NMO
		9iFB ME ex Isr/Iran/Arab, **9iFD** Iranian, **9iFE** Kurdish, **9iFG** Lati n American, **9iFH** South/Central American, **9iFJ** Multi-ethnic islands: Mauritian or Seychellois or Maldivian or St Helena, **9iFK** Any other - ethn categ	

6. Not stated	17. (16+1) Not stated	**9iG** Ethn cat not stated	**9S** Ethnic groups census,**9SD** Ethnic group - patient refused, **9SE** Ethnic group not recorded, **9SZ** Ethnic groups census NOS

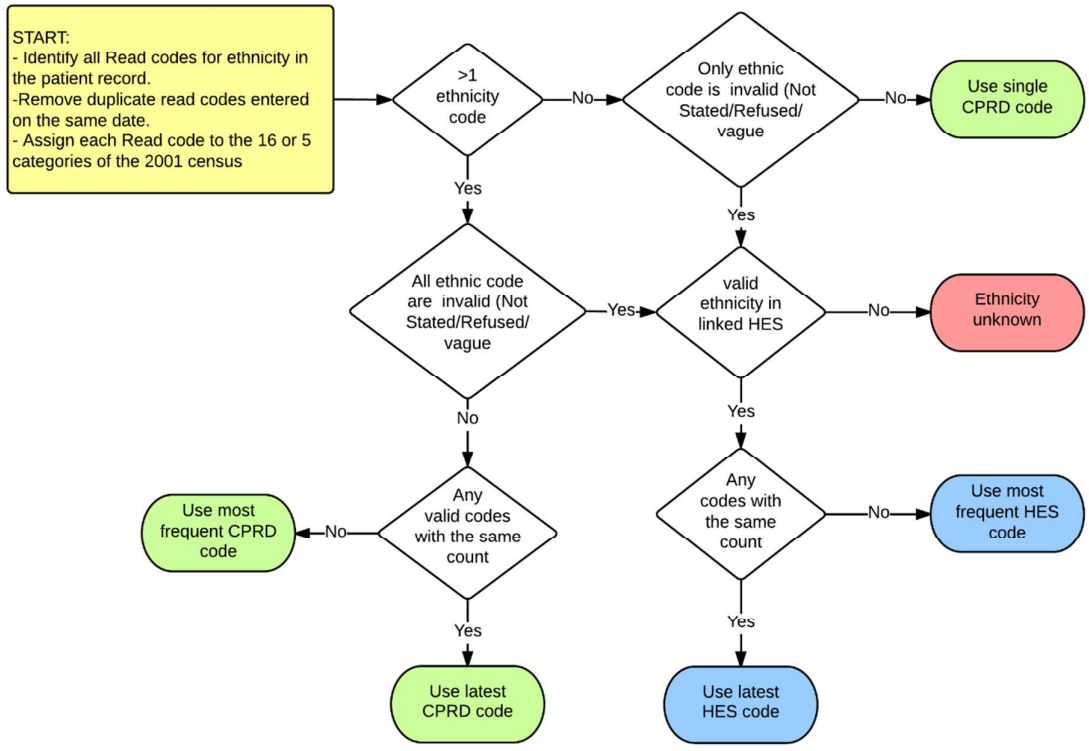


Figure 5. Classification of Ethnicity in the CPRD (From Mathur et al. Journal of Public Health, 2013)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	page
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3
Objectives	3	State specific objectives, including any prespecified hypotheses	3
Methods			
Study design	4	Present key elements of study design early in the paper	3
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	3
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	4-5
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	4-5
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	*4-5*
Bias	9	Describe any efforts to address potential sources of bias	5
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	5
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	5
		(*b*) Describe any methods used to examine subgroups and interactions	5
		(*c*) Explain how missing data were addressed	5
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	5
		(*e*) Describe any sensitivity analyses	

Results			page
Participants6	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	6
		(b) Give reasons for non-participation at each stage	6
		(c) Consider use of a flow diagram	n/a
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table1,2
		(b) Indicate number of participants with missing data for each variable of interest	Table1,2
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Fig 2. Fig 3
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	
		Cross-sectional study—Report numbers of outcome events or summary measures	
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2, Fig 2, Fig 3
		(*b*) Report category boundaries when continuous variables were categorized	7
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	11
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	7-8
Discussion			
Key results	18	Summarise key results with reference to study objectives	9
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	9-10
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	12

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at

http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.