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Ethnic differences in CKD progression among people with type 2 diabetes and rapid eGFR decline: A secondary data analysis

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Abstract

Background People with type 2 diabetes mellitus (T2DM) and chronic kidney disease (CKD) exhibit diverse patterns of kidney function decline. However, there is limited evidence on the impact of ethnicity and diabetic retinopathy on the rate of estimated glomerular filtration rate (eGFR) decline and the progression of CKD.

Methods We analysed 14,489 people with T2DM and baseline eGFR ≥ 45 ml/min/1.73 m² attending outpatient clinics at south London hospitals from 2004 to 2018. The ethnically diverse cohort included 45% White, 37.8% Black, 9.1% Asian, 2.7% Mixed, and 5.2% Other ethnicities. The latent class analysis approach, Group Based Trajectory Model (GBTM) was used to identify eGFR trajectories, and multinomial logistic models assessed CKD progression to stages 4 and 5 among those with faster eGFR decline (≥ 1.92 ml/min/year).

Results Four eGFR trajectories were identified from each ethnic group. Those with the fastest decline ($n=2,531$) were older, had higher urine albumin-to-creatinine ratio (ACR), and lower baseline eGFR. Of this group, 368 (14.53%) progressed to stage 5 CKD. Relative risk ratios (95% CI) of progression compared to White individuals were 1.64 (1.22–2.21) for Black, 2.39 (1.57–3.64) for Asian, 1.97 (1.11–3.50) for Mixed, and 3.72 (2.11–6.57) for other ethnicities. Diabetic retinopathy at baseline was present in 17.58% of this group, and linked to faster CKD progression, particularly among Black individuals.

Conclusion Non-White ethnicities experience faster CKD progression, with diabetic retinopathy contributing significantly, especially in Black individuals. These findings highlight the need for tailored strategies of prevention and intervention to address disparities in CKD outcomes.

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Key messages

- Limited data exists on Estimated glomerular filtration rate (eGFR) decline patterns in ethnically diverse cohorts with T2DM.
- In our study of over 14,000 people with T2DM, we identified four eGFR trajectories. The fastest-progressing group (17% of the cohort) showed higher Albumin Creatinine Ratio (ACR), elevated systolic blood pressure, lower baseline eGFR, more males, and older age.
- Diabetic retinopathy was linked to chronic kidney disease (CKD) progression, with advanced retinopathy stages (R2M0, R3M0, R3M1) most prevalent among Black and Asian groups, who experienced faster eGFR decline.

Keywords Type 2 diabetes, Estimated glomerular filtration rate (eGFR), Chronic kidney disease (CKD), Diabetes retinopathy, Latent class modelling, Group based trajectory models (GBTMs)

Introduction

Type 2 Diabetes Mellitus (T2DM) is linked to a wide range of complications, including microvascular and macrovascular damage. Among these, chronic kidney disease (CKD) is a prevalent and serious condition, with significant variability in progression patterns across individuals. Understanding the factors that drive these trajectories is essential for optimizing patient outcomes.

Ethnicity has often been identified as a significant determinant of T2DM complications [1] with certain ethnic groups, including African Americans and South Asians having higher prevalence of complications in comparison to White [2]. Variations in study methods, regions, diabetes duration, and the aggregation or omission of ethnic populations may have skewed findings. As a result, the reported outcomes might not accurately capture the true extent of ethnic differences.

In our previous study, we did a systematic review and meta-analysis of 27 studies found that overall Diabetic Nephropathy (DN) prevalence of 18%, with no significant differences across ethnic groups, while Diabetic Retinopathy (DR) prevalence was higher among Afro-Caribbeans (28%), and Asians (25%) compared to Whites (19%) [3].

People with T2DM who develop chronic kidney disease (CKD) exhibit heterogeneous patterns of progression to advanced stages of CKD. Recent studies indicate that 70–80% of people with T2DM do not experience a significant decline in eGFR (>1 ml/min/1.73 m² per year) over time, classifying them as non-progressors [4]. However, variations have been observed across ethnically diverse cohorts in the UK. For instance, [2] a study by Mathur et al. (2022) in East London reported that South Asian and Black populations experienced significantly faster eGFR decline compared to White individuals, with an annual loss of approximately 1.52 ml/min/1.73 m² in Black individuals and 1.38 ml/min/1.73 m² in South Asians, compared to 0.98 ml/min/1.73 m² in White individuals. These differences highlight disparities in kidney function decline across ethnic groups [5].

Several studies have explored the progression of kidney function decline in people with type 2 diabetes mellitus (T2DM), revealing both common patterns and significant variability influenced by demographic, clinical, and socioeconomic factors [6]. Afkarian et al. (2014) demonstrated that most individuals with T2DM maintain stable kidney function, with only a minority experiencing rapid decline in estimated glomerular filtration rate (eGFR). However, other studies, such as Mathur et al. (2022), highlight ethnic disparities in eGFR trajectories, reporting faster declines among South Asian and Black populations compared to White individuals [7]. Similarly, Raymond et al. (2011) observed a higher prevalence of proteinuria in South Asian individuals with T2DM, which is a strong predictor of CKD progression [8].

Tarver-Carr et al. (2002) and Ward (2005) further emphasized the disproportionate burden of CKD risk factors among African-Caribbean and South Asian populations, including higher rates of hypertension, metabolic syndrome, and proteinuria [9, 10]. Despite these findings, the literature remains fragmented, with variations in methodologies, sample populations, and definitions of eGFR decline complicating cross-study comparisons. Additionally, many studies aggregate ethnic groups or exclude minority populations, limiting the generalizability of their findings.

This diversity of evidence highlights the need for studies that account for ethnic differences while addressing gaps in understanding the relationship between diabetic retinopathy, proteinuria, and CKD progression. Our study aims to address these gaps by examining eGFR trajectories in a large, ethnically diverse cohort, providing a more comprehensive understanding of the factors driving CKD progression in people with T2DM [9, 11]. Additionally, we aimed to explore the characteristics of subgroups at elevated risk of eGFR progression, from each ethnicity and to explore the role of diabetic retinopathy and other traditional risk factors for CKD, in the rates of progression to CKD stages 4 and 5.

Materials and methods

Study population and setting

This study included 14,489 individuals with type 2 diabetes, drawn from routine secondary care outpatient clinics in South London hospitals (Guy's, St. Thomas, and King's College Hospitals) between 2004 and 2018 (Median follow up was 4 years). Inclusion criteria required a baseline $\text{eGFR} \geq 45$ ml/min/1.73 m², age ≥ 18 years old, ensuring that participants started with preserved renal function. Participants were included if they had at least two eGFR measurements per year over a minimum of two years, ensuring sufficient data density for reliable trajectory modelling. All eligible patients were consecutively included from the database based on inclusion and exclusion criteria, ensuring a representative cohort.

The cohort was ethnically diverse, comprising 45% White, 37.8% Black, 9.1% Asian, 2.7% of Mixed ethnicity, and 5.2% Other ethnicities. The 'Other' category likely includes individuals of Middle Eastern, Arab, Latin American, and East or Southeast Asian backgrounds, based on local demographics. Ethnicity was self-reported by participants using predefined NHS categories and recorded in electronic health records.

Participants were excluded from the study if they met any of the following criteria: a baseline estimated glomerular filtration rate (eGFR) below 45 ml/min/1.73 m², age under 18 years, documented non-diabetic kidney disease, fewer than two eGFR measurements per year, missing baseline data within two years of their initial creatinine measurement, or pregnancy, due to its unique effects on eGFR.

Data were extracted from Electronic Health Records (EHRs) and encompassed both demographic and clinical variables. "All EHR data underwent systematic cleaning, including plausibility checks, removal of outliers based on clinical thresholds, and validation to ensure data integrity." Standardized processes across all participating hospitals ensured comprehensive data collection, spanning baseline characteristics and regular follow-up measurements for reliable and continuous monitoring. Key health indicators included demographics (age, gender, ethnicity, and diabetes diagnosis date), anthropometric data (weight and Body Mass Index), blood pressure (systolic and diastolic measurements), and laboratory measures. These laboratory assessments included eGFR (calculated using the CKD-EPI 2019 equation- which is a race free equation) [12], urine albumin-to-creatinine ratio (ACR), HbA1c, and lipid profiles (LDL, HDL, total cholesterol, and triglycerides).

eGFR values were used to define chronic kidney disease (CKD) stages per KDIGO 2012 guidelines [13]: G1 (>90 ml/min/1.73 m²), G2 (60–89), G3 (30–59), G4 (15–29), and G5 (≤ 15). G4 and G5 is referred to CKD stages 4 and 5. Albuminuria was assessed using spot urine

ACR. KDIGO categories (A1–A3) were applied based on ACR thresholds, without conversion to 24-hour albumin excretion [8].

Diabetic retinopathy and maculopathy severity were assessed using retinal digital imaging, following UK National Diabetic Eye Screening guidelines [14]. Retinopathy stages ranged from R0M0 (no retinopathy) to R3M1 (severe proliferative retinopathy with maculopathy). For analysis, stages R2M0 with R2M1 as well as R3M0 with R3M1 were combined due to sample size considerations and to simplify the findings. In contrast, stages R1M0 and R1M1 were retained as separate categories.

The follow-up duration was between 2004–2018. Last follow up was defined as the date of last available creatinine measurement and estimated glomerular filtration rate (eGFR) or date of death.

Statistical analysis

Trajectory analysis using group-based trajectory modelling (GBTM)

We applied the Group-Based Trajectory Modelling (GBTM) approach to investigate eGFR progression patterns across the full sample, encompassing the main ethnic groups—White, Black, Asian, Mixed ethnicity, and Others [15]. This analysis aimed to identify distinct trajectories within the population while accounting for ethnic variations. The model was conducted separately for each individual ethnicity across the entire cohort. This approach ensures that distinct eGFR progression patterns were identified within each ethnic group, and this methodology is consistently described throughout the paper, including in the text, tables, and figures. Stata 18 was used for the analysis [16]. GBTM is particularly suited for heterogeneous populations, enabling robust subgroup identification without assuming a homogeneous rate of decline across the cohort [15].

Trajectory group assignments

Participants were assigned to trajectory groups using maximum likelihood estimation. This approach utilises the longitudinal sequence of measurements on individual providing high classification accuracy.

Model selection and validation

Various models were tested with differing trajectory numbers and shapes (linear and quadratic), using the lowest Bayesian Information Criterion (BIC) and a low Akaike Information Criterion (AIC) to identify optimal model fit. High entropy values (≥ 0.85) validated further group separability, and group size, with each trajectory group representing at least 5% of the cohort to maintain statistical relevance, has been observed [17]. Characteristics of the defined trajectory groups at baseline were compared using one-way ANOVA for continuous, normally

distributed variables, and the Kruskal-Wallis test for non-normally distributed data, such as ACR. Categorical variables were analysed with chi-square tests. Multinomial logistic regression models were applied to the trajectories of fastest decline from each ethnic group to estimate the Relative Risk Ratio (RRR) of the outcomes, 1] CKD progression to stages 4 and 5 using earlier CKD stages as reference, and 2] baseline retinopathy stages R1M0, R1M1, RM2(R2M0 + R2M1, and RM3(R3M0 + R3M1) using R0M0 as reference. RRRs were calculated to compare the relative risks for each ethnic group with that for the White. The models adjusted for baseline health indicators, including age, gender, HbA1c, and ACR. Data available was sufficient for the use of GBTMs by ethnic groups (> 500 participants) [3]. The only exception was the mixed ethnicity group, which had a sample size of $n=387$. This size was considered adequate given the proportion of this group in the overall population. Although estimates will be cautiously interpreted but models for this group were stable and have achieved good fits.

Results

The clinical database included 14,489 patients. Table 1 shows the Summary of the demographic and clinical Characteristics of the whole study population at baseline. The cohort had an average diabetes duration of 6.5 years ($SD=6.95$) The mean age was 54.9 years ($SD=13.64$) and 50.31 % were females. Renal function, as measured by eGFR, average was 74.95 ml/min/1.73 m² ($SD=20.24$). Glycemic control varied widely, with an average HbA1c of 64.5 ($SD=22.46$) mmol/mol, median of 58.5 (Interquartile Range(IQR) 48.5–76), and albumin-creatinine ratio (ACR) average was 38.83($SD=39.24$) mg/mmol with median of 39 (IQR 11–45). Black and Other groups had higher ACR (65.2mg/g and 59.8mg/g) and HbA1c (8.4% and 8.3%) compared to Whites (ACR 43.7mg/g, HbA1c

Table 1 Summary of clinical baseline characteristics

Variable	Mean	Std. dev.	Min	Max
Diabetes Duration (years)	6.54	6.95	0.50	69.00
Age (years)	54.97	13.64	19.00	98.00
eGFR (ml/min/1.73 m ²)	74.95	20.24	45.00	150.20
HbA1c (mmol/mol)	64.52	22.46	21.31	192.90
ACR (mg/mmol)	38.83	39.24	0.10	200.00
Cholesterol (mmol/L)	4.57	1.13	1.20	10.00
Triglycerides (mmol/L)	1.84	1.21	0.20	10.00
DIASTOLIC BP (mmHg)	77.40	10.24	17.00	129.00
SYSTOLIC BP (mmHg)	133.21	18.16	71.00	230.00
BMI (kg/m ²)	31.77	7.35	14.53	94.20
Weight (kg)	88.97	22.55	1.00	272.00
HDL (mmol/L)	1.23	0.36	0.20	4.56
LDL (mmol/L)	2.54	0.95	0.05	10.80

Note: ACR: Albumin Creatinine Ratio; eGFR: estimated Glomerular Filtration Rate; SBP: Systolic Blood Pressure

Table 2 The distribution of people with Type 2 diabetes mellitus (T2DM) across four trajectories of eGFR over time (2004–2018)

Ethnicity	Traj.1	Traj.2	Traj.3	Traj.4	Total
White	1,279	2,330	1,977	995	6,581
%	19.43	35.4	30.04	15.12	100
Black	820	2,062	1,564	1,019	5,465
%	15.00	37.73	28.62	18.65	100
Asian	239	402	411	265	1,317
%	18.15	30.52	31.21	20.12	100
Mixed	78	109	150	43	380
%	20.53	28.68	39.47	11.32	100
Others	115	197	271	163	746
%	15.42	26.41	36.33	21.85	100
Total	2531	5100	4373	2485	14489
%	17.47	35.2	30.18	17.15	100

8.1%), and were younger on average (62.1 and 63.3 years vs. 66.2 years) (Supplementary Table S6). For the entire cohort, four eGFR trajectories were identified, highlighting differences in patterns of kidney function decline Using group-based trajectory modelling, four distinct eGFR trajectories were identified for the overall population: Trajectory 1: Low eGFR/Steep decline (slope: -1.86 mL/min/1.73 m² per year; SE: 0.09), Trajectory 2: low GFR /Stable (slope: $+1.77$; SE: 0.08; quadratic term: -0.14), Trajectory 3: Moderate eGFR/Stable (slope: $+3.50$; SE: 0.08; quadratic: -0.22), and Trajectory 4: High eGFR/Stable (slope: $+3.49$; SE: 0.12; quadratic: -0.20).

The distribution of people across four eGFR trajectories differs by ethnic group (Table 2) (Fig. 1). Among the White participants ($n=6,581$), the largest proportion (35.2%) fell into trajectory 2, followed by trajectory 3 (30.04 %), 19.43% in trajectories 1, while 15.12 % were assigned to trajectory 4. Black participants ($n=5,465$) similarly had a large share in trajectory 2 (37.7%) and trajectory 3 (28.62%), with smaller proportions in trajectory 1 (15%) and trajectory 4 (18.65%). In the Asian group ($n=1,317$), the highest proportion (31.21%) was in trajectory 3, followed closely by trajectory 2 (30.52%) and trajectory 4 (20.12%). Mixed ethnicity participants ($n=380$) had the largest percentage in trajectory 3 (38.73%), and those in the “Other ethnicities” ($n=754$), also have a majority in trajectory 3 (39.47%) followed by trajectory 4 (11.32%). Overall, trajectory 2 had the highest representation across all groups (35.2%), indicating some commonality in eGFR patterns despite ethnic differences.

Trajectory 1 has mean eGFR of 56.32 ml/min/1.73 m², and the steepest decline. Trajectory 2 has low eGFR and stable (mean 64.12), Trajectory 3 remains stable (mean 81.47), and Trajectory 4 shows normal kidney function (mean 106.45) throughout the study follow up time.

Focusing on trajectory I slopes, for each ethnicity group, it showed a steady linear eGFR progression where eGFR declined by, -1.92 (Standard Error SE:0.03),

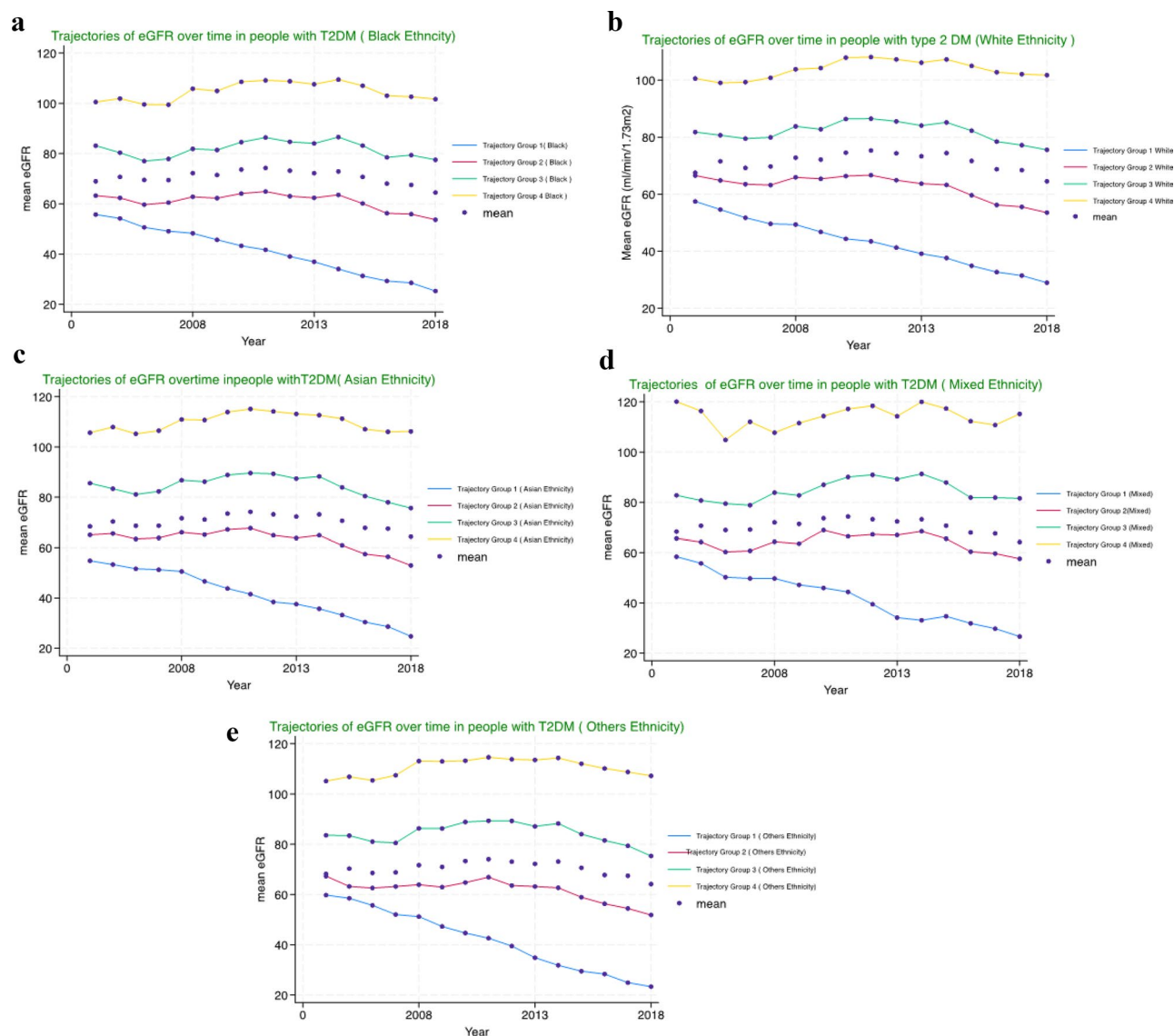


Fig. 1 Trajectories of eGFR over time in people with type 2 DM (Ethnicity-Specific). **(a)** Trajectories of eGFR in White individuals with T2DM Traj 1: mean eGFR 56.67, Traj 2: mean eGFR 65.90, Traj 3: mean eGFR 81.83, Traj 4: mean eGFR 107.04 (ml/min/1.73 m²). **(b)** Trajectories of eGFR in Black individuals with T2DM. Traj 1: mean eGFR 55.85, Traj 2: mean eGFR 62.02, Traj 3: mean eGFR 79.06, Traj 4: mean eGFR 104.67 (ml/min/1.73 m²). **(c)** Trajectories of eGFR in individuals of Asian ethnicities with T2DM. Traj 1: mean eGFR 56.33, Traj 2: mean eGFR 64.91, Traj 3: mean eGFR 83.16, Traj 4: mean eGFR 110.40 (ml/min/1.73 m²). **(d)** Trajectories of eGFR in individuals of Mixed ethnicity with T2DM. Traj 1: mean eGFR 57.44, Traj 2: mean eGFR 64.72, Traj 3: mean eGFR 83.34, Traj 4: mean eGFR 112.94 (ml/min/1.73 m²). **(e)** Trajectories of eGFR in individuals of Other ethnicities with T2DM. Traj 1: mean eGFR 58.52, Traj 2: mean eGFR 66.16, Traj 3: mean eGFR 83.84, Traj 4: mean eGFR 111.56 (ml/min/1.73 m²)

Table 3 Trajectory 1, estimates of slopes of eGFR by ethnicity, based on group based trajectory models (GBTM)

Group Ethnicity	Parameter Trajectory 1 Slope	Estimate	Standard Error	T for H0: Parameter=0	Prob>T
White	Linear	-1.92	0.03	-56.94	0.00
Black	Linear	-2.17	0.04	-48.40	0.00
Asian	Linear	-2.20	0.08	-27.84	0.00
Mixed	Linear	-2.19	0.12	-17.94	0.00
Others	Linear	-2.78	0.11	-25.94	0.00

- 2.17 (0.04), -2.20 (0.08), -2.19 (0.12), - 2.78(0.11) ml/min/1.73 m², for the five ethnic groups, respectively. (Table 3). The other three trajectories have shown similar shapes of growth across all ethnicities that are mostly stable in eGFR progression over time. The models that fit best were of quadratic type showing a steady but modest increase in eGFR halfway through the follow-up time, followed by a steady but modest decrease. The average eGFR for Trajectory II (Stable/Low) was between 56 ml/min/1.73 m² for those of mixed ethnicity to 60 ml/min/1.73 m² for the White at baseline. Trajectories III

(Moderate eGFR) and IV (High eGFR) have an average $\text{eGFR} \geq 70 \text{ ml/min/1.73 m}^2$ and $\geq 90 \text{ ml/min/1.73 m}^2$, respectively for all ethnic groups.

We examined the primary features of trajectory 1, that has shown the fastest decline in eGFR across the 5 ethnic groups. These include traditional risk factors, retinopathy stages at baseline, and the risk of reaching chronic kidney disease (CKD) stages 4 or 5 at some point during follow up.

Age was similar across ethnic groups for this fastest eGFR decline's trajectory, with the White being slightly older, with mean age (SD) of 66.48(10.03) followed by others, 64.35(10.82), Asian, 64.34 (9.96), Black, 63.06(11.38) and Mixed 62.15(11.46) (Table 4).

Among this group of 2,531 participants (those with the most progressive decline in eGFR across all five ethnic groups), 944 (37.3%) progressed to stage 4 CKD, and 368 (14.5%) advanced to stage 5 CKD during the follow-up period (Supplementary Table S1 and S3).

Analyzing the clinical features of this high-risk group across ethnicities—adjusted for age, gender, blood pressure, albuminuria, HbA1c, diabetes duration, and baseline eGFR—showed no differences in the risk of reaching stage 4 CKD across ethnic groups, except for individuals categorized as “Others,” who had a significantly higher

risk compared to White participants, with a relative risk ratio (RRR) of 2.23(95% CI: 1.39–3.35).

Reaching stage 5 CKD, on the other hand differed significantly by ethnicity, after adjusting for the above traditional risk factors; the RRRs and (95% CI), were: 1.64 (1.22–2.21); 2.39 (1.57–3.64); 1.97 (2.11–6.57), and 3.72 (2.11–6.57) for the Black, Asian, Mixed, and Others respectively, compared to the White. (Table 5A).

Retinopathy stages at baseline vary across ethnic groups; Others ethnicity individuals exhibited the highest prevalence of R1M1 stage (14.78%) followed by Black (14.51%) and Asian (9.62%), while the White had a lower prevalence at (7.35%). For R2M0 stage, Mixed individuals had the highest prevalence at (5.13%), followed by Asian individuals (3.77%), and Others (1.74%).

White individuals had the lowest prevalence (1.72%) of severe eye disease (R2M1 stage), while Mixed ethnicity had the highest (8.97%), followed by “other ethnicities” (7.83%) and Asian (6.69%) (Supplementary Table S2). Using multinomial logistic regression with R0M0 as reference, the risk of severe eye disease (yes vs. no) was significantly higher for Asian and “other ethnicities” with RRRs of 3.49 (95% CI: 1.59–7.62) and 2.36 (95% CI: 0.68–8.22), respectively, compared to White individuals. Similarly, individuals of Mixed, Asian, and “other ethnicities”, had higher risks of being in moderate/severe stages

Table 4 Baseline clinical characteristics of participant in trajectory group 1 by ethnicity

Ethnicity	White	Black	Asian	Mixed	Others
Age					
mean (years)	66.48	63.06	64.34	62.15	64.21
SD	10.03	11.38	9.96	11.46	10.82
ACR					
mean (mg/mmol)	47.37	48.24	52.52	50.56	59.48
SD	50.1	49.41	52.5	46.96	58.2
median (IQR)*	40(17–51)	42(25–61)	42(28–56)	43.5(16.5–51.5)	42.5(37–60)
eGFR					
mean(ml/min/1.73 m ²)	56.67	55.85	56.33	57.44	58.52
SD	10.29	10.24	11.48	9.37	10.61
BMI					
mean (kg/m ²)	31.51	30.24	27.63	30.95	29.01
SD	6.56	6.08	4.65	8.55	5.65
SBP					
mean (mmHg)	137.16	141.55	136.54	140.74	136.93
SD	19.81	20.71	20.36	20.00	19.43
DBP					
mean (mmHg)	75.09	77.87	74.22	77.41	75.17
SD	10.50	10.78	10.50	10.82	10.13
HbA1C					
mean (mmol/mol)	62.83	68.76	65.55	69.22	60.70
SD	20.22	23.96	21.10	24.79	17.88
median (IQR)*	59.6 (49.7–73.8)	66.12 (53–89.1)	66 (53–80.33)	64 (52–81)	56 (46.4–72.8)
Total (n)	1279	820	239	78	115
%	50.52	32.40	9.44	3.08	4.54

Note IQR: Interquartile Range; ACR: Albumin Creatinine Ratio; eGFR: estimated Glomerular Filtration Rate; SBP: Systolic Blood Pressure

Table 5A CKD progression to stage 4 and 5 by ethnicity (using multinomial logistic regression)

Stage (outcome)	RRR unadjusted*	RRR adjusted**	95% CI*		P-value°
Stage I-III (Base Outcome)					
Stage IV					
Ethnicity (Ref. White)					
Black	1.07	0.95	0.77	1.16	0.592
Asian	1.27	1.20	0.87	1.65	0.260
Mixed	1.40	1.23	0.73	2.08	0.444
Others	2.23	2.16	1.39	3.35	0.001
Stage V					
Ethnicity (Ref. White)					
Black	2.21	1.47	1.10	1.97	0.009
Asian	2.64	2.26	1.49	3.43	≤0.001
Mixed	2.76	1.76	0.89	3.47	0.104
Others	4.09	3.75	2.14	6.56	≤0.001

* Unadjusted Relative Risk Ratio, ** Adjusted Relative Risk Ratio (adjusted for Risk factors: Age, sex, Baseline eGFR, HbA1C, BP, Chol.), ° p-value of the adjusted model, • Confident interval or adjusted model

Table 5B Retinopathy stages at baseline by ethnicity (Using Multinomial Logistic Regression)

Retinopathy stage (RM)	RRR-unadjusted*	RRR-adjusted**	95% CI*		P-value [°]
R0M0 (Base Outcome)					
R1M0					
Ethnicity (Ref. White)					
Black	1.14	1.08	0.87	1.33	0.510
Asian	1.60	1.48	1.07	2.05	0.019
Mixed	0.92	0.86	0.47	1.59	0.633
Others	1.76	1.86	1.18	2.93	0.008
R1M1					
Ethnicity (Ref. White)					
Black	2.40	1.95	1.42	2.68	≤0.001
Asian	1.79	1.43	0.85	2.41	0.172
Mixed	3.11	2.40	1.20	4.81	0.013
Others	2.99	3.04	1.63	5.67	≤0.001
RM2 (R2M0 + R2M1)					
Ethnicity (Ref. White)					
Black	1.76	1.25	0.84	1.84	0.267
Asian	2.61	2.18	1.28	3.70	0.004
Mixed	3.28	2.23	1.02	4.86	0.045
Others	2.59	2.66	1.27	5.58	0.009
RM3(R3M0 + R3M1)					
Ethnicity (Ref. White)					
Black	2.61	1.97	1.08	0.027	0.027
Asian	3.49	2.80	1.26	0.011	0.011
Mixed	1.99	1.47	0.32	0.618	0.618
Others	2.36	2.21	0.63	0.218	0.218

* Unadjusted Relative Risk ratio, ** Adjusted Relative Risk Ratio (adjusted for Risk factors: Age, sex, Baseline eGFR, HbA1C, BP, Chol.), ° p-value of the adjusted model, • Confident interval or adjusted model

of eye disease (RM2 & RM3), with RRRs of 3.23 (95% CI: 1.59–6.67), 2.61 (95% CI: 1.58–4.33), and 2.59 (95% CI: 1.28–5.26), respectively, compared to White individuals (Table 5B). In general, higher retinopathy severity is associated with greater prevalence of advanced CKD stages among all populations. (Supplementary Table S5).

Discussion

We identified four distinct trajectories of eGFR decline for each of five ethnic groups in a large cohort of people with type 2 diabetes. The average diabetes duration was 6.5 years, and mean age was 54.7 years. Most participants maintained moderate renal function, with an average eGFR of 75.2 ml/min/1.73 m². Glycaemic control showed considerable variation, with a mean HbA1c of

64.5 mmol/mol (SD 22.48) with median of 58.5 (Interquartile Range(IQR) 48.5–76). Additionally, the albumin-creatinine ratio (ACR) highlighted a wide range of risks for kidney disease progression within the population (mean = 38.83 mg/mmol, SD 39.24) with median of 39 (IQR 11–45). The GBTMs analysis revealed distinct patterns of eGFR progression over time, and different characteristics of people within each trajectory.

Where the full cohort was considered, Trajectory I (steepest decline in eGFR) comprised between 15% of participants from the Black ethnicity, to 19.43% from the White. Trajectory II (Stable/Low) and III (stable moderate) comprised a majority across all groups. Of the fast eGFR decline group (Trajectory I) 37.3% progressed to stage 4 CKD, and 14.5% to stage 5 at some point during follow up. The baseline clinical characteristics of the group showed an older age, and higher prevalence of males. White participants, of trajectory I, had lower ACR levels at baseline, increased BMI, and lower retinopathy severity than other ethnic groups. Advanced retinopathy stages were more common among Asian, Mixed, and “other ethnicities” ethnicities, with notably higher risk of severe stages (R3M0/R3M1) among Asian and “other ethnicities” ethnicities’ groups compared to the Whites.

This study adds unique insights into CKD progression across diverse ethnic groups by initially identifying specific eGFR trajectory patterns, then examining the risk of progression to CKD stages 4 and 5 among people with fast eGFR decline in people with T2DM. It reveals that non-White ethnicity, who fell within the fastest eGFR decline trajectory (Trajectory I), were at high-risk for advanced CKD stages. This group showed a significantly increased likelihood of reaching stages 4 and 5 CKD, particularly among the “other ethnicities” ethnicities, which displayed the highest relative risk. Additionally, Asian, Mixed, and other ethnic groups showed a higher tendency to severe Diabetic Retinopathy (DR) stages, highlighting the need for ethnicity-specific management and monitoring to further understand the reasons behind these higher rates of microvascular complications, and to pave the way for appropriate interventions. These findings align with previous literature that identified higher risks of CKD and DR in non-White ethnicities with diabetes. For instance, Hsu et al. (2003) found an accelerated CKD progression among African American populations due to genetic and socioeconomic factors [18]. Similarly, Mathur et al. (2018) noted that Black and South Asian populations in the UK face rapid renal decline, supporting our findings [2]. The importance of traditional risk factors, such as albuminuria and HbA1c, as predictors of CKD, is also consistent with established research. Perkins et al. (2003) and Skupien et al. (2012) showed that elevated baseline albuminuria and HbA1c levels, respectively, are strongly associated with kidney

function decline [19, 20]. The high prevalence of severe DR in ethnic minorities observed here aligns with findings from Varma et al. (2004) and Raymond et al. (2011), who documented increased DR severity among Hispanic, African American, and South Asian populations [8, 21]. The rapid eGFR decline observed in Trajectory I among Black and Asian ethnicities aligns with findings from extensive datasets like the UK Biobank and the Chronic Renal Insufficiency Cohort (CRIC) in the U.S. The CRIC study, for example, found that African American individuals with diabetes have a 2- to 3-fold higher risk of eGFR decline and progression to ESRD compared to White individuals (Feldman et al., 2013) [22]. Powe et al (2016) study explored disparities in CKD progression among racial groups and documented a notably higher risk of ESRD among African Americans compared to White individuals [23]. This study highlights the ethnic groups most likely to experience the most rapid decline in kidney function, with a particular emphasis on the elevated risk observed in the “other ethnicities” group—an aspect less explored in previous datasets. While previous research, such as the UK Biobank study by Banerjee et al. (2017), documented a rapid decline in kidney function among South Asian populations linked to genetic predispositions and socio-environmental factors [24], and the CRIC study emphasised genetic and socioeconomic contributors to CKD disparities, our findings provide additional granularity. By identifying distinct ethnic groups within the fastest progression category, this study enhances the understanding of CKD risk disparities within multiethnic populations [25]. Although the presence of Black, Asian, and Other ethnic groups in Trajectory Group I is low compared to White participants, this presence reflects the actual population structure. Our findings indicate that higher proportions from the Black, Asian and Other are at higher risk of progressing to stage 4 and 5 CKD compared to the White. Trajectory modeling used here provides a robust framework for understanding these progression patterns over time and allows for precise risk stratification, supporting targeted clinical interventions based on ethnic-specific needs and highlighting the importance of further research. The observed faster decline in kidney function among ethnic minority participants likely reflects a complex interplay of biological factors (such as genetic predispositions, e.g., APOL1 variants), socioeconomic determinants, and healthcare access disparities. A tailored management approaches may be needed. These could include earlier risk identification, culturally appropriate education, aggressive control of modifiable risk factors, and improved access to specialist care. Incorporating social determinants of health into risk assessment may further support targeted interventions for high-risk ethnic groups”.

An exploratory analysis was conducted in our study and showed that mortality was highest in the group with the steepest eGFR decline (Trajectory 1) and decreased across more stable trajectories (Supplementary Table S4).

The role of advanced DR stages (R2M0, R2M1, R3M0, R3M1) was linked to faster eGFR decline, especially among non-White ethnicities. The study found that Asian, Mixed, and “other ethnicities” groups in the fastest progression trajectory were more likely to present with severe retinopathy stages than White individuals. This association suggests that DR severity may play a significant role in accelerating CKD progression in these groups. This finding adds depth to the understanding of DR as an indicator of microvascular complications, potentially serving as an early marker of rapid renal deterioration in high-risk ethnic groups. These results align with prior research by Pop-Busui et al. (2016) and Kramer et al. (2003), who documented that advanced DR is associated with faster CKD progression due to shared microvascular damage pathways [26, 27]. Studies have consistently shown higher DR prevalence in non-White ethnicities, often due to genetic and socioeconomic disparities, as observed in the work of Varma et al. (2004) and Raymond et al. (2011) [8, 21]. While our analysis focused on retinopathy within Trajectory 1, future work could examine its distribution across all trajectories to explore broader kidney-eye disease interactions.

Limitations and strengths

This study has several limitations. The self-reported ethnicity data, while common in clinical settings, may not capture the full scope of genetic and environmental factors affecting CKD and DR progression. While standardized care protocols were in place, we acknowledge that potential differences in follow-up duration or frequency of eGFR testing across ethnic groups were not directly assessed. Such differences, potentially reflecting patients' need and likely that there are disparities in healthcare access or engagement based on need alongside care access known differences. We have however standardised the number of measurements as an average per year, as described in the methods section. The study was conducted in South London hospitals, limiting the generalizability of findings to other regions with different ethnic and socioeconomic profiles. Moreover, this hospital-based cohort may differ from primary care populations in disease severity and healthcare access, which may affect generalizability. Additionally, the sample size within certain ethnic subgroups, such as Mixed and “other ethnicities”, may reduce the statistical power to detect nuanced differences. Only baseline measurements for key covariates such as HbA1c and ACR were available for adjustment. Future studies should incorporate longitudinal risk factor trajectories to better understand

dynamic predictors of CKD progression. Although adjustments were made for known risk factors, potentially confounding factors, such as socioeconomic status and healthcare access, may still influence results. While death was not addressed as a competing risk in this study, this limitation is acknowledged and will be explored in future work”.

Despite these limitations, the study has significant strengths. Its focus on an ethnically diverse cohort provides valuable insights into CKD and DR progression in various populations within a real-world setting. The use of Group-Based Trajectory Modeling (GBTM) to identify distinct eGFR trajectories is a methodological strength, as it allows for a more nuanced understanding of CKD progression patterns. The use of retinal digital imaging enhances DR assessment accuracy, strengthening the analysis of DR and renal decline relationships. Additionally, the large sample size and extended follow-up period (2004–2018) support the reliability of findings, offering a comprehensive view of disease progression over time. By focusing on ethnicity-specific analyses, this study provides critical insights to guide more tailored approaches to managing diabetes complications across diverse populations.

Conclusion

The findings emphasize the need for integrated DR and CKD screening, particularly in non-White ethnic groups with diabetes who are at increased risk of rapid renal decline. Severe DR could serve as an early indicator of renal risk in these populations, suggesting that regular retinal assessments could enable early identification of individuals at high risk for CKD progression. Incorporating retinal screening into standard diabetes care for these groups could facilitate timely interventions and closer renal monitoring. The study highlights the importance of ethnicity-specific risk assessment tools to guide clinicians in identifying high-risk individuals, deeper understanding of reasons behind these, and developing tailored management plans to address the unique needs of diverse diabetic populations.

Supplementary information

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Supplementary Material 1

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Author contributions

T.A. was the main author, responsible for conceptualizing the study, conducting the experiments, and drafting the manuscript. S.A. performed the data analysis, contributed to the methodology, and reviewed the manuscript. J.K. provided additional analysis, contributed to the discussion, and reviewed the manuscript. M.O. critically reviewed the manuscript and provided editorial input. All authors reviewed and approved the final version of the manuscript.

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Data availability

The datasets generated and analysed during the current study are available from the corresponding author upon reasonable request.

Declaration

Ethical approval

This study, which involves human participants, was conducted as a retrospective analysis in accordance with local audit protocols. It utilized existing anonymized routine clinical data, which was accessed solely by the clinical care teams. The project received approval from the data governance committees of Guy's and St. Thomas' Hospital and King's College Hospital. Informed consent was obtained from all participants prior to their involvement in the study.

Consent for publication

Not applicable. No individual personal data is included in this manuscript.

Disclosure

Nothing to disclose.

Competing interests

The authors declare that they have no competing interests.

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