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Original Article

ORIGINAL ARTICLE

Association of deprivation and its individual domains on outcomes in people with chronic kidney disease

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ABSTRACT

Background. Due to the high correlation of chronic kidney disease (CKD) with other comorbidities, the sole effect of CKD on deprived people is not clear. In addition, there is a paucity of evidence in the literature linking isolated domains of deprivation to outcomes. This study aimed to examine whether deprivation was associated with adverse outcomes in patients with CKD, independent of cardiometabolic morbidities. Individual domains of deprivation were also evaluated.
Methods. A retrospective study of patients with non-dialysis-dependent CKD (ND-CKD) in the Salford Kidney Study to investigate the association of deprivation with outcomes. The English Indices of Deprivation was used for the comparative analysis of the five quintiles of deprivation. Two propensity score methods were used to attenuate the confounding effect of cardiometabolic morbidities between the least and the most deprived groups.
Results. People living in the least deprived areas ($n = 319$) had a lower risk of combined outcomes (all-cause mortality and renal replacement therapy) when compared with the most deprived group ($n = 813$) [hazard ratio (HR) 0.83; 95% confidence interval (CI) 0.71–0.98]. The negative association of deprivation remained after matching but with mixed statistical significance when using different propensity methods (HR 0.85; 95% CI 0.70–1.03 for propensity score matching and HR 0.77; 95% CI 0.61–0.98 for inverse probability weighting). The association of combined outcomes varied across component index of multiple deprivation domains with wide CIs. However, areas with lower scores for education, income and employment were significantly associated with a higher risk.
Conclusions. This study has identified that in people with ND-CKD, unemployment, poor educational attainment and lower household income were associated with poor outcomes. The association of deprivation with adverse outcomes persists despite adjustment for cardiometabolic morbidities.

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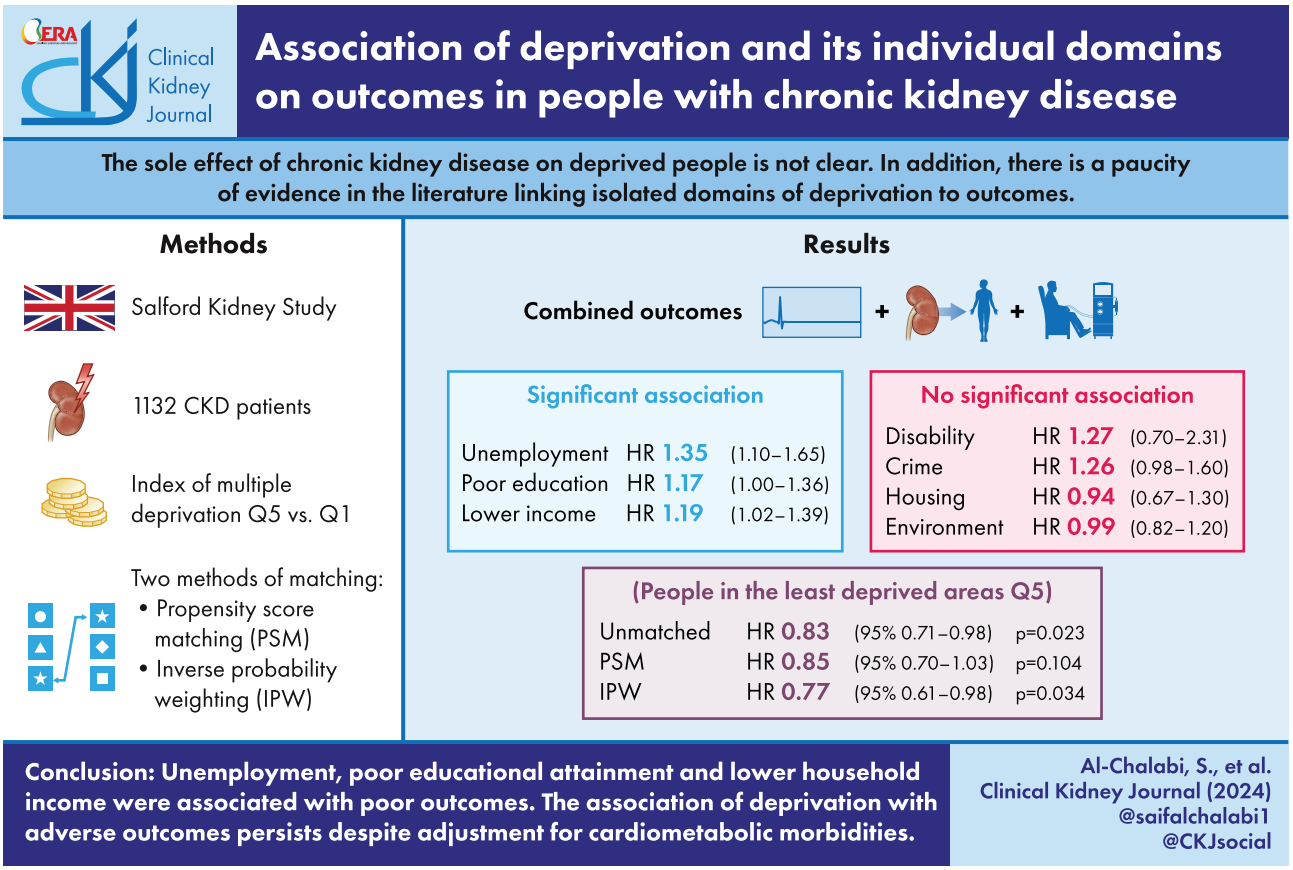
GRAPHICAL ABSTRACT



Keywords: chronic kidney disease, deprivation, domains of deprivation, multimorbidity, socioeconomic status

KEY LEARNING POINTS

What was known:

- People with chronic kidney disease (CKD) who are living in deprived areas are at higher risk of multimorbidity and poorer health outcomes.
- It is not clear whether CKD has a direct impact on outcomes independent of other comorbidities.
- There is a paucity of evidence on the impact of different aspects of deprivation on outcomes in people with non-dialysis-dependent CKD.

This study adds:

- The association of combined outcomes differs across component parts of the summary index of multiple deprivation measure, which warrants investigation in further analysis.
- Association of deprivation on adverse outcomes in patients with CKD persists despite adjustment for cardiometabolic morbidities such as obesity and diabetes mellitus.

Potential impact:

- The study findings indicate the need for healthcare researchers and policymakers to undertake further research and interventions which specifically target the unemployed, the poorly educated and those on low incomes with CKD, given that they are at risk of worse outcomes.

INTRODUCTION

Chronic kidney disease (CKD) is estimated to affect more than 800 million individuals worldwide [1]. It is also predicted to be the fifth leading cause of death by 2040 [2]. Associated conditions such as diabetes mellitus (DM), obesity and cardiovascular diseases are also increasing. A cross-sectional study of US adults showed a significant rise in the prevalence of cardiorenal metabolic disease cluster between 1999–2000 and 2017–20 (5.3% to 8.0%) [3]. This may represent an overarching epidemic of cardiorenal metabolic diseases that are highly connected through common pathophysiological pathways [4].

Socioeconomic status (SES) is known to be a key determinant of health outcomes [5]. People living in deprived areas have a higher likelihood of developing multimorbidity, the presence of two or more long-term conditions, which occurs at an earlier age than in those living in less deprived areas [6]. Individuals living in the most deprived areas have equivalent rates of multimorbidity to those aged 10–15 years older in the least deprived areas [7].

Measures of SES are based on individual or area indicators. Individual SES level is time-consuming and may be difficult to replicate in subsequent studies. Moreover, individual SES level may not be a better determiner of health outcomes when compared with area SES level [8]. Irrespective of the method of SES measurement, people with lower SES have a higher prevalence of CKD, higher risk of end-stage kidney disease and higher levels of albuminuria [9, 10]. However, there is limited evidence on the effect of socioeconomic deprivation on outcomes in patients with CKD, independent of other comorbidities [5, 11, 12].

The detrimental effect of deprivation on outcomes in people with CKD is well known. However, there is a paucity of evidence linking isolated domains of deprivation such as income and employment to outcomes [13]. The impact of deprivation on the population is multifaceted with complex connections between personal (e.g. smoking, alcohol, exercise) and area determinants (e.g. access to health, quality of the environment, housing). However, studying each domain of deprivation in isolation may allow for targeted intervention for high-risk groups. We hypothesized that people living in deprived areas with CKD would have a higher risk of worse outcomes independent of cardiometabolic morbidities. In addition, different domains of deprivation would have different association with outcomes.

This study aimed to examine whether deprivation was associated with adverse outcomes in patients with CKD, independent of cardiometabolic morbidities. Individual domains of deprivation were also evaluated.

MATERIALS AND METHODS

Study population

This study was undertaken using data from patients recruited to the Salford Kidney Study (SKS), which is an extension of the Chronic Renal Insufficiency Standards Implementations Study (CRISIS) [14]. The CRISIS study was inaugurated in 2002 and was renamed the SKS in February 2016. SKS is a prospective epidemiological cohort study with over 3000 patients with non-dialysis-dependent CKD (ND-CKD). Inclusion criteria were patients aged 18 years or older and referred to the renal department at Salford Royal Hospital (a tertiary renal centre with a catchment population of 1.55 million in the northwest of England) with estimated glomerular filtration rate (eGFR) <60 mL/min/1.73 m^2. Ethical approval was granted by a regional ethics committee (REC15/NW/0818). All patients recruited into the SKS between October 2002 and December 2016 with a recorded body mass index (BMI) level at baseline were included in this study.

Data collection and definitions

Exposure

Baseline data collection included demographics, comorbid conditions, medications and laboratory data. Patients were followed up annually until death, the incidence of renal replacement therapy (RRT) or until the censoring date (31 December 2021). The last clinic date was taken as the endpoint date for patients who were lost to follow-up. The eGFR was calculated using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation [15]. A positive smoking history was defined as a current smoker or a history of previous smoking. A positive alcohol history was defined as taking alcohol over the recommended limit of 14 units per week.

Outcomes

An RRT outcome was reached if a patient started on haemodialysis, peritoneal dialysis or received a kidney transplant. All-cause mortality (ACM) was reported for total follow-up and for 5 years. The combined outcome was reached if a patient reached either ACM or RRT or both. The rate of eGFR decline was calculated for all patients with a minimum of three eGFR measurements and at least 1-year follow-up until 31 December 2021.

Deprivation metrics

Data for the index of multiple deprivation (IMD) was obtained from The English Indices of Deprivation 2019 report (IoD 2019), the official measure of relative deprivation for small areas in England [16]. IoD 2019 ranks areas in England from 1 (most deprived) to 32 844 (least deprived). The study population were derived from six boroughs in Greater Manchester with a total population of more than 1.5 million (Fig. 1). The IoD 2019 is a nationally recognized method to assess area deprivation in the UK. It was based on 39 area indicators organized across seven domains of deprivation. These domains were combined and weighted to calculate the overall IMD. The assigned weight for each domain was adopted from the IoD 2019. The weights were assigned based on their impact on the overall IMD and the level of robustness of specific indicators for each domain [16]. The following is a short description of the domains used to construct the IoD metrics:

- Domain 1: Income (proportion of the population experiencing deprivation relating to low income).
- Domain 2: Employment (measures the proportion of the working-age population in an area involuntarily excluded from the labour market).
- Domain 3: Education (measures the lack of attainment and skills in the local population).
- Domain 4: Health and disability (measure the risk of premature death and the impairment of quality of life through poor physical or mental health).
- Domain 5: Crime (measures the risk of personal and material victimisation at a local level).
- Domain 6 Barriers to housing and services (measures the physical and financial accessibility of housing and local services).

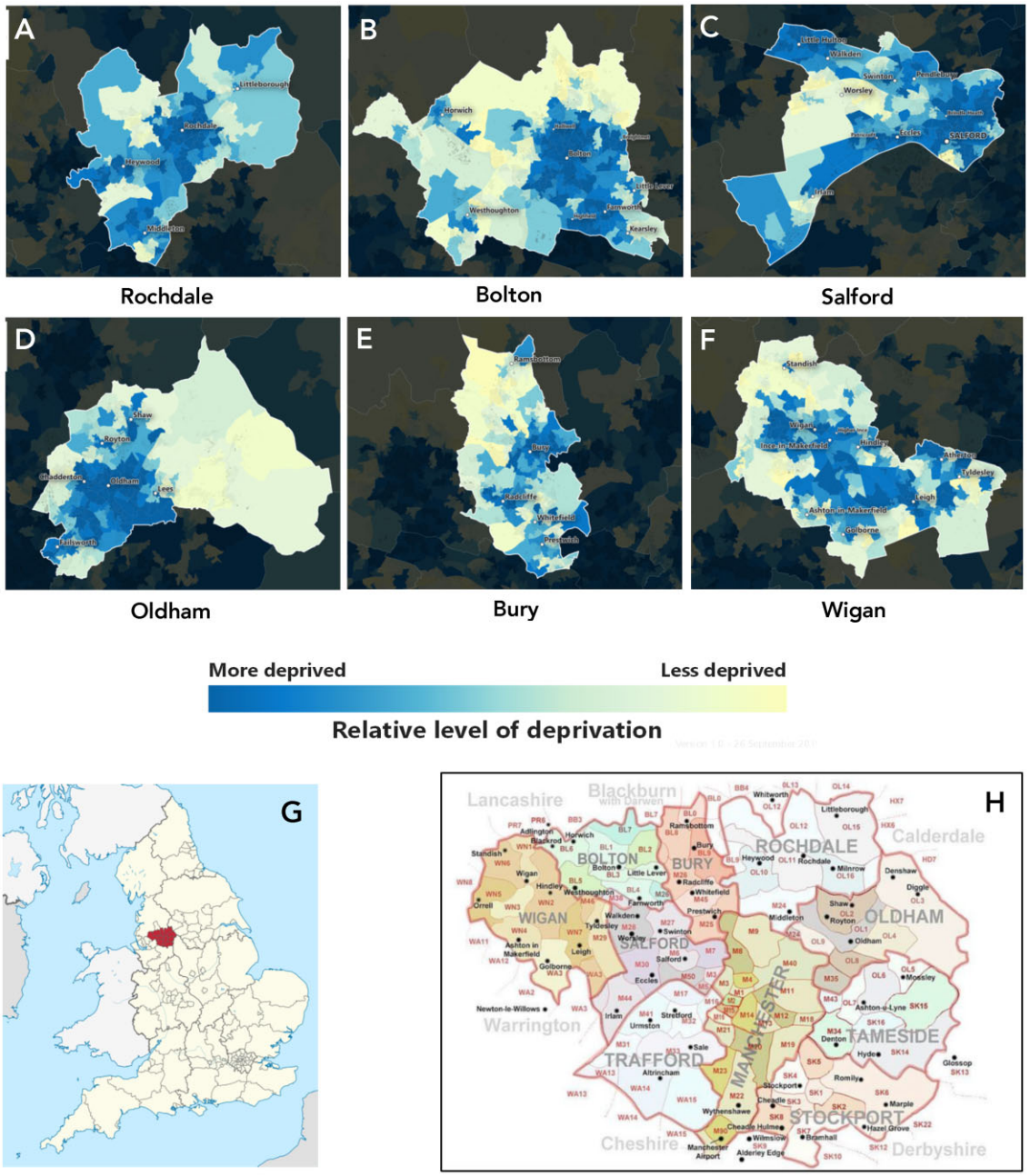


Figure 1: (**A–F**) The distribution of deprivation index in the boroughs served by the renal department at Salford Care Organisation. (**G**) map of England where Greater Manchester is highlighted in red. (**H**) Greater Manchester map showing the boroughs boundaries.

- Doman 7: Living environment (measures the quality of both the indoor and outdoor local environment).

Further details pertaining to the statistical methods and domain indicators can be found in the Supplementary file, Appendix 1 and the technical report released with the IoD 2019 publication [17].

Statistical analysis

Continuous variables were presented as median with interquartile range (IQR). Mann–Whitney U test and Kruskal–Wallis H test were used to compare statistical significance. Categorical values were expressed as percentages and the chi-square test was used to determine significance. The IoD 2019 grouped people into deciles. For this analysis we aggregated the data into quintiles; this approach has previously been adopted by Hossain *et al.* [18]. Baseline variables were compared across the 5 quintiles of the IMD (1 = most deprived areas, 5 = least deprived areas). Due to the wide distribution of the IMD values, a log scale of 2 was used for the comparative analysis. Multivariate regression analysis has several limitations such as conditional selection (overfitting) [19]. Therefore, two propensity score methods were used in our study to correct for differences in confounding factors—propensity score matching (PSM) and inverse probability weighting (IPW) [20]. Propensity scores for PSM were

Table 1: Baseline characteristics by quintiles of deprivation (Q1 most deprived, Q5 least deprived).

	Total ($n = 2416$)	Q1 ($n = 813$)	Q2 ($n = 472$)	Q3 ($n = 380$)	Q4 ($n = 432$)	Q5 ($n = 319$)	*P*-value
Age (years)	67.3 (55.9–75.6)	66.5 (54.6–75.1)	67.7 (57.6–75.9)	68.2 (57.1–76.4)	68.6 (57.4–76.3)	66.9 (52.6–74.8)	.101
Male, *n* (%)	1494 (61.8)	477 (58.7)	296 (62.7)	237 (62.4)	277 (64.1)	207 (64.9)	.209
Serum creatinine, µmol/L	177 (134–247)	179 (135.5)	176 (133.3–251.8)	186.5 (130–267)	169 (134.3–254.8)	173 (134–236)	.658
eGFR (CKD-EPI)	30.7 (20.4–43.6)	30.3 (20.5–41.8)	30.1 (20.4–44.6)	29.2 (18.9–44.0)	31.2 (19.6–44.7)	32.3 (21.9–45.7)	.290
White ethnicity (%)	2330 (96.40)	774 (95.2)	457 (96.8)	372 (97.9)	417 (96.5)	310 (97.2)	.154
Smoking, *n* (%)	1589 (65.8)	569 (70)	311 (65.9)	252 (66.3)	258 (59.7)	199 (62.4)	**.004**
Alcohol, *n* (%)	1132 (46.9)	315 (38.7)	217 (46.0)	183 (48.2)	237 (54.9)	180 (56.4)	**<.001**
SBP, mmHg	138 (124–152)	139 (125–154.5)	138 (122–152)	138 (122.3–155)	138 (125–152)	138 (120–151)	.474
DBP, mmHg	72 (65–80)	71 (65–80)	74 (65–80)	75 (65–80)	70 (65–80)	75 (68–80)	**.029**
DM	807 (33.4)	324 (39.9)	144 (30.50	120 (31.6)	125 (28.9)	94 (29.5)	**<.001**
HF	227 (9.4)	82 (10.1)	51 (10.8)	32 (8.4)	37 (8.6)	25 (7.8)	.518
BMI	28.1 (24.7–32.6)	28.7 (25.2–33.7)	28.1 (24.9–32.8)	28.1 (24.5–32.5)	27.3 (24.2–31.4)	27.5 (24.5–31.9)	**<.001**
Hypertension, *n* (%)	2182 (90.3)	745 (91.6)	422 (89.4)	345 (90.8)	392 (90.7)	278 (87.1)	.206
Angina, *n* (%)	444 (18.4)	175 (21.5)	89 (18.9)	69 (18.2)	67 (15.5)	44 (13.8)	**.015**
MI, *n* (%)	365 (15.1)	130 (16.0)	77 (16.3)	55 (14.5)	54 (12.5)34 (7.9)	49 (15.4)	.485
CVA, *n* (%)	180 (7.5)	39 (7.3)	36 (7.6)	32 (8.4)	34 (7.9)	19 (6.0)	.786
PVD, *n* (%)	312 (12.9)	129 (15.9)	64 (13.6)	37 (9.7)	51 (11.8)	31 (9.7)	**.010**
COPD, *n* (%)	457 (18.9)	184 (22.6)	93 (19.7)	67 (17.6)	67 (15.5)	46 (14.4)	**.004**
Liver disease, *n* (%)	80 (3.3)	35 (4.3)	10 (2.1)	10 (2.6)	12 (2.8)	13 (4.1)	.190
Malignancy, *n* (%)	276 (11.4)	82 (10.1)	53 (11.2)	53 (13.9)	50 (11.6)	38 (11.9)	.415
EPO, *n* (%)	324 (13.4)	99 (12.2)	69 (14.6)	50 (13.2)	68 (15.7)	38 (11.9)	.365
ACEi/ARB, *n* (%)	1487 (61.5)	507 (62.4)	288 (61)	227 (59.7)	260 (60.2)	205 (64.3)	.709
Statin, *n* (%)	1448 (59.9)	521 (64.1)	286 (60.6)	218 (57.4)	249 (57.6)	174 (54.5)	**.019**
Albumin, g/L	43 (41–45)	43 (40–45)	42 (41–45)	43 (40.5–45)	43 (40–45)	43 (41–46)	.383
Haemoglobin, g/L	123 (111–134)	122 (110–132.5)	122 (113–134)	123 (113–135.8)	122 (110–135)	124 (112–137)	.123
ALP, IU/L	82 (66–104)	85 (68–107)	81 (65–102)	81 (62–101)	79 (64.3–104)	82 (63–101)	.069
Calcium, mmol/L	2.29 (2.20–2.38)	2.30 (2.21–2.38)	2.29 (2.20–2.37)	2.30 (2.22–2.39)	2.29 (2.20–2.39)	2.29 (2.20–2.38)	.379
Phosphate, mmol/L	1.11 (0.97–1.28)	1.11 (0.97–1.29)	1.12 (0.98–1.27)	1.10 (0.96–1.28)	1.11 (0.97–1.28)	1.07 (0.93–1.26)	.296
UPCR, mg/mmol	28.6 (12.2–95.7)	31.1 (12.5–106.1)	25.3 (11.4–80.1)	27.7 (11.7–112.5)	29.7 (12.8–103.1)	27.5 (12.7–88.9)	.356

Continuous variables are presented as median (interquartile range), *P*-value by Kruskal–Wallis H test. Categorical variables presented as number (percentage), *P*-value by chi-squared test.

Missing values are as follows: albumin in 89 patients, haemoglobin in 85 patients, ALP in 125 patients, calcium in 96 patients, phosphate in 95 patients and UPCR in 213 patients.

SBP: systolic BP; MI: myocardial infarction; CVA: cerebrovascular accident; EPO: erythropoietin; ACEi/ARB; angiotensin-converting enzyme inhibitor and angiotensin-receptor blocker drug intake; ALP: alkaline phosphatase; UPCR: urinary protein creatinine ratio; HF: heart failure.

Bold values denote statistical significance at the $P < .05$ level.

Table 2: Outcomes by quintiles of deprivation (Q1 most deprived, Q5 least deprived).

	Total ($n = 2416$)	Q1 ($n = 813$)	Q2 ($n = 472$)	Q3 ($n = 380$)	Q4 ($n = 432$)	Q5 ($n = 319$)	*P*-value
Follow-up (months)	51.5 (25–94)	49 (24–94.5)	52 (26–93)	49.5 (26–90.8)	56 (24–100.8)	55 (29–96)	.545
ACM	1120 (46.4)	400 (49.2)	227 (48.1)	165 (43.4)	198 (45.8)	130 (40.8)	.071
5 years ACM	599 (24.8)	224 (27.6)	120 (27.6)	78 (20.5)	105 (24.3)	72 (22.6)	.088
RRT	563 (23.3)	189 (23.2)	102 (21.6)	100 (26.3)	100 (23.1)	72 (22.6)	.594
Combined ACM/RRT	1683 (69.6)	589 (72.5)	329 (69.7)	265 (69.7)	298 (68.9)	202 (63.4)	.305
Delta eGFR, mL/min/1.73 m^2/year	−1.09 (−3.23–0.36)	−1.09 (−3.57–0.44)	−0.87 (−2.72–0.72)	−1.24 (−3.23–0.25)	−1.26 (−3.12–0.00)	−0.86 (−3.50–0.54)	.217

Continuous variables are presented as median (interquartile range) , *P*-value by Kruskal–Wallis H test. Categorical variables presented as number (percentage) , *P*-value by chi-squared test.

generated by matching people in the least deprived (quintile 5) with a pool of people in the most deprived (quintile 1) using binary logistic regression analysis. We utilized 11 variables that were significantly different between Q1 and Q5 groups in the matching process: age, smoking, alcohol, DM, BMI, hypertension, angina, peripheral vascular disease (PVD), chronic obstructive pulmonary disease (COPD), use of statin and diastolic blood pressure (DBP). Matching was performed in a 1:1 ratio using the nearest neighbour method with a calliper width of 0.1. The distribution of propensity scores before and after matching is shown in the Supplementary data, Fig. S1. The robust standard errors (Huber White) for the propensity score matching are given in the Supplementary data, Table S2. The association of IMD quintile groups ACM and incidence of RRT was calculated using univariate Cox proportional hazard to determine hazard ratios (HRs), 95% confidence intervals (CIs) and statistical significance. IPW was utilized to mitigate the impact of selection biases within the study sample by including all the subjects

Table 3: Baseline characteristics for total and matched Q1 (most deprived) and Q5 (least deprived) using PSM.

	Q1 ($n = 813$)	Q5 ($n = 319$)	*P*-value	Matched Q1 ($n = 310$)	Matched Q5 ($n = 310$)	*P*-value
Age (years)	66.5 (54.6–75.1)	66.9 (52.6–74.8)	.765	66.7 (53.9–75.2)	67.2 (52.9–74.9)	.965
Male, *n* (%)	477 (58.7)	207 (64.9)	.054	194 (62.6)	203 (65.6)	.451
Serum creatinine, µmol/L	179 (135.5)	173 (134–236)	.304	178 (136.8–251.3)	173 (136–237.3)	.544
eGFR (CKD-EPI)	30.3 (20.5–41.8)	32.3 (21.9–45.7)	.072	31.1 (19.9–41.7)	32.0 (21.7–44.2)	.341
White ethnicity (%)	774 (95.2)	310 (97.2)	.138	298 (96.1)	301 (97.1)	.505
Smoking, *n* (%)	569 (70)	199 (62.4)	**.014**	192 (61.9)	197 (63.5)	.678
Alcohol, *n* (%)	315 (38.7)	180 (56.4)	**<.001**	174 (56.1)	171 (55.2)	.808
SBP, mmHg	139 (125–154.5)	138 (120–151)	.097	138 (124–155)	138 (120–151.3)	.211
DBP, mmHg	71 (65–80)	75 (68–80)	**.004**	75 (66–80)	75 (66–80)	.937
DM	324 (39.9)	94 (29.5)	**.001**	89 (28.7)	94 (30.3)	.660
HF	82 (10.1)	25 (7.8)	.245	27 (8.7)	25 (8.1)	.772
BMI	28.7 (25.2–33.7)	27.5 (24.5–31.9)	**<.001**	27.4 (24.5–31.7)	27.6 (24.7–32.0)	.566
Hypertension, *n* (%)	745 (91.6)	278 (87.1)	**.021**	281 (90.6)	273 (88.1)	.298
Angina, *n* (%)	175 (21.5)	44 (13.8)	**.003**	62 (20)	44 (14.2)	.055
MI, *n* (%)	130 (16.0)	49 (15.4)	.794	43 (13.9)	48 (15.5)	.570
CVA, *n* (%)	39 (7.3)	19 (6.0)	.437	12 (3.9)	19 (6.1)	.197
PVD, *n* (%)	129 (15.9)	31 (9.7)	**.008**	28 (9.0)	31 (10)	.681
COPD, *n* (%)	184 (22.6)	46 (14.4)	**.002**	53 (17.1)	46 (14.8)	.443
Liver disease, *n* (%)	35 (4.3)	13 (4.1)	.863	14 (4.5)	12 (3.9)	.689
Malignancy, *n* (%)	82 (10.1)	38 (11.9)	.369	42 (13.5)	36 (11.6)	.467
EPO, *n* (%)	99 (12.2)	38 (11.9)	.902	39 (12.6)	38 (12.3)	.903
ACEi/ARB, *n* (%)	507 (62.4)	205 (64.3)	.551	185 (59.7)	201 (64.8)	.185
Statin, *n* (%)	521 (64.1)	174 (54.5)	**.003**	175 (56.5)	173 (55.8)	.871
Albumin, g/L	43 (40–45)	43 (41–46)	.086	43 (41–45)	43 (41–46)	.739
Haemoglobin, g/L	122 (110–132.5)	124 (112–137)	**.014**	123 (110–133)	123.5 (112–137)	.093
ALP, IU/L	85 (68–107)	82 (63–101)	.060	83 (66–102)	83 (63–101.5)	.744
Calcium, mmol/L	2.30 (2.21–2.38)	2.29 (2.20–2.38)	.455	2.29 (2.21–2.38)	2.28 (2.20–2.38)	.774
Phosphate, mmol/L	1.11 (0.97–1.29)	1.07 (0.93–1.26)	**.045**	1.12 (0.97–1.27)	1.07 (0.93–1.26)	.169
UPCR, mg/mmol	31.1 (12.5–106.1)	27.5 (12.7–88.9)	.453	26.5 (11.7–72.9)	29.5 (12.9–91.2)	.406

Continuous variables are presented as median (interquartile range), *P*-value by Mann–Whitney U test. Categorical variables presented as number (percentage), *P*-value by chi-squared test.

SBP: systolic blood pressure; MI: myocardial infarction; CVA: cerebrovascular accident; EPO: erythropoietin; ACEi/ARB: angiotensin-converting enzyme inhibitor and angiotensin -receptor blocker drug intake; ALP; alkaline phosphatase, UPCR; urinary protein creatinine ratio.

Bold values denote statistical significance at the $P < .05$ level.

in the analysis without exclusion [21]. We used the same 11 variables to generate propensity scores using binary logistic regression analysis. The inverse probability weight was computed as 1/propensity score for the Q1 group and 1/(1 – propensity score) for the Q5 group. HRs were estimated using weighted Cox regression analysis. The progression of CKD was computed using the rate of change of eGFR (eGFR slope) from baseline to study endpoint in the linear regression slope. The HR for combined outcomes (ACM and RRT) was calculated for each quintile in each IMD domain using the quintile 5 group as a reference. There was only a small percentage of missing data with no identifiable pattern. Therefore, data imputation was not undertaken (Supplementary data, Table S3). Information on missing data is also available within each table. A *P*-value <.05 was considered statistically significant. Statistical analysis was performed using IBM SPSS (Version 28.0.1.1) provided by the University of Manchester (2021) and the R Statistical Software (v4.2.1; R Core Team 2021).

RESULTS

Baseline characteristics

A total of 2416 patients were included in the analysis with a median age of 67.3 (IQR 55.9–75.6) years. A significant proportion of patients reside in the most deprived areas (34%). There was a predominance of males, 61.8% ($n = 1494$) (Table 1). The most common associated comorbidities were hypertension (90.3%), DM (33.4%) and ischaemic heart disease (18.4% angina and 15.1% myocardial infarction). Median eGFR was 30.7 (IQR 20.4–43.6) mL/min/1.73 m^2. There was a higher prevalence of intake of alcohol above recommended limits in the least deprived group (quintile 5 group; 56.4%) compared with 38.7% in quintile 1, *P*-value <.001. The least deprived group (quintile 1) had a significantly higher prevalence of DM and angina with a higher median BMI at baseline compared with the other groups.

Outcomes

The risk of ACM was lower in the least deprived group compared with the most deprived group but with no statistical significance (Q1, 49.2% vs Q5, 40.8%; *P*-value = .071) (Table 2).

Comparison between the least deprived and the most deprived groups

We compared the most deprived group (Q1) with the least deprived group (Q5) in an unmatched and two-matched comparative analysis.

Unmatched Q1 vs Q5 groups

People in the least deprived group (Q5) had a lower median urine protein creatinine ratio at baseline (Q5, 27.5 vs Q1, 31.1 mg/mmol; $P = .453$) (Table 3). Median eGFR was higher in the least deprived group (Q5, 32.3 vs Q1, 30.3 mL/min/1.73 m^2; $P = .072$). ACM and combined outcomes were significantly lower in the Q5 group (40.8% vs 49.2%; $P = .010$ and 63.4% vs 72.5%;

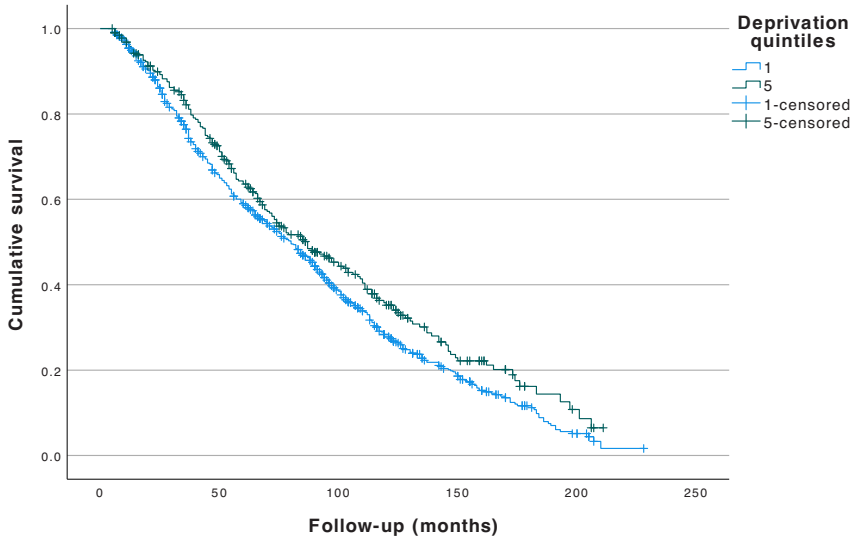


Figure 2: KM curves for combined outcomes between unmatched Q1 and Q5 groups.

Table 4: Outcomes for total and matched Q1 (most deprived) and Q5 (least deprived) using PSM.

	Q1 ($n = 813$)	Q5 ($n = 319$)	*P*-value	Matched Q1 ($n = 310$)	Matched Q5 ($n = 310$)	*P*-value
Follow-up (months)	49 (24–94.5)	55 (29–96)	.111	65 (29–108)	66 (36.8–110.3)	.561
ACM	400 (49.2)	130 (40.8)	**.010**	150 (48.4)	126 (40.6)	.052
5 years ACM	224 (27.6)	72 (22.6)	.086	84 (27.1)	69 (22.3)	.162
RRT	189 (23.2)	72 (22.6)	.808	77 (24.8)	70 (22.6)	.509
Combined ACM/RRT	589 (72.5)	202 (63.4)	**.010**	225 (72.6)	196 (63.1)	**.044**
Delta eGFR, mL/min/1.73 m^2/year	−1.09 (−3.57–0.44)	−0.86 (−3.50–0.54)	.403	−0.96 (−3.53–0.57)	−0.84 (−3.39–0.54)	.642

Continuous variables are presented as median (interquartile range), *P*-value by Kruskal–Wallis H test. Categorical variables presented as number (percentage), *P*-value by chi-squared test.
Bold values denote statistical significance at the $P < .05$ level.

$P = .010$, respectively). There was no significant difference in the incidence of RRT. In the univariate analysis, the Q5 group had a significantly lower incidence of combined outcomes compared with the Q1 group (HR 0.83; 95% CI 0.71–0.98; $P = .023$). The Kaplan–Meier (KM) curve indicated a significant difference in the survival probabilities for the combined outcomes, with better survival in Q5 (log rank = 0.022) (Fig. 2).

Matching Q1 and Q5 using PSM

A total of 620 patients were included in the propensity score matched cohort (310 in the Q1 group vs 310 in the Q5 group) (Table 3). The combined outcomes remained significantly lower (63.1% vs 72.6%; $P = .044$) in Q5 compared with Q1 after correcting for the following confounding factors: age, smoking, alcohol, DM, BMI, hypertension, angina, PVD, COPD, use of statin and DBP (Table 4). The rate of decline in eGFR was lower in Q5 compared with Q1 but was not statistically significant (−0.84 vs −0.96 mL/min/1.73 m^2/year; $P = .642$). In the univariate analysis, the Q5 group continued to have a lower incidence of combined outcomes compared with the Q1 group, but this difference was not statistically significant (HR 0.85; 95% CI 0.70–1.03; $P = .104$). The survival probabilities using the KM curve were not significantly different between the two groups with a log rank of 0.102 (Fig. 3).

Matching Q1 and Q5 using IPW

Propensity scores were generated using the same covariates used for PSM. The standard mean difference between the Q1 and Q5 groups has improved significantly with only four variables >0.1 compared with 16 variables in the unmatched cohort (Table 5). The weighted Cox regression analysis showed that the Q5 group had a significantly lower incidence of combined outcomes compared with the Q1 group (HR 0.77; 95% CI 0.61–0.98; $P = .034$).

Domains of area deprivation

The hazard of combined outcomes for total IMD and each of its domains were compared among the quintile groups using the least deprived group (Q5) as a reference (Fig. 4). In the total IMD analysis, the hazard of combined outcomes was significantly higher in the Q1 group (HR 1.2; 95% CI 1.02–1.41; $P = .027$). The risk of combined outcomes declined with higher IMD (less deprivation) (Fig. 4). Education and income domains were also associated with a significantly higher risk of combined outcomes in the most deprived group (Q1) (HR 1.17; 95% CI 1.00–1.36; $P = .046$ and HR 1.19; 95% CI 1.02–1.39; $P = .024$, respectively). The domain with the most significant association was employment (HR for Q1 group 1.35; 95% CI 1.10–1.65; $P = .003$). There were

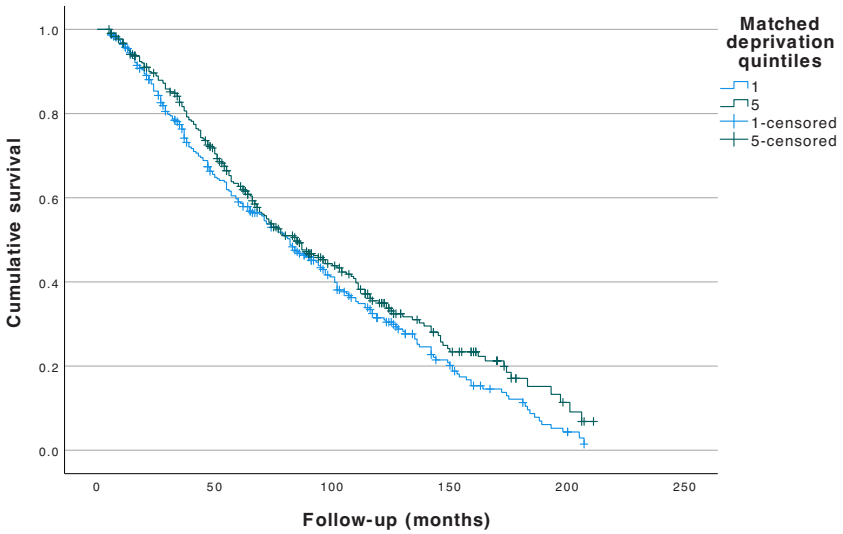


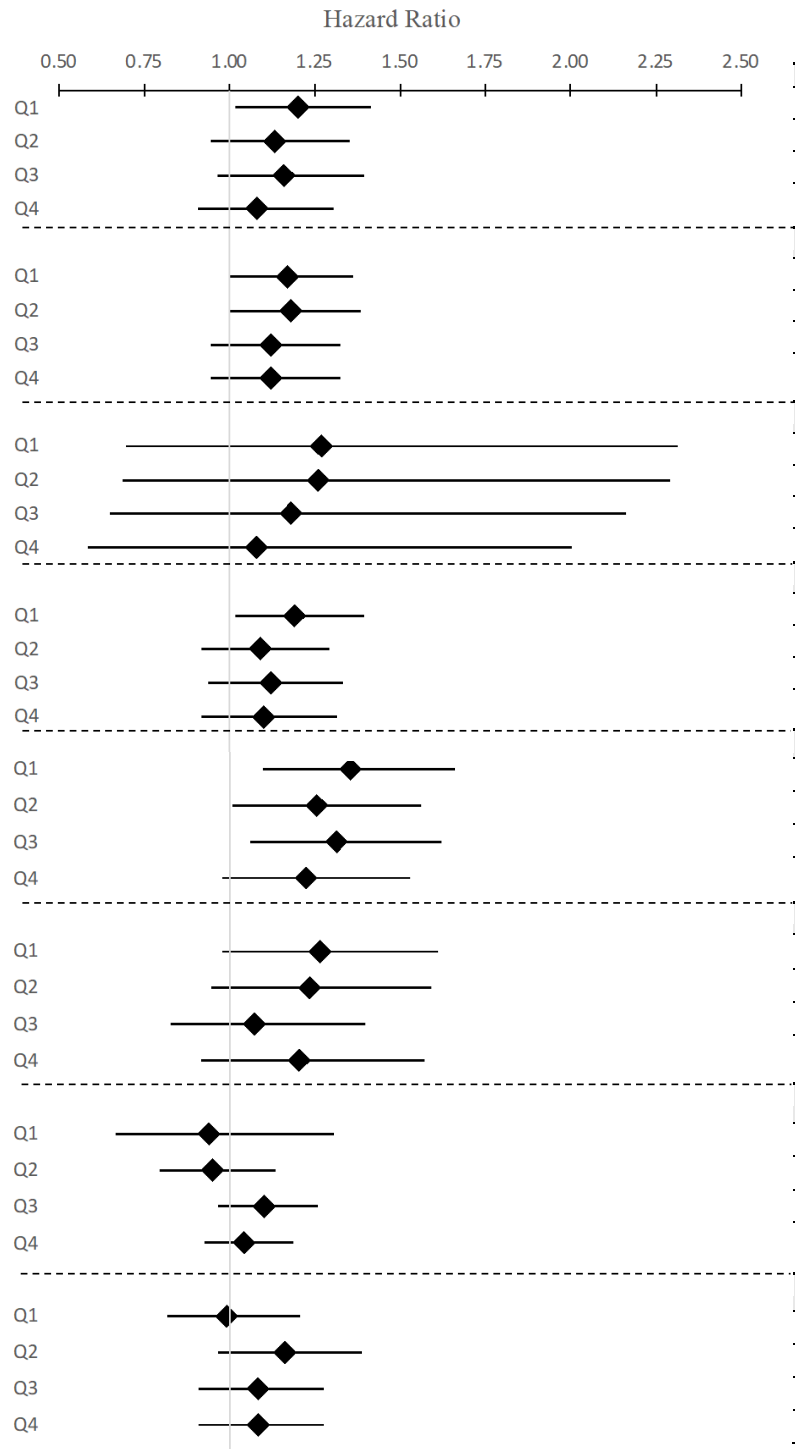
Figure 3: KM curves for combined outcomes between matched Q1 and Q5 groups.

Table 5: Baseline characteristics for the total and matched Q1 (most deprived) and Q5 (least deprived) using IPW.

	Q1 $n = 813$	Q5 $n = 319$	SMD for unmatched	Q1 IPW $n = 1332$	Q5 IPW $n = 1133$	SMD for matched
Age (years)	66.5 (54.6–75.1)	66.9 (52.6–74.8)	0.049	66.2 (54.4–75.1)	67.7 (54.5–75.3)	0.024
Male, *n* (%)	477 (58.7)	207 (64.9)	0.128	670 (59.2)	738 (65.1)	0.122
Serum creatinine, µmol/L	179 (135.5)	173 (134–236)	0.061	179 (135–245)	173 (137.4–235)	0.028
eGFR (CKD-EPI)	30.3 (20.5–41.8)	32.3 (21.9–45.7)	0.107	30.7 (20.9–42.0)	32.4 (21.7–43.5)	0.061
White ethnicity, *n* (%)	774 (95.2)	310 (97.2)	0.103	1079 (95.4)	1095 (96.6)	0.063
Smoking, *n* (%)	569 (70)	199 (62.4)	0.161	772 (68.2)	779 (68.7)	0.012
Alcohol, *n* (%)	315 (38.7)	180 (56.4)	0.359	494 (43.6)	489 (43.1)	0.010
SBP, mmHg	139 (125–154.5)	138 (120–151)	0.078	139.5 (125–155)	137.2 (120–152)	0.142
DBP, mmHg	71 (65–80)	75 (68–80)	0.152	72 (65–80)	73.7 (66–80)	0.016
DM	324 (39.9)	94 (29.5)	0.219	417 (36.8)	406 (35.8)	0.021
HF	82 (10.1)	25 (7.8)	0.107	121 (10.7)	114 (10.1)	0.019
BMI	28.7 (25.2–33.7)	27.5 (24.5–31.9)	0.224	28.4 (24.9–33.3)	28.2 (25.2–32.9)	0.010
Hypertension, *n* (%)	745 (91.6)	278 (87.1)	0.146	1022 (90.3)	1021 (90.1)	0.008
Angina, *n* (%)	175 (21.5)	44 (13.8)	0.204	218 (19.3)	215 (18.9)	0.009
MI, *n* (%)	130 (16.0)	49 (15.4)	0.017	170 (15.1)	217 (19.1)	0.108
CVA, *n* (%)	39 (7.3)	19 (6.0)	0.052	78 (6.9)	77 (6.8)	0.004
PVD, *n* (%)	129 (15.9)	31 (9.7)	0.185	160 (14.2)	171 (15.1)	0.025
COPD, *n* (%)	184 (22.6)	46 (14.4)	0.212	230 (20.4)	226 (19.9)	0.010
Liver disease, *n* (%)	35 (4.3)	13 (4.1)	0.011	49 (4.4)	43 (3.8)	0.028
Malignancy, *n* (%)	82 (10.1)	38 (11.9)	0.058	118 (10.4)	128 (11.3)	0.029
EPO, *n* (%)	99 (12.2)	38 (11.9)	0.008	134 (11.9)	161 (14.2)	0.069
ACEi/ARB, *n* (%)	507 (62.4)	205 (64.3)	0.039	696 (61.5)	736 (64.9)	0.071
Statin, *n* (%)	521 (64.1)	174 (54.5)	0.195	693 (61.3)	690 (60.9)	0.008
Albumin, g/L	43 (40–45)	43 (41–46)	0.058	43 (40–45)	43 (41–45)	0.052
Haemoglobin, g/L	122 (110–132.5)	124 (112–137)	0.190	122.6 (110–133)	122 (111–136)	0.121
ALP, IU/L	85 (68–107)	82 (63–101)	0.117	84 (68–106)	84 (63.5–103)	0.071
Calcium, mmol/L	2.30 (2.21–2.38)	2.29 (2.20–2.38)	0.048	2.30 (2.21–2.38)	2.28 (2.19–2.38)	0.124
Phosphate, mmol/L	1.11 (0.97–1.29)	1.07 (0.93–1.26)	0.141	1.11 (0.97–1.29)	1.08 (0.93–1.26)	0.093
UPCR, mg/mmol	31.1 (12.5–106.1)	27.5 (12.7–88.9)	0.005	31.2 (12.5–102.8)	27.5 (13.0–90.9)	0.050

Missing values in Q1 IPW: albumin 48, haemoglobin 44, ALP 73, Ca 54, PO_4 51, UPCR 121. Missing values Q5 IPW: albumin 45, haemoglobin 34, ALP 55, Ca 45, PO_4 47, UPCR 74.

SMD: standard mean difference; SBP: systolic blood pressure; MI: myocardial infarction; CVA: cerebrovascular accident; EPO: erythropoietin; ACEi/ARB: angiotensin-converting enzyme inhibitor and angiotensin-receptor blocker drug intake; ALP; alkaline phosphatase, UPCR; urinary protein creatinine ratio.



	HR (95% CI)	P value
Deprivation index		
Q1	1.2 (1.02-1.41)	**0.027**
Q2	1.13 (0.95-1.35)	0.161
Q3	1.16 (0.97-1.39)	0.113
Q4	1.08 (0.91-1.30)	0.375
Education		
Q1	1.17 (1.00-1.36)	**0.046**
Q2	1.18 (1.00-1.38)	**0.046**
Q3	1.12 (0.95-1.32)	0.186
Q4	1.12 (0.95-1.32)	0.184
Disability		
Q1	1.27 (0.70-2.31)	0.428
Q2	1.26 (0.69-2.29)	0.451
Q3	1.18 (0.65-2.16)	0.584
Q4	1.08 (0.59-2.00)	0.804
Income		
Q1	1.19 (1.02-1.39)	**0.024**
Q2	1.09 (0.92-1.29)	0.316
Q3	1.12 (0.94-1.33)	0.207
Q4	1.10 (0.92-1.31)	0.307
Employment		
Q1	1.35 (1.10-1.65)	**0.003**
Q2	1.25 (1.01-1.55)	**0.038**
Q3	1.31 (1.06-1.61)	**0.013**
Q4	1.22 (0.98-1.52)	0.078
Crime		
Q1	1.26 (0.98-1.60)	0.068
Q2	1.23 (0.95-1.58)	0.115
Q3	1.07 (0.83-1.39)	0.601
Q4	1.20 (0.92-1.56)	0.172
Housing		
Q1	0.94 (0.67-1.30)	0.696
Q2	0.95 (0.80-1.13)	0.549
Q3	1.10 (0.97-1.25)	0.129
Q4	1.04 (0.93-1.18)	0.480
Environment		
Q1	0.99 (0.82-1.20)	0.936
Q2	1.16 (0.97-1.38)	0.097
Q3	1.08 (0.91-1.27)	0.389
Q4	1.08 (0.91-1.27)	0.404

Figure 4: HR for combined outcomes for deprivation index and its seven domains.

no significant associations in disability, crime, housing and environment domains.

DISCUSSION

This study showed that people living in the least deprived areas had a borderline but significantly lower risk of combined outcomes for ACM and RRT than people living in the most deprived areas. The association was consistent among the different methods used to attenuate the risk of bias by correcting for cardiometabolic morbidities. Further detailed analysis was undertaken on the association of social determinants of deprivation and combined outcomes. Our study showed that lower ranks of employment, educational attainment and household

income were associated with worse combined outcomes in people with ND-CKD. However, there was no association with area indices of crime, access to housing, disability or living environment.

Due to the strong link between CKD, multimorbidity and lower SES, it is difficult to evaluate the direct effects of SES on outcomes in people with CKD, independent of other CKD-related comorbidities. Several studies corrected these factors by using stepwise multivariate regression analysis yielding mixed results [22, 23]. In a study using the Scottish Deprivation Index, a higher index of deprivation was not associated with significantly higher cardiovascular mortality (HR 1.48; 95% CI 0.56–3.94; $P = .44$) or incidence of RRT (HR 0.95; 95% CI 0.26–3.46; $P = .94$) after correcting for associated morbidities (DM, obesity, coronary artery disease and blood pressure) using multivariate analysis models [23]. Another study on people referred to a renal specialist centre in Italy showed that the most socioeconomically deprived patients had a higher rate of ACM independent of cardiac and metabolic comorbidities (HR 1.38; 95% CI 1.01–1.90; $P = .047$) [22]. The discrepancies in results might be due to the differences in the criteria used to define the index of deprivation between different countries. Our PSM results showed that combined outcomes of ACM and RRT trended towards being better in patients living in the least deprived areas when matched with those in the most deprived areas, but without statistical significance (HR 0.85; 95% CI = 0.70–1.03; $P = .104$). However, applying the IPW method revealed a significantly lower risk of combined outcomes in the least deprived group when compared with the most deprived group (HR 0.77; 95% CI = 0.61–0.98; $P = .034$).

Studies have examined the effects of selected domains of deprivation on CKD outcomes [13]. Only one published study has examined the influence of employment on CKD, and it found no association with mortality or the incidence of RRT [16]. Notably, this study categorized individuals as skilled or unskilled workers, with no representation of unemployed participants. Our analysis showed a significant association between the rate of employment in the area and the risk of worse combined outcomes (HR for the most deprived group compared with the least deprived group 1.35; 95% CI 1.10–1.65; $P = .003$).

While it is widely acknowledged that income inequality can affect health outcomes, the precise connection remains unclear and is likely to vary across different countries and healthcare systems [24]. Our study showed that only the most deprived group had a significantly higher risk of combined outcomes (HR 1.19; 95% CI 1.02–1.39; $P = .024$). There was no impact on other groups. This may, in part, be attributed to the accessibility of healthcare services in the UK via the National Health Service (NHS).

To our knowledge, this is the first study that assess the impact of all domains of deprivation in a cohort of patients with ND-CKD. However, there are several limitations to consider. The cohort is predominantly of white ethnicity (96.4%), limiting generalizability to other ethnic groups. The focus on referred CKD patients in secondary care may not represent those in the community without nephrology service care. The relatively small sample size, due to focused population selection, affects result consistency by creating volunteer bias. Despite efforts to match deprived groups, residual confounding and selection bias remain a risk after employing the PSM method as Cox models CIs do not cover for uncertainties that can arise during the PSM process. However, the use of the IPW method helps mitigate this risk by including all subjects in the analysis. IoD metrics varied over the period of 2002–21; IoD 2019 was chosen for its recent, consistent and relative measure nature. However, risk of misclassification bias remain as it is not possible to link subjects with corresponding year metrics due to data collection spanning multiple years, and patient relocations add complexity in assigning appropriate metrics.

In conclusion, people with ND-CKD living in areas of increased socioeconomic deprivation in the northwest of England were found to be at increased risk of poor outcomes. This was specifically associated with areas with the lowest levels of employment, income and education. However, the accessibility of housing and the quality of the area environment did not have a significant association. Importantly, the effect of deprivation on adverse outcomes in patients with ND-CKD persists despite adjustment for cardiometabolic morbidities. These findings may highlight the need to specifically target the unemployed, the poorly educated and those on low incomes with CKD given that they are at risk of worse outcomes.

SUPPLEMENTARY DATA

Supplementary data are available at *Clinical Kidney Journal* online.

AUTHORS' CONTRIBUTIONS

S.A.C. conceptualized the study, performed the data analysis and drafted the manuscript. E.P. participated in data collection and performed the preliminary analysis. R.C. contributed to the design of the study and participated in critically revising the manuscript. P.A.K. and S.S. participated in critically revising the manuscript. All authors read and approved the final manuscript.

DATA AVAILABILITY STATEMENT

The data underlying this article will be shared on reasonable request to the corresponding author.

CONFLICT OF INTEREST STATEMENT

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