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Original Article

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Diagnosis, treatment, and survival from kidney cancer: real-world National Health Service England data between 2013 and 2019

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Objectives

To report the NHS Digital (NHSD) data for patients diagnosed with kidney cancer (KC) in England. We explore the incidence, route to diagnosis (RTD), treatment, and survival patterns from 2013 to 2019.

Materials and Methods

Data was extracted from the Cancer Data NHSD portal for International Classification of Diseases, 10th edition coded KC; this included Cancer Registry data, Hospital Episode Statistics, and cancer waiting times data.

Results

Registrations included 66 696 individuals with KC. Incidence of new KC diagnoses increased (8998 in 2013, to 10 232 in 2019), but the age-standardised rates were stable (18.7–19.4/100 000 population). Almost half of patients (30 340 [45.5%]) were aged 0–70 years and the cohort were most frequently diagnosed with Stage 1–2 KC (n = 26 297 [39.4%]). Most patients were diagnosed through non-urgent general practitioner referrals (n = 16 814 [30.4%]), followed by 2-week-wait (n = 15 472 [28.0%]) and emergency routes (n = 11 796 [21.3%]), with older patients (aged ≥70 years), Stage 4 KCs, and patients with non-specified renal cell carcinoma being significantly more likely to present through the emergency route (all $P < 0.001$). Invasive treatment (surgery or ablation), radiotherapy, or systemic anti-cancer therapy use varied with disease stage, patient factors, and treatment network (Cancer Alliance). Survival outcomes differed by Stage, histological subtype, and social deprivation class ($P < 0.001$). Age-standardised mortality rates did not change over the study duration, although immunotherapy usage is likely not captured in this study timeline.

Conclusion

The NHSD resource provides useful insight about the incidence, diagnostic pathways, treatment, and survival of patients with KC in England and a useful benchmark for the upcoming commissioned National Kidney Cancer Audit. The RTD data may be limited by incidental diagnoses, which could confound the high proportion of 'emergency' diagnoses. Importantly, survival outcomes remained relatively unchanged.

Keywords

kidney cancer, radical nephrectomy, radiotherapy, chemotherapy, surveillance, incidence, prevalence, stage, renal cancer

Patient Summary

Over 400 000 people per year worldwide are diagnosed with kidney cancer (KC) and over four out of 10 people affected die with the disease. Here, we have used anonymous and routinely collected NHS data in England to look at trends between 2013 and 2019 at:

- The number of people diagnosed with KC every year.
- The different types (subtypes) of KC diagnosed every year.
- The journey a person takes to reach their diagnosis (e.g., through urgent cancer pathways [2-week wait], non-urgent GP referrals, or accident and emergency).
- The treatments (surgery, anti-cancer drug therapy, or radiotherapy) that people with KC receive.
- How many people die with or because of KC.

Over 66 000 people were diagnosed with KC in England in the 7-year period. Less aggressive cancers (Stage 1–2) were most common. More people were diagnosed through non-urgent GP referrals than urgent cancer pathways. We are unsure of the reason for this, but it might be because of the symptoms people experience, problems with the referral pathway, or that KC can be found by scans done for other reasons. One fifth of people were diagnosed with KC through emergency pathways. These people were more likely to have advanced (Stage 4) cancer, be older (aged >70 years) and were less likely to have a confirmed type of KC (which likely mean they did not have a biopsy of their cancer). Treatments were different depending on the aggressiveness of the cancer (Stage), individual patient characteristics (e.g., age and other medical problems), and changed in different regions around the country. A persons' chance of surviving with KC was different depending on the aggressiveness of the KC (Stage), the type of KC, and individual patient social circumstances; survival was also different depending on the region patients were treated. Between 2013 and 2019, survival for patients with KC did not seem to improve. It is important to note that this study period does not include some of the newer treatments that are now available in 2023. We also note in this report that some of the data were incomplete or not detailed enough and have suggested some ways to improve data collection in the future.

Introduction

Each year, kidney cancer (KC) affects 431 288 patients globally, with 179 368 dying from the disease [1]. KC is most common in Europe and North America, in older patients (median age of diagnosis is 74 years [UK]) and has a two-fold higher incidence in men than women [2]. KCs are usually sporadic and associated with modifiable risk factors, such as smoking, obesity, hypertension, and diabetes [3]. Around 5–8% of KCs are hereditary [4]. The age-standardised incidence of KC in the UK has doubled since 1993 [5], which could reflect increased opportunistic diagnosis (through widespread use of abdominal imaging) or rising levels of risk factor exposure (particularly obesity). However, despite improved access to imaging, advances in surgical techniques and widespread adoption of systemic therapies, the age-standardised mortality rate in the UK increased by 5% between 2007 and 2009 and 2017–2019 [6]. In addition, patients with KC have some of the worst patient-reported experiences of all cancers in England [7]. Hence, further population-based research is warranted to understand why outcomes are stagnant and how to improve patient experiences.

The analysis of population-level data can be used to explore real-world presentations, treatments, and outcomes in a timely fashion to inform clinical practice and health policy. In the UK, real-world data (RWD) relating to cancer is routinely collected, quality assured, and published, by the National Cancer Registry and Analysis Service (NCRAS). Therefore, RWD provides an accessible low-cost resource for interrogation [8], which better reflects the clinical environments in which patients are treated, and unlike clinical trials, is more inclusive and reflective of population demographics [9]. In addition, interrogation of RWD provide insight about cancer-specific diagnostic pathways and patient flow, which may impact on patient outcomes and experiences. As part of the expanding portfolio of audits run by the National Cancer Audit Collaborating Centre, KC has recently been commissioned as one of five new cancer audits to enhance our understanding of the real-world experiences of patients in England and Wales [10]. In this report, we present a summary of the most contemporary NHS England data for KC from 2013 to 2019.

Materials and Methods

Methods for this study are similar to previously published work using the NHS Digital (NHSD) database on the diagnosis, treatment, and survival trends for bladder, upper urinary tract, and urethral cancers [11].

Data Extraction

We extracted data from the NHSD Get Data Out (GDO) tables, which has been provided by patients and collected by the NHS as part of their care and support. The data are

collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of NHSD (Appendix S1). The results presented use routinely collected cancer data, which are retrospectively annotated with NHS patient outcomes [12]. The data starts in 2013, the year that the Cancer Outcomes and Survival Dataset was established, which promoted consistent reporting (hence, reducing data error and bias) [13]. As coded data were annotated retrospectively, there were more missing data in the 2019 cohort due to the COVID-19 pandemic.

Cancers in the KC dataset were considered for inclusion based on the following International Classification of Diseases, 10th edition (ICD-10) codes: C64, invasive kidney; D41.0, uncertain kidney; and D09.1, in situ other urinary organ with a location code (ICD-for Oncology-third edition first revision [ICD-O-3.1] code) of C64 (kidney). TCCs of the kidney (ICD-O-3.18120, 8122, 8130, 8131) were not included. KCs of uncertain behaviour (ICD-10 coded D41.0) were removed from overall totals; they accounted for <100 diagnoses/year. KCs were annotated according to the year of first diagnosis and ICD-O-3.1 2011 morphology (clear cell RCC [ccRCC], papillary RCC [pRCC], chromophobe RCC [chRCC], RCC non-specified [RCC-NOS], Wilms or 'other'). The subclass of 'renal non-specified' meant that either a distinct histological morphology could not be microscopically confirmed, or histological tissue was not obtained; <20 cases (per 5-year period) in this group related to lack of information. Staging data at diagnosis (Stages 1–2, 3, or 4) were available for ccRCC and RCC-NOS. Stage was allocated using a combination (where available) of pathological and radiological data; whereby if surgery was within 3 months of radiological diagnosis, and no neoadjuvant treatment was delivered, then diagnostic Stage included surgical pathology. Of note, the TNM classification of tumours moved from seventh to eighth version between 2017 and 2018, which slightly altered the wording around T3a tumours; however, KC Stages remained constant [14].

Route to diagnosis (RTD) was allocated, as previously described [15], to one of the following categories: screen detected, 2-week-wait (2WW) pathway (urgent GP referral where there is a suspicion of cancer), GP referral, emergency presentation, 'other' outpatient, inpatient elective (where no earlier information can be found prior to admission from a planned waiting list), death certificate only, and unknown. As there is no national screening programme for KC in England, no patients were allocated to the 'screen detected' RTD; hence, this class was not described in this manuscript. The RTD was described by age (Stage 3 RCC-NOS was the only KC class that was not annotated with age data, and so were not included in the age analysis), Stage, and histological subtype.

Treatments received were described between 2013 and 2018, where NCRAS uses Hospital Episode Statistics information to annotate cancer statistics. In brief, surgical or ablative procedures were allocated using NHS Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures, version 4 (OPCS-4) codes (https://www.datadictionary.nhs.uk/data_elements/opcs-4_code.html). The data described 'tumour resection' as any of the following procedures to the primary tumour site: nephrectomy (M021, M023, M025, M028, M029), partial nephrectomy (M038, M039, M042), heminephrectomy (M024), or focal ablative therapy (cryoablation M104 or radiofrequency ablation M137). These treatments will subsequently be classified as 'Invasive Treatment' (IT) in the manuscript. Systemic treatments were assigned using the systemic anti-cancer therapy (SACT) source data (https://www.datadictionary.nhs.uk/data_sets/clinical_data_sets/systemic_anti-cancer_therapy_data_set.html). The SACT details the systemic delivery of all anti-cancer agents delivered to solid or haematological cancers, including patients on clinical trials. Radiotherapy regimens were extracted using the Radiotherapy Data Set (https://www.datadictionary.nhs.uk/data_sets/clinical_data_sets/radiotherapy_data_set.html).

Analysis and Statistics

Data were extracted from the above sources and analysed within Excel (Version 16.69.1; Microsoft Corp., Redmond, WA, USA). Graphs were generated and statistical analyses performed using GraphPad Prism 9.5.1 (GraphPad Software Inc., San Diego, CA, USA). Kaplan–Meier overall survival from 3 to 60 months was available for KC by Stage and histological subtype. Age-standardised net survival rates from 12 to 60 months were available for KC survival by gender, and Index of Multiple Deprivation (IMD) classification. Survival outcomes were compared using a two-way ANOVA. Patterns of disease were compared using chi-squared tests or *t*-tests (variable dependant). A $P < 0.05$ was taken as statistically significant.

Ethical Approval, Consent, and Data Availability

All data used in this study are publicly available, routinely collected for service assessment, and patients are not identifiable. Datasets available to download are documented in Appendix S1.

Results

New Diagnoses of KC

A total of 66 696 new cases of KC were diagnosed in England between 2013 and 2019 (Table 1). The number of cases diagnosed increased from 8998 in 2013, to 10 232 in 2019 (13.7% increase). The age-standardised incidence rate

Table 1 New KC diagnoses between 2013 and 2019 in England.

Variable	KC, *n* (%)	ccRCC, *n* (%)	pRCC, *n* (%)	chRCC, *n* (%)	RCC-NOS*, *n* (%)	Wilms/'other', *n* (%)
Total	66 696	29 780 (45)	3822 (5.7)	2511 (3.8)	29 248 (44)	1335 (2)
Year						
2013	8998	3476 (39)	433 (4.8)	299 (3.3)	4621 (51)	169 (1.9)
2014	9407	3974 (42)	504 (5.4)	330 (3.5)	4400 (47)	199 (2.1)
2015	9303	4155 (45)	529 (5.7)	379 (4.1)	4021 (43)	219 (2.4)
2016	9522	4428 (47)	560 (5.9)	365 (3.8)	3979 (42)	190 (2.0)
2017	9564	4558 (48)	572 (6.0)	359 (3.8)	3866 (40)	209 (2.2)
2018	9670	4554 (47)	560 (5.8)	372 (3.8)	3996 (43)	188 (1.9)
2019	10 232	4635 (45)	664 (6.5)	407 (4.0)	4365 (44)	161 (1.6)

**Of the RCC-NOS, 64.4% had no histology record.*

(ASIR) in England was 18.7 (95% CI [18.3–19.1])/100 000 population in 2013 and 19.4 (95% CI [19.0–19.8])/100 000 population in 2019. Age annotation was available for 55 011 patients diagnosed with KC. Most patients diagnosed with KC were aged 0–69 years (n = 30 340 [45.5%]), fewer were ≥70 years (n = 24 671 [37.0%]), and in 11 658 (17.5%) age was unknown. Most KCs were ccRCC (n = 29 760 [44.6%]); however, a substantial proportion were deemed RCC-NOS (n = 29 248 [43.8%]), of which 18 826 (64.4%) had no histology record.

Tumour Stage at diagnosis was available for 88.5% (n = 59 028) of the cohort, which included the ccRCC and RCC-NOS groups (Table S1). Most KCs were Stage 1–2 (n = 26 297 [39.4%]), followed by Stage 4 (n = 12 009 [18.0%]), and then Stage 3 (n = 9188 [13.7%]). Stage was documented 'unknown' in 11 534 (17.3%). The number of patients, per Stage, remained relatively unchanged (Fig. S1). The RCC-NOS group had significantly more patients with Stage 4 (Wilcoxon P = 0.016) and unknown Stage diagnoses (Wilcoxon P = 0.015) than the ccRCC group (Fig. S2). In 2019, KC was the 10th most prevalent cancer in England (10-year prevalence per 100 000 population, Fig. S3), which differed by age, gender, ethnicity and IMD classification (Fig. S4).

The RTD for Patients with KC

The RTD data were available between 2013 and 2018 for 55 328 patients and are summarised in Fig. 1. In all, 15 472 (28.0%) patients with KC received their diagnosis through the urgent cancer pathway (2WW) route, indications for which include: patients aged ≥45 years with unexplained visible haematuria (without UTI), or that persists/recurs after treatment of UTI [16]. Most patients (n = 16 814 [30.4%]) were diagnosed outside the 2WW route, through GP pathways. A high proportion of KCs presented through the emergency route (n = 11 796 [21.3%]). There was a marginal decrease in emergency presentation over the study period (22.1% [range 21.2–23.0] in 2013 to 19.6% [range 18.8–20.4] in 2019).

The RTD by Age

The RTD data, dichotomised by age, was available for 55 011 patients (aged 0–69 years, n = 30 340; aged ≥70 years, n = 24 671; Fig. S5). Patients aged ≥70 years were significantly less likely to present by the 2WW route (25.4% [95% CI [23.1–27.8]] compared to 30.0% [95% CI 28.8–31.3] in the 0–69 years group, P = 0.0004), GP route (28.8% [95% CI 27.3–30.3] compared to 31.4% [95% CI 29.5–33.2] in the 0–69 years group, P = 0.0002) and 'other' outpatient route (12.8% [95% CI 11.8–13.8] compared to 18.5% [95% CI 17.8–19.2] in the 0–69 years group, P < 0.0001). Older patients were more likely to present via the emergency route (27.1% [95% CI 25.0–29.1] compared to 14.3% [95% CI 13.3–15.4] in the 0–69 years group, P < 0.0001; Fig. S6).

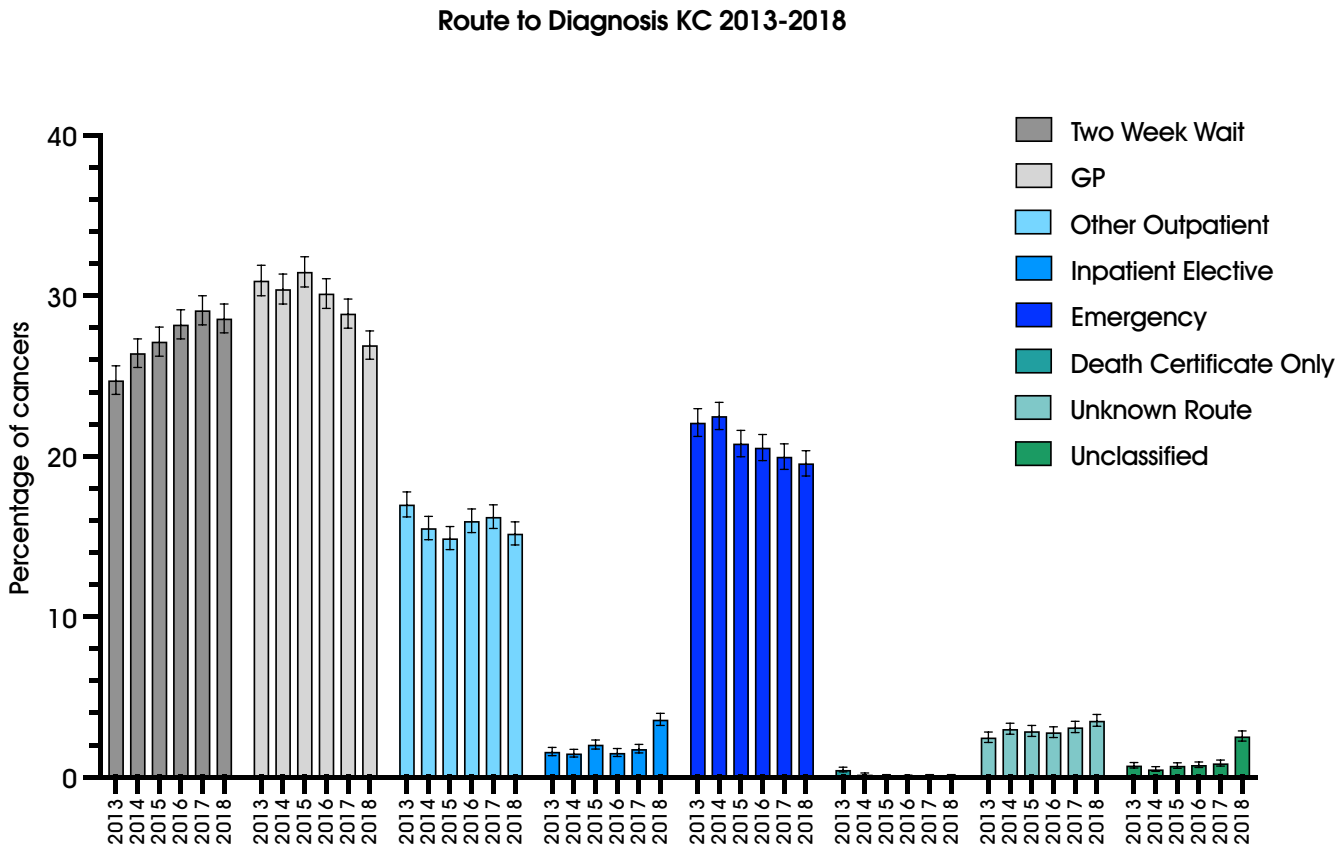
The RTD by Stage

The RTD by Stage was available for 41 216 patients (Stage 1–2, n = 22 885; Stage 3, n = 7879; Stage 4, n = 10 452; Fig. S7). There was a significant difference in the proportion of patients diagnosed through 2WW, GP, 'other' outpatient, and emergency routes by Stage (ANOVA P < 0.001; Fig. S8). Patients with Stage 3 KC were most likely to be diagnosed through 2WW (37.3% [95% CI 34.5–40.0]) and patients with Stage 4 KC were the least likely (25.8% [95% CI 24.2–27.5]). Patients with Stage 1–2 KC were the most likely to be diagnosed through the GP referral pathway (33.8% [95% CI 32.0–35.5]) and patients with Stage 4 the least likely (22.6% [95% CI 20.3–24.8]). Patients with Stage 4 KC were the least likely to be diagnosed through 'other' outpatient routes (10.3% [95% CI 9.7–10.9]) and most likely to be diagnosed through the emergency route (36.8% [95% CI 35.8–37.7]).

The RTD by Histological Subtype

The RTD by KC subtype was available for 55 290 patients (ccRCC, n = 25 145; pRCC, n = 3158; chRCC, n = 2104; RCC-NOS, n = 24 883; Fig. S9). The pRCC and RCC-NOS were less likely to be diagnosed by the 2WW pathway (25.3%

Fig. 1 The RTD of KC in England between 2013 and 2018 for 55 328 patients diagnosed with KC.



[95% CI 22.9–27.8] and 22.9% [95% CI 21.6–24.3], respectively) than ccRCC or chRCC (32.2% [95% CI 30.8–33.7] and 33% [95% CI 29.5–36.6], respectively; ANOVA $P < 0.001$). Those with RCC-NOS were also less likely to be diagnosed through the GP (26.9% [95% CI 24.9–28.8]) or 'other' outpatient routes (11.0% [95% CI 9.8–12.2]) and were most likely to be diagnosed through emergency presentation (31.9% [95% CI 31.0–32.9]; ANOVA $P < 0.0001$) (Fig. S10).

Treatment Received for KC

Data regarding modality of treatment for KC was available from 2013 to 2018 (n = 41 216). Treatments received were broadly divided into IT (surgery or ablative therapies), SACT, RT, and other treatment. These were documented either in isolation or as combined treatments. Treatments received were divided by Stage at diagnosis, patient characteristics, including: age, gender, ethnicity, year diagnosed, comorbidity index, IMD classification, and Cancer Alliances.

Treatment Received for KC by Stage

As Stage data were only available for ccRCC and RCC-NOS, treatments by Stage only relate to these groups. Treatments differed by Stage (Fig. 2). Stage 1–2 KCs were treated almost unanimously with either IT (n = 14 703 [64.2%]) or other treatment (n = 7968 [34.8%]; Fig. 3). There was a reciprocal relationship where the number of patients undergoing any IT reduced from 70.2% to 60.5%, and 'other' treatment rose from 29.1% to 38.8%. Other treatment in the context of Stage 1–2 KC likely reflects active surveillance, suggesting a trend towards more conservative treatment of lower Stage KC; whereas, IT in this context could represent focal therapy or surgical resection.

For Stage 3 KC, a higher proportion of patients underwent IT (n = 6795 [86.2%]) and fewer patients had other treatment (n = 900 [11.4%]; Fig. 2); IT here likely reflects surgical rather than ablative IT (as ablative therapies are not indicated in Stage 3 KC [17]), and other treatment likely represents unfit or frail patients who are unsuitable for IT. Slightly more patients had combined IT and SACT (n = 541 [6.9%]), highlighting the use of neoadjuvant and adjuvant treatment (Fig. 3).

Stage 4 disease had a much broader distribution of treatments (Figs 2,3). The most frequent treatment for patients with Stage 4 KC was any SACT (in isolation or combination; n = 4303 [41.2%]), followed by other treatment (n = 4073 [39.0%]; which likely reflects patients receiving

palliative treatment approaches), and then any RT (n = 2692 [25.8%]). A total of 2339 (22.4%) patients with Stage 4 KC were treated with IT, which reduced over the study period from 24.7% to 18.8%. In total, 1891 (18.1%) patients received SACT only (Fig. 3); this almost doubled from 12.6% in 2013 to 21.8%, which mirrored increases in the use of any SACT (95% CI 35.4–45.8) and likely represents increasing use of tyrosine kinase inhibitors, or indeed a small number of patients being treated with immunotherapies in clinical trials. Unfortunately, data on the type of SACT received were not available. RT use seemed curtailed to those with Stage 4 KC.

Treatment Received for KC by Patient Characteristics

Data regarding the treatment received by patient characteristics are summarised in Fig. 4. The greatest degree of treatment variation was by age and Charlson Comorbidity Index, with increasing proportions of other treatment (although the two were not completely matched). Treatment patterns did not differ by gender, year of diagnosis, or IMD classification. There was a slight difference in treatment based on broad ethnicity, where White patients were treated slightly less frequently with IT (47.4%) than other ethnicities (55.4%).

Treatment Received for Kidney Cancer by Cancer Alliance

There were differences in the treatment of KC by Cancer Alliance (Fig. S11). The South East and North West/South West London had the highest proportion of IT only treatment at 51.9% and 51.7%, respectively. Whereas, Wessex had the lowest proportion of IT only treatment at 43.2% and the highest proportion of other treatment at 43.4%.

Survival Outcomes

Survival data was available for 64 390 patients with KC between 2013 and 2019. There was no change in survival by date of diagnosis (Fig. S12), with an unchanged age-standardised mortality rate of 6.5/100 000 patients.

Survival Outcomes by Patient and Tumour Characteristics

When exploring survival outcomes by Stage, patients with Stage 4 KC had significantly worse survival (ANOVA $P < 0.0001$; Fig. 5). When the Stage 4 KC survival outcomes were mapped by year, outcomes seemed to be worse in 2016 than they were in 2013 (Fig. S13). In terms of histological subtypes of KC, patients diagnosed with RCC-NOS had the poorest survival (ANOVA $P < 0.001$; Fig. 5). There was no difference in age-standardised net survival between men and women (ANOVA $P = 0.94$). Patients from lower IMD class (more deprived) had poorer survival outcomes ($P < 0.001$; Fig. 5).

Survival Outcomes by Geographical Location

Data were available for 1–4 year age-standardised net survival for all Cancer Alliances, which showed a degree of

Fig. 2 Treatment of kidney cancer (KC) in England from 2013 to 2018 by Stage. (**A**) Stage 1–2 (n = 22 885); (**B**) Stage 3 (n = 7879); (**C**) Stage 4 (n = 10 452). IT, invasive treatment (surgery or ablative therapy); SACT, systemic anti-cancer therapy; RT, radiotherapy.

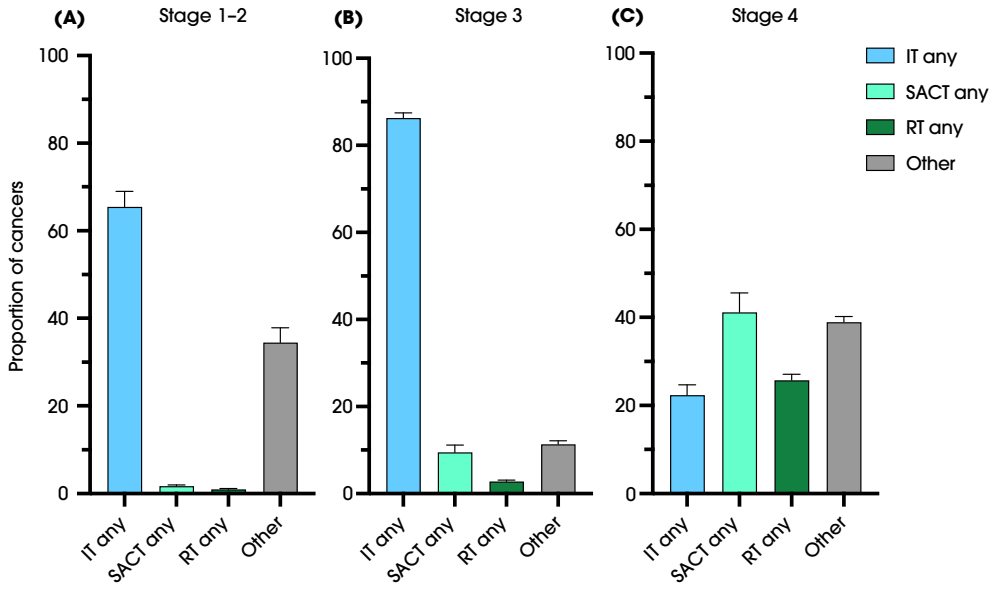
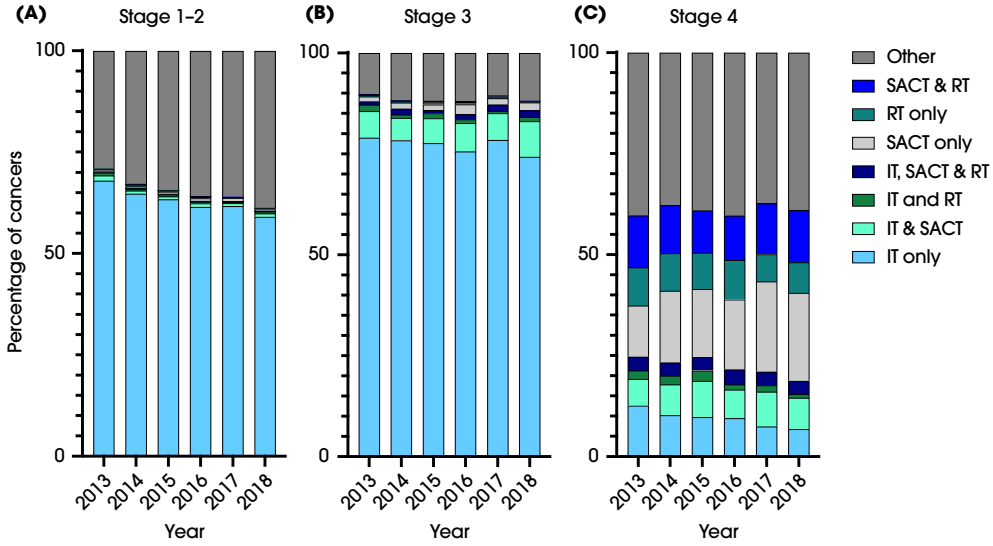


Fig. 3 Combined treatment of KC in England from 2013 to 2018 by Stage. (**A**) Stage 1–2 (n = 22 885); (**B**) Stage 3 (n = 7879); (**C**) Stage 4 (n = 10 452). IT, invasive treatment (surgery or ablative therapy); SACT, systemic anti-cancer therapy; RT, radiotherapy.



geographical variation (Fig. S14). The highest net survival rates (1–4 years) were seen in London (North Central, 81.5% [95% CI 74.0–99.8]; North West and South West, 78.8% [95% CI 71.7–85.9]; and North East, 76.8% [95% CI 68.9–84.6], respectively); whereas the lowest were seen in the East Midlands (70.0% [95% CI 61.1–78.7]), Northern (71.4% [95% CI 62.3–80.4]), and South Yorkshire and Bassetlaw (72.3% [95% CI 63.8–80.9]), respectively.

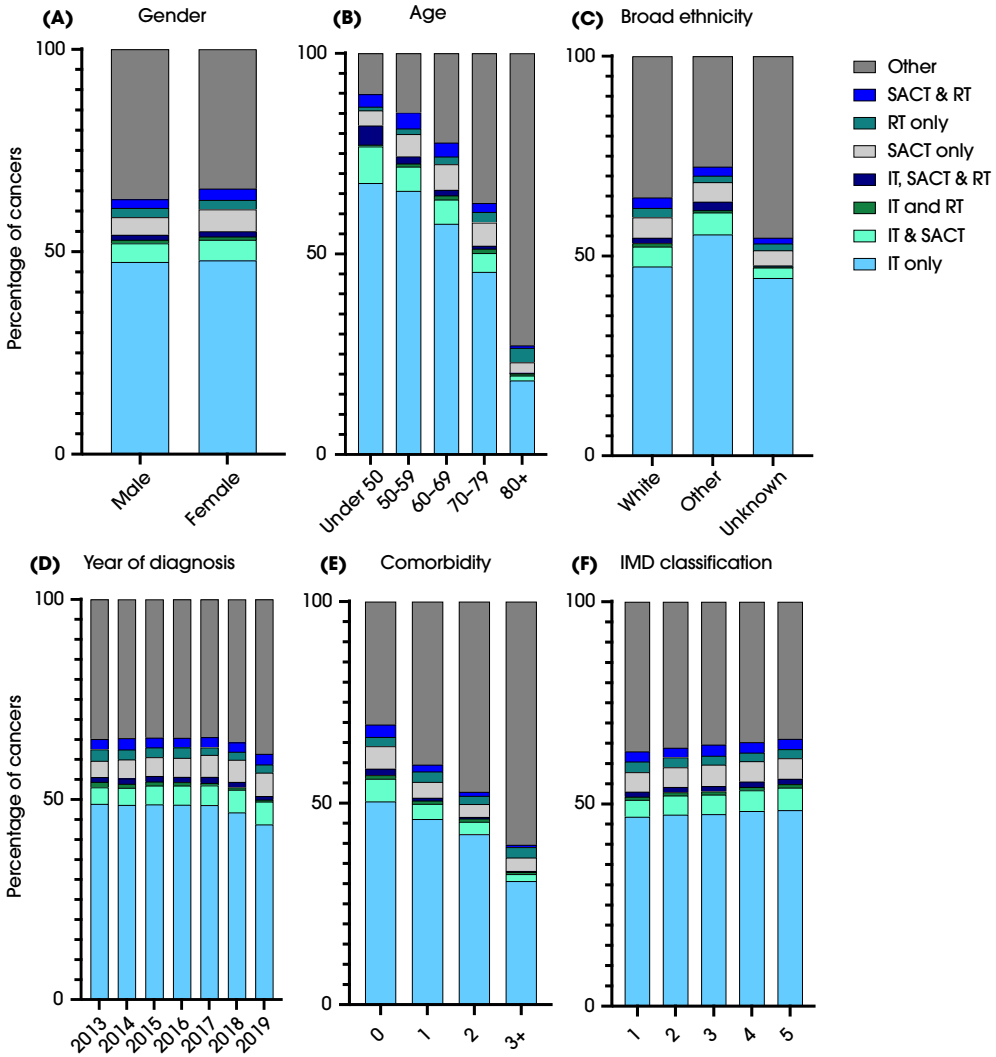
Discussion

Routinely collected, RWD has become increasingly useful in objectively understanding presentation, diagnosis, and treatment of diseases. Through interrogation of the NHSD and NCRAS data resources, we have summarised important information about KC incidence, staging, RTD, treatment, and survival in England. KC incidence has risen 13.7% in England, mirroring global [18–20] and UK trends [19,21], which is likely multifactorial (ageing and growing population; increased cross-sectional imaging; exposure to risk factors) [18]. The change in the ASIR was more modest (18.7–19.4/100 000 people), consistent with a plateaued ASIR in England since 2014 (NHS Cancer Data, Incidence and Mortality) and Western Europe [20]. Despite the rising incidence, there was no clear evidence of Stage migration, unlike trends seen in the United States [22]. However, staging data did not include pRCC and chRCC; had high proportions of unknown Stage—particularly in 2013 and 2019; which was further confounded by subtle changes in T3 TNM subtyping between 2017 and 2018 [14].
In addition, the raw data combined Stage 1 and 2 KCs (T1aN0M0-T3N0M0), which limited downstream subgroup analysis.

Prolonged diagnostic intervals have been associated with poorer survival in cancer [23]. The use of urgent cancer referral pathways (termed 2WW in England) [16,24] increases cancer detection and reduces diagnostic delays [25,26]; thus, interrogation of their real-world application is essential. The 2WW pathways often rely on indicative cancer symptom signatures or validated diagnostic biomarkers. Challenges arise around the 2WW pathway for suspected KC [27], as it has a broad symptom signature [28,29]. The most compelling symptom is visible haematuria, but even this only generates a pooled incidence of KC of 2% (95% CI 1–2%) [30]. Hence, it is unsurprising that only 28.0% (15 472 patients) of the patients with KC were diagnosed through the 2WW pathway and more were diagnosed through non-urgent GP routes (n = 16 814 [30.4%]). Current RTD metrics do not include a category for incidental diagnoses [15], which is common in KC [20,31] and has recently provided scope to identify KCs during other screening studies, such as lung cancer [32]. In this study, there is insufficient clarity by which incidental KC diagnoses have presented, as an incidental KC could fall into one of many routes. For example, when considering older patients (aged >70 years), they were significantly less likely to be diagnosed through 2WW, this could reflect that older patients are more likely to be investigated for other competing comorbidities and may be more likely to receive an incidental diagnosis. Finally, the NHSD RTD datasheet currently does not provide diagnostic interval data for individual routes, which is a critical pathway metric that impacts on patient outcomes and experiences [23].

Another area to explore is the proportion of emergency presentations, as this is associated with worse outcomes [15,33,34], poorer patient experiences [35,36], and is an

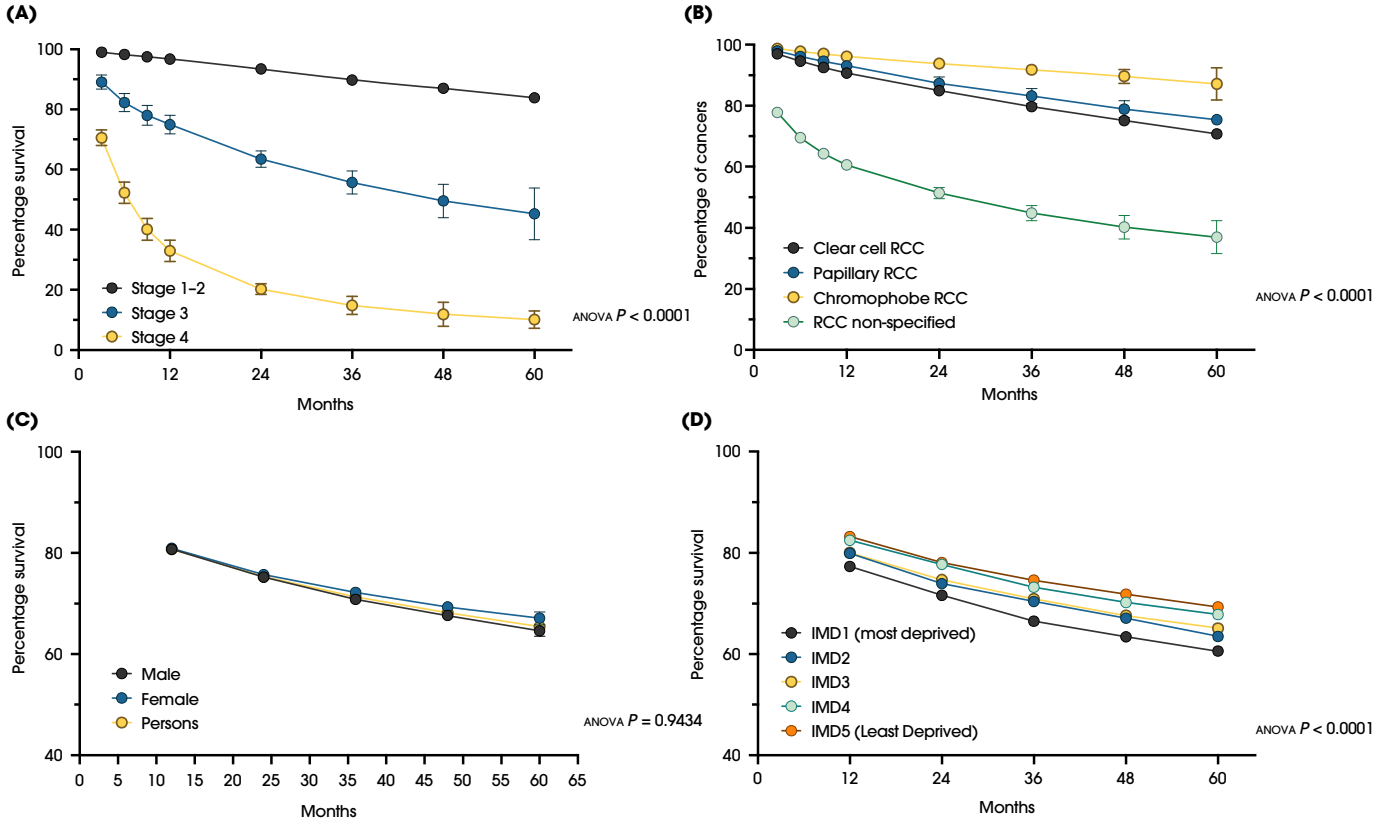
Fig. 4 Treatment of KC in England from 2013 to 2018 by: (**A**) gender; (**B**) age; (**C**) broad ethnicity; (**D**) year of diagnosis; (**E**) Charlson Comorbidity Index; and (**F**) IMD classification. IT - invasive treatment (surgery or ablative therapy; SACT - systemic anti-cancer therapy; RT - radiotherapy.



independent predictor of survival [33]. Over one-fifth of the patients with KC presented through emergency routes (n = 11 796 [21.3%]), which decreased over the study period. It was noted that older patients and patients with more advanced Stage were significantly more likely to present as emergencies, which is consistent across a range of cancers [34,37,38]. This finding could reflect one of two things: patients admitted to hospital symptomatic of another comorbidity, who receive an incidental diagnosis of KC (asymptomatic) during their admission; or emergency admission for a symptomatic KC with local or systemic sequalae. The former most likely reflects the emergency presentation trend by age, and the latter for more advanced Stages of KC. Nonetheless, further evaluation of the underlying mechanisms of these presentation in KC are warranted.

The landscape of KC treatment has changed dramatically in the last 20 years [17]. In this study, treatment by Stage was mapped against international guideline recommendations [17,39]. There were several interesting trends noted. Firstly, in patients with Stage 1–2 KC there was a reduction in the proportion of patients having IT and increased other treatment; this likely reflects increased uptake of active surveillance in selected patients [40,41] or a tendency towards expectant management in patients with low cancer-specific mortality and competing comorbidity [42]. Very few patients with Stage 1–2 (n = 213 [0.9%]) or indeed Stage 3 (n = 231 [2.8%]) KC received RT (Fig. 2); however, this may change in future considering recent developments in stereotactic ablative RT techniques [43]. Secondly, the number of patients receiving SACT either in isolation or in combination was increasing in patients with Stage 4 KC. Recent randomised trials have shown

Fig. 5 Overall survival plotted using the Kaplan–Meier method for patients with KC with respect to: (**A**) KC Stage; (**B**) KC histological subtype; (**C**) sex; and (**D**) IMD social deprivation index.



improved survival for patients with metastatic RCC treated with dual immunotherapy or combined targeted and immunotherapy [44–47]; however, this report pre-dates many of those clinical trials [48]. Hence, changes in SACT treatment likely reflect changes in targeted therapy use, as sunitinib (National Institute for Health and Care Excellence [NICE] Technology Appraisal [TA]-169), pazopanib (NICE TA-215), were approved as first-line treatment in 2009 and 2011, and axitinib as second-line treatment (NICE TA-333) in 2015 for metastatic RCC by NICE. In addition, some patients may have received combined targeted and immunotherapy or dual immunotherapy SACT as part of NICE evaluations or clinical trials. Finally, IT for patients with Stage 4 KC was high at 22.4%, albeit decreasing over the study duration. Again, the Cancer du Rein Metastatique Nephrectomie et Antiangiogéniques (CARMENA) trial showing non-inferiority of sunitinib compared to sunitinib and cytoreductive nephrectomy was only published in 2018 [49]; thus, changes in surgical practice in this study largely pre-date this and may reflect a clinical paradigm shift towards systemic therapies in these patients. There were notable differences in treatment by age, Charlson Comorbidity Index, ethnicity, and geographical location.

Survival outcomes did not differ by gender similar to previous reports of KC survival in England [50]. It was noted that survival rates worsened with increasing levels of deprivation; this is a consistent finding across all cancers [50,51]. However, many other factors, which are unavailable in this dataset could influence this, such as, KC Stage and competing comorbidity. Nonetheless, this warrants further investigation into how socioeconomic disparities lead to such health inequality. As anticipated, more advanced Stage was associated with poorer survival, most notably for patients with Stage 4 KC, whose survival outcomes seemed to be worsening rather than improving (Fig. S14). Although this finding is unexpected, it is important to note that, often SACT treatment in patients with advanced KC is limited to patients with good performance status (0/1); whereas, in some other cancers treated with hormonal therapy, patients with poorer performance status may still receive life-prolonging SACT. Hence, this may contribute to the lack of progression in clinical outcomes in patients with Stage 4 KC. Of the histological subtypes, chRCC had the most favourable survival, followed by pRCC, and ccRCC. The RCC-NOS group had the poorest outcomes; as the majority did not have a histological report available, this group may include patients

with poor performance status, who were managed expectantly, in whom a biopsy was not appropriate. There was also geographical variation in the 1–4 year survival outcomes by Cancer Alliance, with an absolute difference of 11.5% from highest to lowest (mean survival East Midland = 70.0% to North Central London = 81.5%); however, this was not adjusted for confounding variables, e.g., deprivation indices.

Limitations

Although this report provides useful information, we must disclose the various limitations that exist. Firstly, the granularity of this large, population-based, RWD study is lacking. For example, OPCS-4 coded surgical procedures for KC are broad, including focal therapy, partial, total, and open nephrectomy, which were not divisible in the dataset; similarly, data for type of SACT (targeted therapy or immunotherapy) and the number of lines of therapy received were not available. Hence, more in depth treatment pattern changes could not be explored. Secondly, the data were incomplete or missing for some variables of interest, e.g., over one-quarter of the cohort had unknown or undisclosed staging data and histological RCC subtype data were not available for almost half of patients—hence why the proportion of ccRCC was lower than expected. This could reflect poor local data collection or submission quality, although NCRAS have detailed quality assurance protocols [52]; alternatively it could represent patients who are unfit for IT, SACT, or RT in whom tissue collection may not change clinical management. In addition, the retrospective data annotation performed by NHSD led to high numbers of missing Stage data in 2019.

Thirdly, grouping of data by the NHSD GDO steering panel created barriers to more in-depth evaluation, e.g., Stage 1–2 KCs were combined, meaning their data could not be interrogated independently; in addition, pRCCs were not divided by subtype. One of the most crucial, is the concern that the current RTD classifiers do not map well onto how patients with KC present in practice. In particular, with respect to the uncertainty of where patients with incidental diagnoses lie, and the fact that many diagnosed under the umbrella of 'emergency' presentation may be presenting with symptoms unrelated to their KC. We also note that the study period pre-dates many practice-changing clinical trials [44–47,49] and as such, this report may not represent the current landscape of treatments being delivered to patients in England in 2023. Crucially, individual biological factors, patient characteristics, and institutional working patterns can only be explored in isolation, meaning that relationships between them are lacking.

Nonetheless, this report provides a summary of large, population-wide, objective datasets and the data presented may be a useful resource to clinicians, institutions, and patients. In particular, we highlight the need for further research into the mechanisms by which patients with KC present, their presenting symptom signatures (if any), diagnostic intervals, and the potential need for further subclassification of RTD. The limitations highlighted stress the need for greater data granularity in the primary NHSD publications, with improved integration of valuable clinical information, such as performance status; as well as, involvement of patients in deciding on the key information that is routinely collected. This report provides data analysis preceding that of the most recently commissioned National Kidney Cancer Audit (National Cancer Audit Collaborating Centre) and allows benchmarking for comparisons to be made.

Conclusions

This NHSD resource provides insight about KC incidence, RTD, treatment, and survival trends in England. Key limitations in the data exist when evaluating the KC RTD; in particular, the lack of incidental diagnosis classification and uncertainty about asymptomatic KC diagnoses made during emergency admissions for competing comorbidities. Importantly, survival outcomes remain relatively unchanged; these may improve with the more recent introduction of systemic immunotherapies not captured in this dataset.

Author Contributions

Samantha Conroy had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of analysis. Concept and design: Samantha Conroy, James W.F. Catto, and Marcus G. Cumberbatch. Acquisition, analysis, or interpretation of data: Samantha Conroy, James W.F. Catto, Axel Bex, Janet E. Brown, Alison Fielding, Rob J. Jones, Vincent Khoo, David Nicol, Grant D. Stewart, Mark Sullivan, Maxine G.B. Tran, Rose Woodward, and Marcus G. Cumberbatch. Drafting of the manuscript: Samantha Conroy, James W.F. Catto, and Marcus G. Cumberbatch drafted the initial manuscript. All authors then read, edited, and commented on the manuscript.

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Disclosure of Interests

James W.F. Catto reported receiving reimbursement for consultancy from AstraZeneca, Ferring, Roche, and Janssen; speaker fees from Bristol Myers Squibb, Pfizer, Merck Sharp & Dohme, Janssen, Astellas, Nucleix, and Roche; honoraria for membership in advisory boards from Ferring, Roche, Gilead, Photocure, Bristol Myers Squibb, QED Therapeutics, and Janssen; and research funding from Roche. Axel Bex is the recipient of a restricted educational grant from Pfizer for a neoadjuvant trial; a steering committee member on adjuvant trials from BMS and Roche/Genentech and has taken part in advisory boards from Ipsen. Grant D. Stewart has received educational grants from Pfizer, AstraZeneca and Intuitive Surgical; consultancy fees from Pfizer, Merck, EUSA Pharma and CMR Surgical; Travel expenses from Pfizer and Speaker fees from Pfizer. Maxine G.B. Tran has received consultancy fees from MSD and Boston Scientific. Janet E. Brown reports having served as a consultant or adviser for Novartis, Ipsen, Amgen, Merck Sharp & Dohme, Bristol-Myers Squibb, and Bayer; honoraria from Novartis, Ipsen, Amgen, Merck Sharp & Dohme, Bristol-Myers Squibb, and Bayer; and travel expenses from Ipsen. Rob J. Jones received consulting and speaker fees from Novartis, Pfizer, Merck Serono, MSD, Roche, Ipsen, and Bristol Myers Squibb. VK receives fees from Accuray, Astellas, Bayer, and Boston Scientific. Axel Bex receives consulting fees from Roche, BMS, and Ipsen. MGC receives consulting fees from Ipsen, Janssen, and Pfizer. RW is a patient, Founder of the ACTION KIDNEY CANCER charity, and Founding Board Director of the International Kidney Cancer Coalition. Alison Fielding is a patient, consumer member of the National Cancer Research Institute (NCRI) Consumer Forum and member of the NCRI Bladder and Renal Group.

References

1 **Sung H, Ferlay J, Siegel RL et al.** Global cancer statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. *CA Cancer J Clin* 2021; 71: 209–49
2 **Bukavina L, Bensalah K, Bray F et al.** Epidemiology of renal cell carcinoma: 2022 update. *Eur Urol* 2022; 82: 529–42
3 **Capitanio U, Bensalah K, Bex A et al.** Epidemiology of renal cell carcinoma. *Eur Urol* 2019; 75: 74–84
4 **Shuch B, Vourganti S, Ricketts CJ et al.** Defining early-onset kidney cancer: implications for germline and somatic mutation testing and clinical management. *J Clin Oncol* 2014; 32: 431–7
5 **Smittenaar CR, Petersen KA, Stewart K, Moitt N.** Cancer incidence and mortality projections in the UK until 2035. *Br J Cancer* 2016; 115: 1147
6 **Cancer Research UK.** Kidney cancer mortality statistics [Internet]. Available at: https://www.cancerresearchuk.org/health-professional/cancer-statistics/statistics-by-cancer-type/kidney-cancer/mortality#heading-Two. Accessed April 2023
7 **Saunders CL, Abel GA, Lyratzopoulos G.** Inequalities in reported cancer patient experience by socio-demographic characteristic and cancer site: evidence from respondents to the English cancer patient experience survey. *Eur J Cancer Care (Engl)* 2015; 24: 85–98
8 **Penberthy LT, Rivera DR, Lund JL, Bruno MA, Meyer A-M.** An overview of real-world data sources for oncology and considerations for research. *CA Cancer J Clin* 2022; 72: 287–300
9 **Bartlett VL, Dhruva SS, Shah ND, Ryan P, Ross JS.** Feasibility of using real-world data to replicate clinical trial evidence. *JAMA Netw Open* 2019; 2: e1912869
10 **Healthcare Quality Improvement Partnership (NHS England).** National Cancer Audit Collaborating Centre, 2021. Available at: https://www.rcseng.ac.uk/standards-and-research/research/clinical-effectiveness-unit/national-cancer-audit-collaborating-centre/. Accessed April 2023
11 **Catto JWF, Mandrik O, Quayle LA et al.** Diagnosis, treatment and survival from bladder, upper urinary tract, and urethral cancers: real-world findings from NHS England between 2013 and 2019. *BJU Int* 2023; 12: 14
12 **Henson KE, Elliss-Brookes L, Coupland VH et al.** Data resource profile: national cancer registration dataset in England. *Int J Epidemiol* 2020; 49: 16–16h
13 **NHS Digital.** Data collection and quality assurance of administrative data about the NDRS, 2021
14 **Swami U, Nussenzveig RH, Haaland B, Agarwal N.** Revisiting AJCC TNM staging for renal cell carcinoma: quest for improvement. *Ann Transl Med* 2019; 7(Suppl 1): S18
15 **Elliss-Brookes L, McPhail S, Ives A et al.** Routes to diagnosis for cancer – determining the patient journey using multiple routine data sets. *Br J Cancer* 2012; 107: 1220
16 **NICE Guideline.** *Suspected Cancer: Recognition and Referral.* NICE Guideline, 2015: 1–378. Available at: https://www.nice.org.uk/guidance/ng12. Accessed April 2023
17 **Ljunberg B, Albiges L, Bedke J et al.** EAU guidelines on: renal cell carcinoma, 2022
18 **Fitzmaurice C, Abate D, Abbasi N et al.** Global, regional, and national cancer incidence, mortality, years of life lost, years lived with disability, and disability-adjusted life-years for 29 cancer groups, 1990–2017: a systematic analysis for the global burden of disease study. *JAMA Oncol* 2019; 5: 1749–68
19 **Wong MCS, Goggins WB, Yip BHK et al.** Incidence and mortality of kidney cancer: temporal patterns and global trends in 39 countries. *Sci Rep* 2017; 7: 15698
20 **Znaor A, Lortet-Tieulent J, Laversanne M, Jemal A, Bray F.** International variations and trends in renal cell carcinoma incidence and mortality. *Eur Urol* 2015; 67: 519–30

21 **Du Z**, **Chen W**, **Xia Q**, **Shi O**, **Chen Q**. Trends and projections of kidney cancer incidence at the global and national levels, 1990–2030: a Bayesian age-period-cohort modeling study. *Biomark Res* 2020; 8: 1–0

22 **Patel HD**, **Gupta M**, **Joice GA et al.** Clinical stage migration and survival for renal cell carcinoma in the United States. *Eur Urol Oncol* 2019; 2: 343–8

23 **Tørring ML**, **Frydenberg M**, **Hansen RP**, **Olesen F**, **Vedsted P**. Evidence of increasing mortality with longer diagnostic intervals for five common cancers: a cohort study in primary care. *Eur J Cancer* 2013; 49: 2187–98

24 **Department of Health**. The NHS Cancer Plan, 2000

25 **Round T**, **Ashworth M**, **Esperance VL**, **Moller H**. Cancer detection via primary care urgent referral and association with practice characteristics: a retrospective cross-sectional study in England from 2009/2010 to 2018/2019. *Br J Gen Pract* 2021; 71: e826–35

26 **Neal RD**, **Tharmanathan P**, **France B et al.** Is increased time to diagnosis and treatment in symptomatic cancer associated with poorer outcomes? Systematic review. *Br J Cancer* 2015; 112: S92–107

27 **Zhou Y**, **Van Melle M**, **Singh H**, **Hamilton W**, **Lyratzopoulos G**, **Walter FM**. Quality of the diagnostic process in patients presenting with symptoms suggestive of bladder or kidney cancer: a systematic review. *BMJ Open* 2019; 9: e029143

28 **Koo MM**, **Hamilton W**, **Walter FM**, **Rubin GP**, **Lyratzopoulos G**. Symptom signatures and diagnostic timeliness in cancer patients: a review of current evidence. *Neoplasia* 2018; 20: 165–74

29 **Koo MM**, **Swann R**, **McPhail S et al.** Presenting symptoms of cancer and stage at diagnosis: evidence from a cross-sectional, population-based study. *Lancet Oncol* 2020; 21: 73–9

30 **Rai BP**, **Luis Dominguez Escrig J**, **Vale L et al.** Systematic review of the incidence of and risk factors for urothelial cancers and renal cell carcinoma among patients with Haematuria. *Eur Urol* 2022; 82: 182–92

31 **Vasudev NS**, **Wilson M**, **Stewart GD et al.** Challenges of early renal cancer detection: Symptom patterns and incidental diagnosis rate in a multicentre prospective UK cohort of patients presenting with suspected renal cancer. *BMJ Open* 2020; 10: e035938

32 **Harrison H**, **Wood A**, **Pennells L et al.** Estimating the effectiveness of kidney cancer screening within lung cancer screening programmes: a validation in UK biobank. *Eur Urol Oncol* 2023; 6: 351–3

33 **Mcphail S**, **Elliss-Brookes L**, **Shelton J et al.** Emergency presentation of cancer and short-term mortality. *Br J Cancer* 2013; 109: 2027

34 **McPhail S**, **Swann R**, **Johnson SA et al.** Risk factors and prognostic implications of diagnosis of cancer within 30 days after an emergency hospital admission (emergency presentation): an international cancer benchmarking partnership (ICBP) population-based study. *Lancet Oncol* 2022; 23: 587–600

35 **Salika T**, **Abel GA**, **Mendonca SC et al.** Associations between diagnostic pathways and care experience in colorectal cancer: evidence from patient-reported data. *Frontline Gastroenterol* 2018; 9: 241–8

36 **Alessy SA**, **Alhajji M**, **Rawlinson J**, **Baker M**, **Davies EA**. Factors influencing cancer patients' experiences of care in the USA, United Kingdom, and Canada: a systematic review. *eClinicalMedicine* 2022; 47: 101405

37 **Herbert A**, **Abel GA**, **Winters S**, **McPhail S**, **Elliss-Brookes L**, **Lyratzopoulos G**. Are inequalities in cancer diagnosis through emergency presentation narrowing, widening or remaining unchanged? Longitudinal analysis of English population-based data 2006–2013. *J Epidemiol Community Heal* 2019; 73: 3–10

38 **Abel GA**, **Shelton J**, **Johnson S**, **Elliss-Brookes L**, **Lyratzopoulos G**. Cancer-specific variation in emergency presentation by sex, age and deprivation across 27 common and rarer cancers. *Br J Cancer* 2015; 112 (Suppl 1): S129

39 **Campbell SC**, **Clark PE**, **Chang SS**, **Karam JA**, **Souter L**, **Uzzo RG**. Renal mass and localized renal cancer: evaluation, management, and follow-up: AUA guideline: Part I. *J Urol [Internet]*. 2021; 206: 199–208

40 **Jewett MAS**, **Mattar K**, **Basiuk J et al.** Active surveillance of small renal masses: progression patterns of early stage kidney cancer. *Eur Urol* 2011; 60: 39–44

41 **McIntosh AG**, **Ristau BT**, **Ruth K et al.** Active surveillance for localized renal masses: tumor growth, delayed intervention rates, and >5-yr clinical outcomes. *Eur Urol* 2018; 74: 157–64

42 **Kutikov A**, **Egleston BL**, **Canter D**, **Smaldone MC**, **Wong YN**, **Uzzo RG**. Competing risks of death in patients with localized renal cell carcinoma: a comorbidity based model. *J Urol* 2012; 188: 2077–83

43 **Hannan R**, **McLaughlin MF**, **Pop LM et al.** Phase 2 trial of stereotactic ablative radiotherapy for patients with primary renal cancer. *Eur Urol* 2023: S0302-2838(23)02625-8. https://doi.org/10.1016/j.eururo.2023.02.016

44 **Motzer RJ**, **Tannir NM**, **McDermott DF et al.** Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Engl J Med* 2018; 378: 1277–90

45 **Choueiri TK**, **Powles T**, **Burotto M et al.** Nivolumab plus cabozantinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med* 2021; 384: 829–41

46 **Rini BI**, **Plimack ER**, **Stus V et al.** Pembrolizumab plus axitinib versus sunitinib for advanced renal-cell carcinoma. *N Engl J Med* 2019; 380: 1116–27

47 **Motzer R**, **Alekseev B**, **Rha S-Y et al.** Lenvatinib plus pembrolizumab or everolimus for advanced renal cell carcinoma. *N Engl J Med* 2021; 384: 1289–300

48 **Department of Health**. Accelerated access review: review of innovative medicines and medical technologies, 2016. Available at: www.nationalarchives.gov.uk/doc/open-government-licence/. Accessed April 2023

49 **Méjean A**, **Ravaud A**, **Thezenas S et al.** Sunitinib alone or after nephrectomy in metastatic renal-cell carcinoma. *N Engl J Med* 2018; 379: 417–27

50 **Exarchakou A**, **Kipourou DK**, **Belot A**, **Rachet B**. Socio-economic inequalities in cancer survival: How do they translate into number of life-years lost? *Br J Cancer* 2022; 126: 1490–8

51 **Singh GK**, **Jemal A**. Socioeconomic and racial/ethnic disparities in cancer mortality, incidence, and survival in the United States, 1950–2014: over six decades of changing patterns and widening inequalities. *J Environ Public Health* 2017; 2017: 1–9

52 **The National Cancer Registration and Analysis Service**. Data collection and quality assurance of administrative data – GOV.UK [Internet], 2021. Available at: https://www.gov.uk/government/publications/ncras-statistical-publications-quality-and-methodology-information/data-collection-and-quality-assurance-of-administrative-data#accuracy-and-quality-of-data-and-estimates. Accessed April 2023

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Abbreviations: 2WW, 2-week-wait pathway; ccRCC, clear cell RCC; chRCC, chromophobe RCC; GDO, Get Data Out; ICD-10, International Classification of Diseases, 10th edition; ICD-O-3.1, International Classification of Diseases for Oncology, third edition, first revision; IMD, Index of Multiple Deprivation; IT, invasive treatment (surgery or ablative therapy); KC, kidney cancer; NCRAS, National Cancer Registry and Analysis Service; NCRI, National Cancer Research Institute; NHSD, NHS Digital; NICE, National Institute for Health and Care Excellence; NIHR, National

Institute for Health and Care Research; OPCS-4, Office of Population Censuses and Surveys Classification of Surgical Operations and Procedures, version 4; pRCC, papillary RCC; RCC-NOS, RCC non-specified; RT, radiotherapy; RTD, route to diagnosis; RWD, real-world data; SACT, systemic anti-cancer therapy; TA, Technology Appraisal.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. Source data used in this report.

Table S1. New KC diagnoses between 2013 and 2019 in England by Stage.

Fig. S1. Number of new KC diagnoses in England between 2013 and 2019 by Stage.

Fig. S2. Diagnoses of KC between 2013 and 2019 by Stage and histological subtype in England.

Fig. S3. The 10-year prevalence of KC compared to other cancers in 2019 in England.

Fig. S4. The 5-, 10- and 20-year prevalence of KC in 2019 in England by: (**A**) gender (rate per 100 000 population); (**B**) age (rate per 100 000 population); 5- and 10-year prevalence counts of KC by: (**C**) ethnicity (counts); and 5-, 10- and 20-year prevalence counts by: (**D**) IMD class (counts).

Fig. S5. The RTD of KC between 2013 and 2018 by age.

Fig. S6. Violin plots of RTD of KC by age for: (**A**) 2WW; (**B**) GP referral; (**C**) 'other' outpatient, (**D**) emergency.

Fig. S7. The RTD of KC between 2013 and 2018 by Stage.

Fig. S8. Violin plots of RTD of KC by Stage for: (**A**) 2WW; (**B**) GP referral, (**C**) 'other' outpatient, (**D**) emergency.

Fig. S9. The RTD of KC between 2013 and 2018 by histological subtype.

Fig. S10. Violin plots of RTD of KC by subtype for: (**A**) 2WW; (**B**) GP referral, (**C**) 'other' outpatient, (**D**) emergency.

Fig. S11. Treatment of patients with KC in England by Cancer Alliance, showing geographical variation.

Fig. S12. Kaplan–Meier survival estimates of overall survival in patients with KC by year of diagnosis.

Fig. S13. Kaplan–Meier survival estimates of overall survival in patients with Stage 4 KC by year of diagnosis from 2013 to 2016 (complete data for 48-month outcomes).

Fig. S14. Age-standardised 1–4 year net survival estimates by Cancer Alliance in England.