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The epidemiology of hospitalised acute kidney injury not requiring dialysis in England from 1998 to 2013: retrospective analysis of hospital episode statistics

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Disclosure
The authors have declared that no competing interests exist.

SUMMARY

Aims: Epidemiology studies of acute kidney injury (AKI) have focused on cases requiring dialysis but those not requiring dialysis represent the majority. To address this gap, we interrogated hospital episode statistics (HES) to investigate population trends in temporal epidemiology of AKI not requiring dialysis between 1998 and 2013. **Methodology:** In this retrospective observational study of HES data covering the entire English National Health Service, we identified 1,136,167 AKI events, not requiring dialysis, diagnosed between 1998 and 2013. We explored the effect of age, gender, ethnicity, Charlson's comorbidity score (CCS), method of admission, diagnosis period and AKI in diagnosis codes on temporal changes in the incidence and case-fatality of AKI with specific examination of its predictors. **Result:** The incidence of AKI increased from 15,463 cases (317 pmp) in 1998–1999 to 213,700 cases (3995 pmp) in 2012–2013. There was increase in proportion of people over 75 years from 51.1% in 1998–1999 to 63.4% in 2012–2013. Overall unadjusted case-fatality decreased from 42.3% in 1998–2003 to 27.1% in 2008–2013, $p < 0.001$. Compared with 1998–2003, the multivariable adjusted odds ratio for death was 0.64 in 2003–2008 (95% CI 0.63–0.65) and 0.35 in 2008–2013 (95% CI 0.34–0.35). Odds for death were higher for patients over 85 years (2.93; 95% CI 2.89–2.97), CCS of more than five (2.75; 95% CI 2.71–2.79), emergency admissions (2.14; 95% CI 2.09–2.18) and AKI in the secondary diagnosis code (1.35; 95% CI 1.33–1.36) and AKI in other diagnoses codes (2.17; 95% CI 2.15–2.20). **Conclusions:** In England, the incidence of AKI not requiring dialysis has increased and case-fatality has decreased over last 15 years. Efforts to reduce the incidence of AKI and improve survival should focus on elderly people, emergency admissions and those with multi-morbidity.

What's known
Temporal epidemiology of acute kidney injury (AKI) not requiring dialysis has been studied only in United States. Most epidemiological studies tend to focus primarily on dialysis requiring AKI and there is no data regarding population epidemiology of AKI not requiring dialysis in England

What's new
This is the first study describing temporal epidemiology of AKI not requiring dialysis in England using national database. Our study has shown that the incidence of AKI not requiring dialysis has increased in England by more than twelve folds and though the case-fatality has decreased it has remained unacceptably high.

Introduction

The International Society of Nephrology (ISN) has recognised acute kidney injury (AKI) as an important cause of death worldwide and has launched a campaign to eradicate preventable death because of AKI in developing countries by 2025 (1). Nevertheless, previous studies indicate that the incidence of AKI is also increasing in developed countries and remains a significant challenge (2–4). To this effect, National Health Service (NHS) in England has launched Acute Kidney Injury Programme, with a primary aim to reduce the risk and burden of AKI (5). It is therefore important to gain a more comprehensive understanding of the epidemiology AKI in all countries to inform strategies to reduce incidence and improve outcomes. Information on AKI and its associated case-fatality in populations from different regions of the world is fragmentary and quite often, inconsistent (6). Moreover, there are no epidemiological studies, other than from USA, describing the temporal epidemiology of AKI (3,4). Previous published studies in developed countries lack population coverage as they are based on selected samples of hospital patients reported in billing or administrative databases or located in selected clinical locations. Also, epidemiological studies tend to focus primarily on dialysis requiring AKI (7–9). In recent years, there has been a paradigm shift in understanding of the effect of a relatively small rise in creatinine, which has led to the introduction of a standardised definition and classification of AKI (10). Despite this, no

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study has examined national trends in the incidence and case-fatality of AKI after the introduction of RIFLE and the Acute Kidney Injury Network (AKIN) classification and staging system for AKI (11,12). A crucial feature of the healthcare system in England is that it is universal, funded from taxation and has a national database of all hospital admissions, which gives an opportunity to compare and study populations of different demographic composition (13). We have recently investigated the epidemiology of AKI severe enough to require dialysis using Hospital Episode Statistics (HES) dataset in England (14). To address the gap in the literature regarding AKI not severe enough to require dialysis, we combined a national database of all hospital discharges with national census data to investigate population trends and the associated case-fatality as well as their determinants in England between 1998 and 2013.

Methods

Data source

We extracted data from the HES repository for the years 1998 through 2012. These data warehouse contain details of all admissions, outpatient appointments and A&E attendances at NHS hospitals in England (15). HES collects a detailed record for each admitted patient care delivered in England, either by NHS hospitals, primary care trusts, mental health trusts or delivered in the independent sector but commissioned by the NHS. The study protocol was examined by the local research and development department and the National Research Ethics Committee, East of England – Cambridge Central and was deemed exempt from ethical approval because the research involved non-identifiable information, previously collected in the course of normal care and available for public use. The study was conducted according to the principles expressed in the Declaration of Helsinki.

Definitions

We identified all cases of AKI by using validated International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) codes in all diagnoses codes in keeping with the objective of the study. Patients with the following codes in any of the diagnoses codes were included: N17.0 for acute renal failure (ARF) with tubular necrosis, N17.1 for ARF with acute cortical necrosis, N17.2 for ARF with medullary necrosis, N17.8 for other ARF and N17.9 for ARF, unspecified. ARF has been replaced by new terminology, AKI, but due to a lack of ICD10 codes for AKI, we used the ICD10 codes for ARF and henceforth, will be referred to as AKI in this study. In addition to demographic data, we extracted secondary diagnoses from 20 available diagnoses codes and 24 available procedure codes based on the Office of Population Censuses and Surveys Classification of Interventions and Procedures, 4th revision (OPCS-4). We also excluded ICD10 codes for chronic kidney disease stage 5 and end stage renal disease along with OPCS code X40.2 for peritoneal dialysis, X40.3 for hemodialysis, X40.4 for hemofiltration and X40.5 for automated peritoneal dialysis and X40.6 for continuous ambulatory peritoneal dialysis in any of the 24 OPCS-4 codes (Figure 1).

Outcome measures

We obtained data on patient demographics, hospital characteristics, in-hospital case-fatality, disposition, length of stay (LOS) and up to 20 diagnosis and 24 procedure codes that are based on the ICD-10-CM and OPCS-4 from the HES database. To calculate population incidence of AKI not requiring dialysis, we obtained mid-year populations of England in each year from 1998 to 2013 from the Office of National Statistics (ONS). We also obtained mean age, LOS and mortality of all patients in England and also of those, who did not have AKI from 1998–1999 to 2012–2013.

Validation

The National Confidential Enquiry of Perioperative Outcome and Death (NCEPOD) undertook a validation of the ICD-10 codes against RIFLE criteria in 2007 when they studied the process of care of patients who died of AKI in NHS hospitals in England (16). Against this standard, the code N17 in 2007 had 74.1% sensitivity, 96% specificity, 90.9% positive predictive value and 87.2% negative predictive value for identifying AKI. Similarly, another study performed in England examined the validity of ICD-10 N17 codes against the KDIGO criteria for AKI occurring in 2005 and 2010 (17). They estimated the positive predictive value of ICD-10 N17 codes to be 95% (95% CI 91–99) in 2005 and 95% in 2010 (95% CI 88–100) with no suggestion of marked changes in coding of AKI between 2005 and 2010.

Statistical analysis

All analyses were performed using Stata Statistical Software: Release 13 (StataCorp LP, College Station, TX). Data were divided into three 5-year periods (April 1988 to March 2003, April 2003 to March 2008 and April 2008 to March 2013) and also presented by individual year. Age was categorised into the groups < 65, 65–74, 75–84 and > 85. Charlson's comorbidity scores (CCS) greater than 5 were grouped into one category (18). Method of admis-

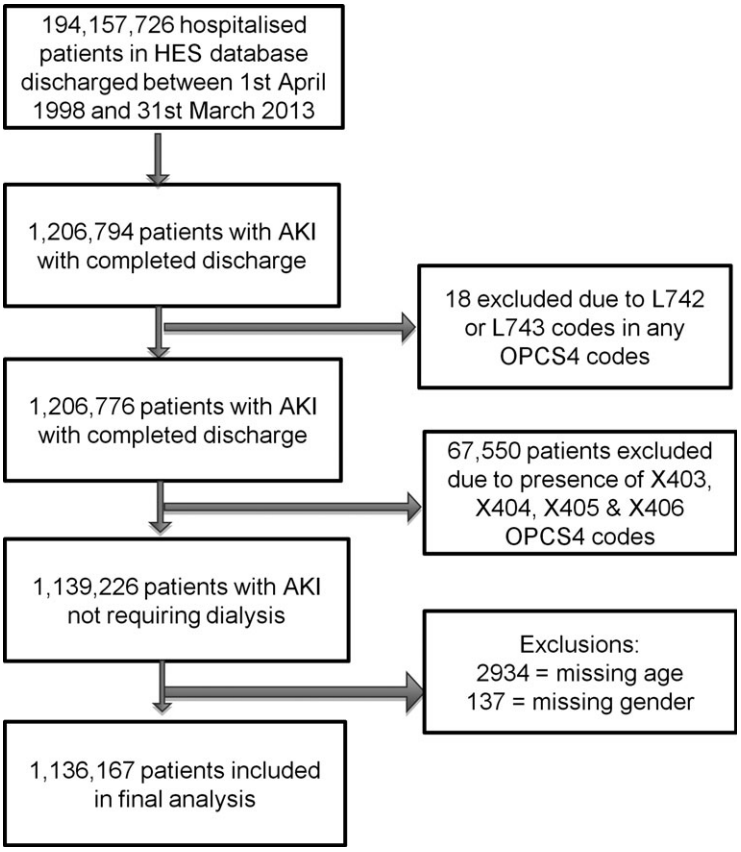

Figure 1 Study flow chart

sion was defined as one of elective admission; emergency admission; maternity admission; other admission or unknown. Ethnicity was grouped as White, Mixed, Asian, Black, other ethnic groups and ethnicity not stated/unknown. AKI in diagnoses codes were categorised as 'AKI in primary diagnosis code', 'AKI in secondary diagnosis code' and 'AKI in all other diagnoses codes'. Continuous variables were expressed as mean with 95% confidence interval (CI); these were compared with the *t*-test under the Central Limit Theorem instead of the Mann–Whitney *U*-test. Categorical variables were expressed as proportions and compared with the chi square test. The associations between discharge status (dead or alive) and gender, age group, period of admission, method of admission, CCS, ethnicity and AKI in diagnosis codes were analysed initially using univariate logistic regression. Multivariate logistic regression was then considered to assess the relative contributions of all these variables simultaneously. Patients with missing data were excluded from analysis.

Sensitivity analysis

The analysis was performed with and without the unknown ethnicity and was repeated separately for all ethnicities and after excluding all patients where ethnicity was not known. We determined whether there was a difference in the effect size with improvement in ethnicity recording in HES (Supplementary file, Table S2). We also performed sensitivity analysis to project estimated cases of AKI with the assumption of constant population incidence of AKI and a sensitivity for ICD-10 N17 code of 74% as identified in NCEPOD study (Table S1). This study is registered with clinicaltrials.gov, number NCT02216695.

Results

Incidence

Between 1 April 1998 and 31 March 2013, there were 1,139,226 coded AKI events, which did not require dialysis in 194,157,726 hospitalised patients in England (Figure 1). Data were incomplete in a small number of patients with AKI, which were excluded from analysis, leaving 1,136,167 for final analysis: age in 2922 cases, age and gender in 12 cases and gender in 125 cases. The number of cases of hospitalised AKI patients increased from 15,463 in 1998–1999 to 213,700 in 2012–2013. The population incidence of hospitalised AKI increased from 317 per million peo-

ple (pmp) in 1998 to 3995 pmp in 2013 (Figure 2). While AKI coded in primary and secondary diagnoses codes decreased in 2003–2008 and 2008–2013, AKI coded in other diagnoses codes increased in both the later 5-year periods (Table 1).

Demographics

Table 1 shows the characteristics of the AKI events over the study period. Compared with 1998–1999, AKI events increased in all age groups, ethnicity and gender. There was a decline in the proportion of males among those developing AKI over the 15-year period. In the AKI population, the proportion of people over 75 years increased from 51.3% in 1998–2003 to 64.3% in 2008–2013 (Figure 3). Coding for ethnicity improved from 1998–2003 to 2008–2013, with 5.5% in the category of 'Not known' in 2008–2013 as compared to 33.7% in 1998–2003. This may account for the increase in proportion of all ethnicities over the 15-year period. The majority of patients who had AKI were admitted as an emergency and the proportion increased from 82.3% in 1998–2003 to 91.3% in 2008–2013. All comorbidities increased significantly over the 15-year period.

The mean age at start of AKI episode increased from 69.3 years (95% CI 69.0–69.5) in 1998–1999 to 76.2 years (95% CI 76.2–76.3) in 2012–2013, $p < 0.001$. In the same period, the mean age of all inpatients in England who did not have AKI was 45.5 years in 1998–1999 and 49.0 years in 2012–2013. The LOS remained high in 1998–2003 at 17.9 days (95% CI 17.8–18.2 days) and 2003–2008 at 17.9 days (95% CI 17.8–18.0 days), but decreased significantly in 2008–2013 to 16.1 days (95% CI 16.0–16.1 days, $p < 0.001$). The LOS for patients who did not have AKI in England decreased from 8.1 days in 1998–2003 to 5.3 days in 2008–2013.

Trend in case-fatality

From 1998–1999 to 2012–2013, overall in-hospital case-fatality in patients who developed AKI in England decreased from 43.5% to 24.1%, $p < 0.001$. The decline in case-fatality was also evident in patients with AKI diagnosis in primary, secondary and all other diagnoses codes and within each age group in the three 5-year period (Table 2) as well as yearly (Figure 4). During the same period, the in-hospital case-fatality for all patients in England without the diagnosis of AKI in any of the diagnoses codes, decreased from 2.4% in 1998–1999 to 1.1% in 2012–2013. Among all people who died with AKI, the proportion of people over the age of 85 years increased from 22.9% to 42.8% from 1998–1999 to 2012–2013. The proportion of deaths decreased in patients

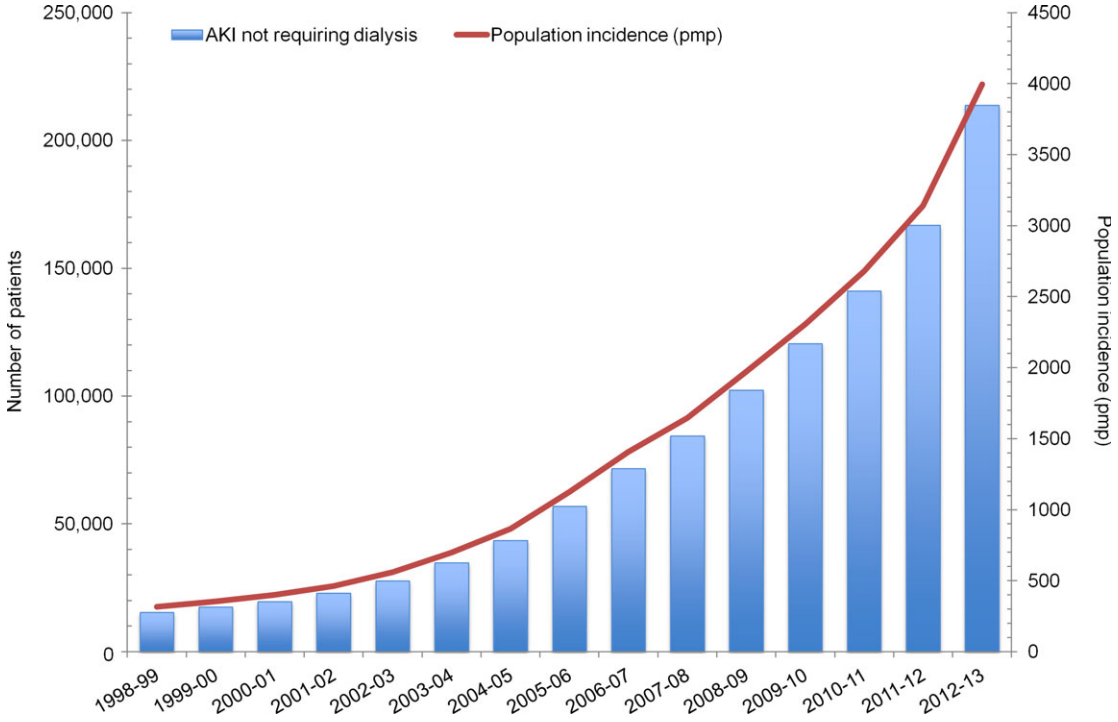

Figure 2 Total number of hospital admissions and population incidence of AKI reported as per million people (pmp) in England

Table 1 Demographic characteristics of non-dialysis requiring AKI patients in England

	Five-year period			
	1998–2003	2003–2008	2008–2013	p-value
AKI in primary diagnosis code	$32{,}546_a$ (31.6)	$74{,}042_b$ (25.4)	$137{,}196_c$ (18.5)	<0.001
AKI in secondary diagnosis code	$24{,}590_a$ (23.9)	$68{,}207_b$ (23.4)	$173{,}507_b$ (23.4)	
AKI in other diagnoses codes	$45{,}858_a$ (44.5)	$148{,}835_b$ (51.1)	$431{,}386_c$ (58.1)	
Total number of AKI cases	102,994	291,084	742,089	na
Age group (years)				
< 65	$26{,}046_a$ (25.3)	$59{,}922_b$ (20.6)	$132{,}387_c$ (17.8)	<0.001
65–74	$24{,}087_a$ (23.4)	$58{,}438_b$ (20.1)	$132{,}430_c$ (17.8)	
75–84	$33{,}491_a$ (32.5)	$100{,}607_b$ (34.6)	$246{,}575_c$ (33.2)	
≥ 85	$19{,}370_a$ (18.8)	$72{,}117_b$ (24.8)	$230{,}697_c$ (31.1)	
Gender: Male	$58{,}079_a$ (56.4)	$158{,}665_b$ (54.5)	$395{,}603_c$ (53.3)	<0.001
Length of stay in days	17.9_a (17.8, 18.2)	17.9_a (17.8, 18.0)	16.1_b (16.0, 16.1)	<0.001
Ethnicity				
White	$64{,}196_a$ (62.3)	$226{,}925_b$ (78.0)	$652{,}953_c$ (88.0)	<0.001
Mixed	71_a (0.1)	760_b (0.3)	2084_b (0.3)	
Asian	1655_a (1.6)	7075_b (2.4)	$24{,}140_c$ (3.3)	
Black	1267_a (1.2)	4725_b (1.6)	$14{,}355_c$ (1.9)	
Other ethnic group	1057_a (1.0)	2514_b (0.9)	8013_a (1.1)	
Not known	$34{,}748_a$ (33.7)	$49{,}085_b$ (16.9)	$40{,}544_c$ (5.5)	
Admission method				
Elective	8417_a (8.2)	$18{,}848_b$ (6.5)	$40{,}177_c$ (5.4)	<0.001
Emergency	$84{,}750_a$ (82.3)	$256{,}121_b$ (88.0)	$677{,}330_c$ (91.3)	
Maternity	64_a (0.1)	101_b (0.01)	246_b (0.01)	
Transfer from other provider	9579_a (9.3)	$15{,}756_b$ (5.4)	$24{,}188_c$ (3.3)	
Not known	179_a (0.2)	252_b (0.1)	115_c (0.01)	
Comorbidities				
Myocardial infarction	9732_a (9.40	$38{,}593_b$ (13.3)	$113{,}600_c$ (15.3)	<0.001
Cerebrovascular disease	5144_a (5.0)	$18{,}253_b$ (6.3)	$58{,}153_c$ (7.8)	<0.001
Congestive cardiac failure	$20{,}431_a$ (19.8)	$57{,}937_a$ (19.9)	$163{,}458_b$ (22.0)	<0.001
Connective tissue disorder	1851_a (1.8)	6682_b (2.3)	$22{,}837_c$ (3.1)	<0.001
Dementia	2920_a (2.8)	$18{,}175_b$ (6.2)	$78{,}769_c$ (10.6)	<0.001
Peptic ulcer	2130_a (2.1)	5167_b (1.8)	$12{,}496_c$ (1.7)	<0.001
Peripheral vascular disease	5137_a (5.0)	$15{,}539_b$ (5.3)	$43{,}553_c$ (5.9)	<0.001
Pulmonary disease	9983_a (9.7)	$40{,}382_b$ (13.9)	$139{,}667_c$ (18.8)	<0.001
Paraplegia	1082_a (1.1)	4011_b (1.4)	$12{,}127_c$ (1.6)	<0.001
Renal disease	$16{,}557_a$ (16.1)	$82{,}267_b$ (28.3)	$268{,}897_c$ (36.2)	<0.001
Diabetes mellitus	$14{,}773_a$ (14.3)	$64{,}708_b$ (22.2)	$203{,}084_c$ (27.4)	<0.001
Liver disease	2221_a (2.2)	6784_b (2.3)	$20{,}475_c$ (2.8)	<0.001
Malignancy	$15{,}443_a$ (15.0)	$43{,}671_a$ (15.0)	$114{,}761_b$ (15.5)	<0.001
HIV	133_a (0.1)	648_b (0.2)	53_c (0.01)	<0.001

Each subscript letter denotes a subset of 5-year period categories whose column proportions do not differ significantly from each other at the 0.05 level.

within age group less than 65 years and 65 to 74 years and remained unchanged in those aged 75–84 years.

Determinants of case-fatality

Both unadjusted and adjusted odds for death were higher for AKI patients in higher age groups. Patients over 85 years of age had adjusted odds ratio (OR) of 2.93 (95% CI 2.89–2.97) as compared to patients under the age of 65 years (Table 3). Patients in all ethnic minority groups had lower odds for death as compared to patients with white ethnicity. Patients with three or more comorbidities showed an incremental increase in the odds for death as compared with patients with no comorbidities. Compared with 1998–2003, the unadjusted odds for death were lower both in 2003–2008 (OR 0.77; 95% CI 0.76–0.78) and 2008–2013 (OR 0.51; 95% CI 0.50–

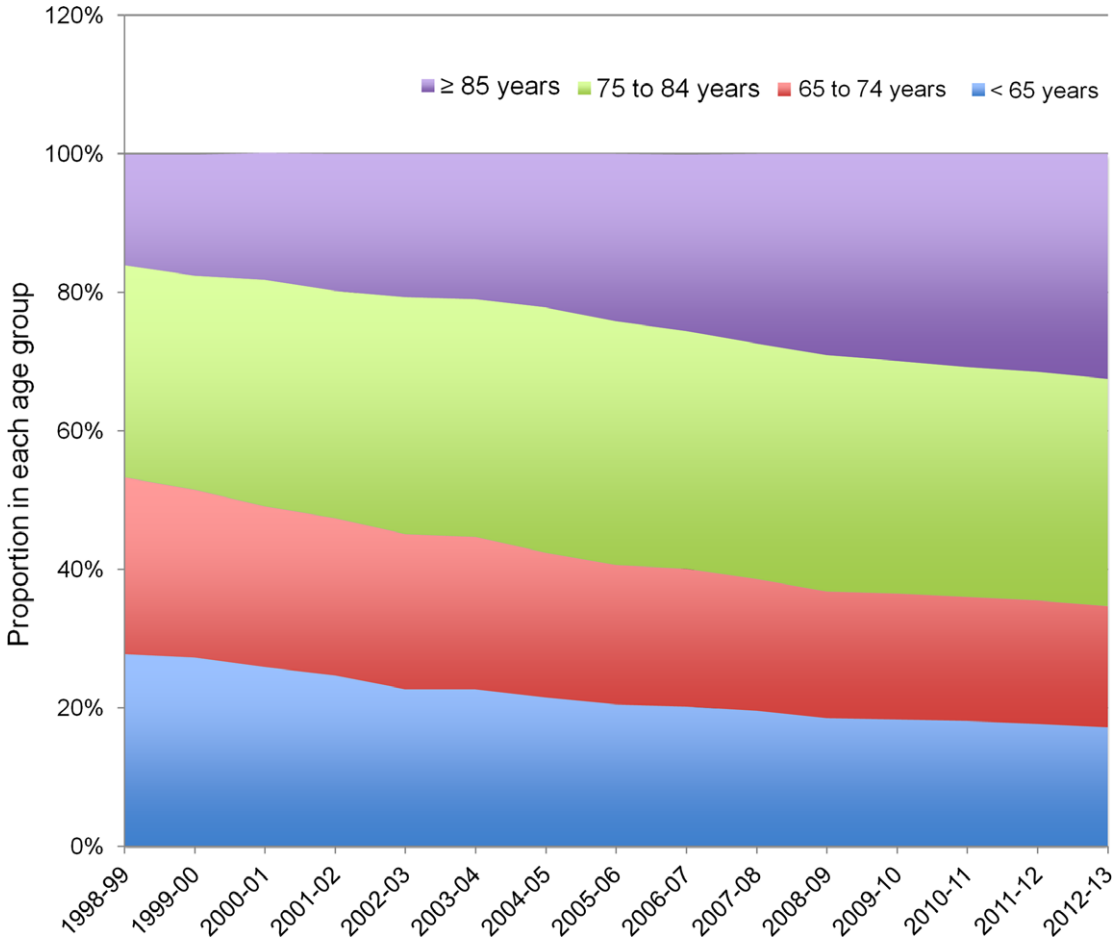

Figure 3 Proportion of AKI patients in each age group from 1998 to 2013

Table 2 Case-fatality in patients with non-dialysis requiring AKI as per diagnoses codes

	Five-year period			
	1998–2003	**2003–2008**	**2008–2013**	**p-value**
AKI in primary diagnosis code	9996_a (30.7)	$18{,}518_b$ (25.0)	$24{,}663_c$ (18.0)	< 0.001
AKI in secondary diagnosis code	$10{,}025_a$ (40.8)	$22{,}407_b$ (32.9)	$37{,}362_c$ (21.5)	< 0.001
AKI in all other diagnoses codes	$23{,}572_a$ (51.4)	$64{,}292_b$ (43.2)	$138{,}754_c$ (32.2)	< 0.001
Overall case-fatality	$43{,}593_a$ (42.3)	$105{,}217_b$ (36.1)	$200{,}779_c$ (27.1)	< 0.001

Each subscript letter denotes a subset of 5-year period categories whose column proportions do not differ significantly from each other at the 0.05 level.

0.51). The adjusted odds for death continued to be significantly lower both in 2003–2008 (OR 0.64; 95% CI 0.63–0.65) and in 2008–2013 (OR 0.35; 95% CI 0.34–0.35). Patients who were admitted in an emergency and transferred from hospital with no nephrology input had higher adjusted odds for death of 2.14 (95% CI 2.09–2.18) and 1.50 (95% CI 1.46–1.54), respectively. The adjusted odds for death were higher when patients had AKI diagnosis in the secondary diagnosis code (OR 1.35; 95% CI 1.33–1.36) and in all other diagnoses codes (OR 2.17; 95% CI 2.15–2.20).

In the sensitivity analysis, we assumed that the population incidence of AKI remained constant and the sensitivity of ICD-10 code for N17 to be 74%, as found in NCEPOD study, from 2006–2007 till 2012–2013. This estimated the number of cases of AKI not

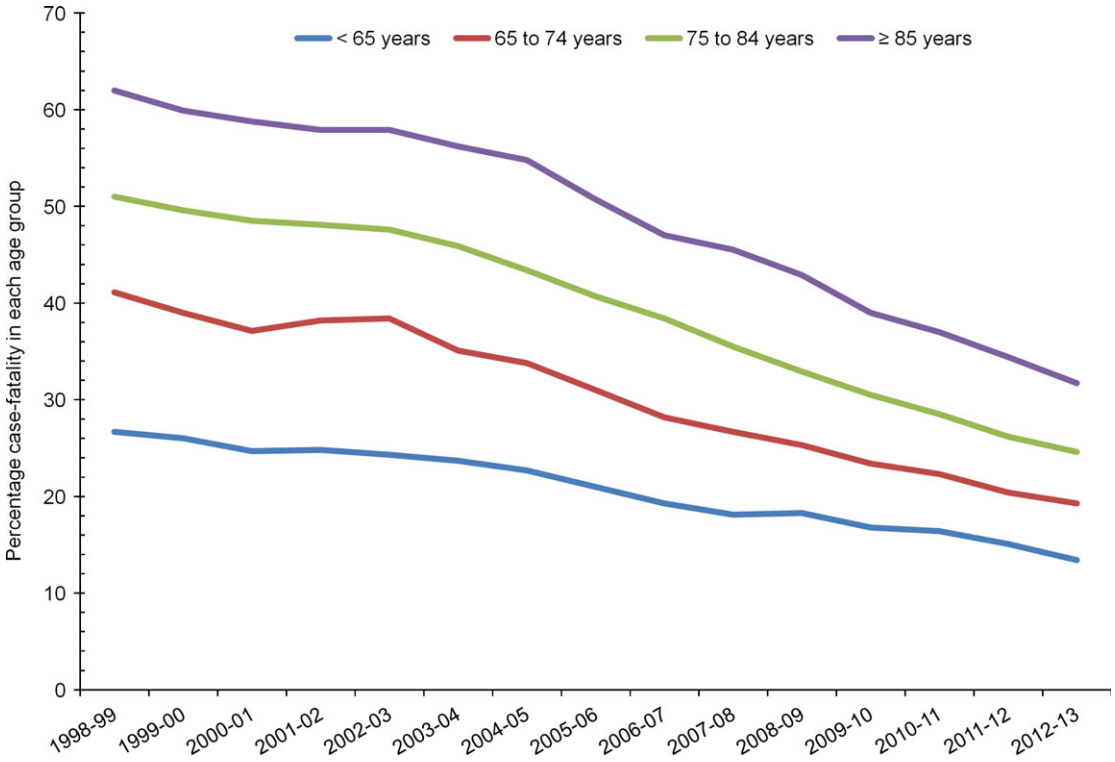

Figure 4 Case-fatality rate of non-dialysis requiring AKI in each age group in England from 1998 to 2013

requiring dialysis in 2012–2013 at 75,310, a figure less than 40% of the number of cases actually observed. The results of multivariable sensitivity analysis were similar to those in the primary analysis and the conclusions remained robust (Tables S2 and S3).

Discussion

We observed a large increase in the population incidence of hospitalised AKI from 317 pmp in 1998–1999 to 3995 pmp in 2012–2013 with most of the increase in those over 75 years. During the same period, there was a significant decrease in case-fatality associated with AKI in all age groups. Over time, people older than 85 years accounted for a greater proportion of those dying with AKI, largely because of increase in the incidence of AKI in this age group.

Comparison with other studies

Our findings are consistent with two other studies, which have used ICD codes to identify patients with AKI in partially overlapping periods (1988–2002 and 1992–2001); one based on the US Renal Data System that covers Medicare patients, and another that covers a Nationwide Inpatient Sample (NIS) database of hospital discharges (3,4). However, the studies reported different incidence and case-fatality rates despite being based on samples from the same population (19). In the NIS, weights were produced to create estimates that approximate a nationally representative sample, but because not all states provide data, some bias in national estimates may have occurred if omitted states had substantially different hospitalisation patterns than states that provided data. The number of states in the NIS of Health Care Utilization Project also varied by year and increased from eight in the first year to 46 in the most recent year (20). Hsu et al. found that the incidence of community AKI increased from 3227 pmp in 1996 to 5224 pmp in 2003 (2,21). Though the study had an advantage of using an updated definition of AKI based on serum creatinine, the average age of this population was only 42 years, much lower than that reported in any of the other AKI studies. In addition, two-thirds of the people of San Francisco bay in Northern California were not members of Kaiser Permanente and this raises questions about the study population representation.

Explaining the rise in the incidence rate of AKI

We found a more than 12-fold increase in the incidence of AKI between 1998–1999 and 2012–2013. It is possible that changes in coding practice contributed to the increased incidence of AKI in this study. In addition to a change in terminology, the

Table 3 Univariate and multivariate determinants of case-fatality in non-dialysis requiring AKI

	Univariate	Multivariate*
Age groups (years)		
< 65	1 (ref)	1 (ref)
65–74	**1.58 (1.56–1.60)**	**1.42 (1.40–1.45)**
75–84	**2.21 (2.18–2.24)**	**2.01 (1.98–2.04)**
≥ 85	**3.05 (3.01–3.09)**	**2.93 (2.89–2.97)**
Gender		
Male	1 (ref)	1 (ref)
Female	**1.11 (1.10–1.12)**	**1.06 (1.05–1.07)**
Five-year period		
1998–2003	1 (ref)	1 (ref)
2003–2008	**0.77 (0.76–0.78)**	**0.64 (0.63–0.65)**
2008–2013	**0.51 (0.50–0.51)**	**0.35 (0.34–0.35)**
Ethnicity		
White	1 (ref)	1 (ref)
Mixed	**0.58 (0.53–0.63)**	**0.74 (0.67–0.82)**
Asian	**0.61 (0.60–0.63)**	**0.73 (0.71–0.75)**
Black	**0.49 (0.47–0.51)**	**0.60 (0.58–0.62)**
Other ethnic group	**0.75 (0.72–0.78)**	**0.85 (0.82–0.89)**
Not known	**1.50 (1.48–1.52)**	**1.35 (1.34–1.37)**
Charlson's comorbidity score		
0	1 (ref)	1 (ref)
1	**1.69 (1.66–1.71)**	**1.54 (1.52–1.56)**
2	**1.61 (1.58–1.63)**	**1.56 (1.54–1.58)**
3	**1.75 (1.72–1.77)**	**1.71 (1.69–1.74)**
4	**1.89 (1.85–1.91)**	**1.91 (1.88–1.94)**
5+	**2.50 (2.47–2.54)**	**2.75 (2.71–2.79)**
Admission method		
Elective	1 (ref)	1 (ref)
Emergency	**2.31 (2.26–2.35)**	**2.14 (2.09–2.18)**
Maternity	**0.32 (0.21–0.48)**	**0.54 (0.36–0.82)**
Transfer from other provider	**1.59 (1.54–1.63)**	**1.50 (1.46–1.54)**
Not known	**2.16 (1.80–2.59)**	**1.58 (1.30–1.91)**
AKI in diagnoses codes		
Primary diagnosis code	1 (ref)	1 (ref)
Secondary diagnosis code	**1.27 (1.26–1.29)**	**1.35 (1.33–1.36)**
All other diagnoses codes	**2.03 (2.01–2.06)**	**2.17 (2.15–2.20)**

*Adjusted for age group, gender, ethnicity, Charlson's score, admission method, 5-year period and AKI in diagnoses codes. Odd ratios and confidence interval in bold indicate statistical significance.

definition of AKI itself was revised in 2003 and 2007 (11,12). This may have led to greater recognition of milder forms of AKI with higher proportion of true cases being diagnosed and identified by coding resulting in the steeper curve in the rate of increase in the number of cases between 2003 and 2013 as compared to that between 1998 and 2003. However, we do not think that increased recognition is the sole explanation for the increased number of AKI cases in this study. First, the Renal Association of UK adopted this definition in its clinical practice guidelines only in June 2008 (22). Second, the RIFLE and AKIN criteria were more widely adopted in clinical practice in UK only after the publication of NCEPOD report in June 2009 with its use in-hospital wide system prospectively for the first time in 2011 (16,23). Third, in our sensitivity analysis, we estimated 75,310 cases of AKI would have occurred in 2012–2013 if we assumed a constant incidence rate but actually observed almost three times this number (213,700). In addition, the accuracy of diagnostic coding in England did not reveal marked changes between 2005 and 2010, a period when there was a steep increase in the incidence of AKI (17). The increase in AKI coded in secondary and other diagnoses codes may represent increasing incidence of

hospital acquired AKI as suggested by Xue et al. where kidney is affected secondarily (4).

Another possible explanation for the observed increase in AKI is the increasing age of the population. This was evident in our study as the mean age increased from 69.3 years in 1998–1999 to 76.2 years in 2012–2013. This is in contrast to other older studies reporting secular trends in the incidence of AKI, where the age did not change much during the study period (3,4). A further possible explanation is a change in the spectrum of comorbidities among people admitted to hospital. Over the last 15 years, the incidence of acute myocardial infarction, stroke and cancer have decreased in England, but the incidence of diabetes mellitus and congestive heart failure has increased (24–27). Moreover, these comorbidities are associated with increased use of drugs that may increase the risk of AKI, including ACE inhibitors (ACEI) and angiotensin receptor blockers (ARBs). Recent evidence suggests that increased prescription of ACEI and ARBs may account for a 15% increase in AKI admissions in England, making this one of the largest preventable causes of AKI (28).

Explaining the decline in case-fatality in AKI

In this study we have shown that case-fatality in patients with AKI decreased significantly from 1998–1999 to 2012–2013. This is consistent with the results of previous two studies, which investigated secular trends in case-fatality (3,4). One reason for the decline in the case-fatality could be the inclusion of less severe cases of AKI discussed above. However, unlike the study by Waikar et al., we observed a higher CCS in each of the previous 5-year period, suggesting that patients were becoming more unwell (3). Despite a decline in case-fatality in last 15 years, the case-fatality rate in 2012–2013 for patients who have AKI remains high even in the absence of a requirement for dialysis at 24.1%. This demonstrates the importance of maintaining a focus on all cases of AKI, whether requiring RRT or not.

Strength and limitations

The strengths of this study include the large size of the cohort, complete national coverage and recent data (29). To the best of our knowledge this is the first study to describe the epidemiology of hospitalised AKI in England using a national database. The main limitation was the reliance on the accuracy and validity of routine data. Nonetheless a systemic review of studies comparing routine hospital discharge statistics with medical records carried out in England, Wales and Scotland reported on average, high accuracy rates for coding (30). NCEPOD reported 74.1% sensitivity, 96% specificity, 90.9% positive predictive value and 87.2% negative predictive value for ICD-10 codes for ARF. Another limitation is that the definition of AKI in this study was not based directly on changes in the serum creatinine and there is likelihood that milder cases of AKI may not have been diagnosed or coded. These data are therefore likely to represent a conservative estimate of the true incidence of hospitalised AKI not requiring dialysis in England.

Conclusions

This study provides the first nationwide investigation of hospitalised AKI not requiring dialysis over a period of 15 years. We have shown that the incidence of hospitalised AKI has increased considerably and although in-hospital case-fatality has decreased over the last 15 years in England, it remains unacceptably high. Most of the increase in incidence was observed in elderly people who also evidenced less improvement in survival. Our data therefore suggest that efforts to reduce the incidence of AKI in England should focus on elderly people with multimorbidity as well as emergency admissions and those requiring transfer from hospitals without a nephrology service.

Author contributions

NVK MWT: Conceived and designed the experiments. NVK AWM MWT: Performed the experiment. NVK SRH: Analysed the data. NVK, SRH: Contributed reagents/materials/analysis tools. NVK MWT AWM, SRH, RJF: Wrote the manuscript. NVK, AWM: Other: Data extraction.

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Transparency statement

Nitin V Kolhe (the manuscript's guarantor) affirms that the manuscript is an honest, accurate and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned (and, if relevant, registered) have been explained.

Data availability

All relevant data are within the paper and its supporting information files.

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Supporting Information

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

Table S1. Number of cases of AKI not requiring dialysis from 2007 onwards with assumption of constant population incidence and a sensitivity of 74% in 2007.

Table S2. Multivariable determinants of case-fatality (after exclusion of all cases where 'Not known' ethnicity).

Table S3. Multivariable determinants of case-fatality (using age and Charlson's score as continuous variable).

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