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*Original Article*

# A simple care bundle for use in acute kidney injury: a propensity score matched cohort study

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## ABSTRACT

**Background.** Consensus guidelines for acute kidney injury (AKI) have recommended prompt treatment including attention to fluid balance, drug dosing and avoidance of nephrotoxins. These simple measures can be incorporated in a care bundle to facilitate early implementation. The objective of this study was to assess the effect of compliance with the AKI care bundle (AKI-CB) on in-hospital case–fatality and AKI progression.

**Methods.** In this larger, propensity score-matched cohort of multifactorial AKI, we examined the impact of compliance with an AKI-CB in 3717 consecutive episodes of AKI in 3518 patients between 1 August 2013 and 31 January 2015. Propensity score matching was performed to match 939 AKI events where the AKI-CB was completed with 1823 AKI events where AKI-CB was not completed.

**Results.** The AKI-CB was completed in 25.6% of patients within 24 h. The unadjusted case–fatality was higher when the AKI-CB was not completed versus when the AKI-CB was completed (24.4 versus 20.4%, P = 0.017). In multivariable analysis, AKI-CB completion within 24 h was associated with lower odds for in-hospital death [odds ratio (OR): 0.76; 95% confidence interval (95% CI): 0.62–0.92]. Increasing age (OR: 1.04; 95% CI: 1.03–1.05), hospital-acquired AKI (OR: 1.28; 95% CI: 1.04–1.58), AKI stage 2 (OR: 1.91; 95% CI: 1.53–2.39) and increasing Charlson's comorbidity index (CCI) [OR: 3.31 (95% CI: 2.37–4.64) for CCI of more than 5 compared with zero] had higher odds for death, whereas AKI during elective admission was associated with lower odds for death (OR: 0.29; 95% CI: 0.16–0.52). Progression to higher AKI stages was lower when the AKI-CB was completed (4.2 versus 6.7%, P = 0.02).

**Conclusions.** Compliance with an AKI-CB was associated with lower mortality and reduced progression of AKI to higher stages. The AKI-CB is simple and inexpensive, and could therefore be applied in all healthcare settings to improve outcomes.

**Keywords:** age, AKI, care bundle, mortality, outcome

## INTRODUCTION

The incidence of acute kidney injury (AKI) has increased considerably in the last two decades, accounting for 13–18% of hospital admissions [1]. Although some studies have reported that outcomes have improved over time [2, 3], AKI is still associated with a high mortality, especially when dialysis is needed [4]. In response, the International Society of Nephrology (ISN) has launched an international campaign to eliminate avoidable deaths due to AKI by 2025 [5]. Frustratingly, trials over the last two decades of various interventions to prevent and treat AKI have proved futile and in some cases deleterious [6–8]. On the other hand, simple measures are quite often enough to prevent AKI, but they are frequently not instituted in the early period of the illness when there is a golden opportunity to change the course. This was confirmed in a landmark report by the National Confidential Enquiry into Patient Outcome and Death (NCEPOD), which found that only 50% of patients with AKI had good care [9]. One intervention for improving the care of patients with AKI has been the implementation of electronic alerting systems to improve early recognition of AKI, but a recent randomized controlled trial (RCT) has found that this alone is insufficient to improve outcomes [10]. It has therefore been proposed that alerts should be used in conjunction with a bundle of diagnostic and therapeutic interventions [11].

The use of such 'care bundles' has been shown to improve survival in patients with sepsis [12] and ventilator-associated pneumonia [13]. In a prospective observational study, we have previously found that implementation of a care bundle, linked to electronic recognition of AKI, was associated with a lower in-hospital case–fatality in patients with AKI, though it is possible that the results were affected by some residual confounding [14]. The objective of this study was to perform a more robust assessment of the effect of compliance with the AKI care bundle (AKI-CB) on in-hospital case–fatality using a larger, prospective propensity score-matched cohort of patients with AKI.

## MATERIALS AND METHODS

This study was conducted in Derby Teaching Hospital NHS Foundation Trust between August 2013 and January 2015. All adult patients who were admitted with or developed AKI, in any location of the hospital, were included. The details of the AKI-CB have been described previously [14]. To briefly summarize, the AKI-CB (Figure 1) was derived from NCEPOD recommendations after consultation between five nephrologist and coupled with an interruptive electronic alert (Supplementary data, Figure S1), which was triggered by the first attempt to order blood tests or medications on patients who had been identified as having AKI by electronic recognition from serum creatinine results [15]. The interruptive alert would warn the clinician about AKI and request them to complete the AKI-CB. The clinician could override the alert by stating a reason. After acknowledging the alert, the doctor can open the AKI-CB to see the elements and complete them. Once the AKI-CB was completed, the clinician was able to request blood tests or medication. Education regarding the recognition and management of AKI and the AKI-CB was provided every 4 months when junior doctors rotated through different specialities and also at clinical governance days. We compared AKI episodes that had the AKI-CB completed early (defined as within 24 h of availability of the blood results) with those who either had the AKI-CB completed late (defined as after 24 h of availability of the blood results) or not completed. The AKI patients who either had the AKI-CB completed late or not completed were considered as not having the AKI-CB completed for this analysis.

### Covariate ascertainment

Race was determined by self-report. Comorbidity information was assembled using International Classification of

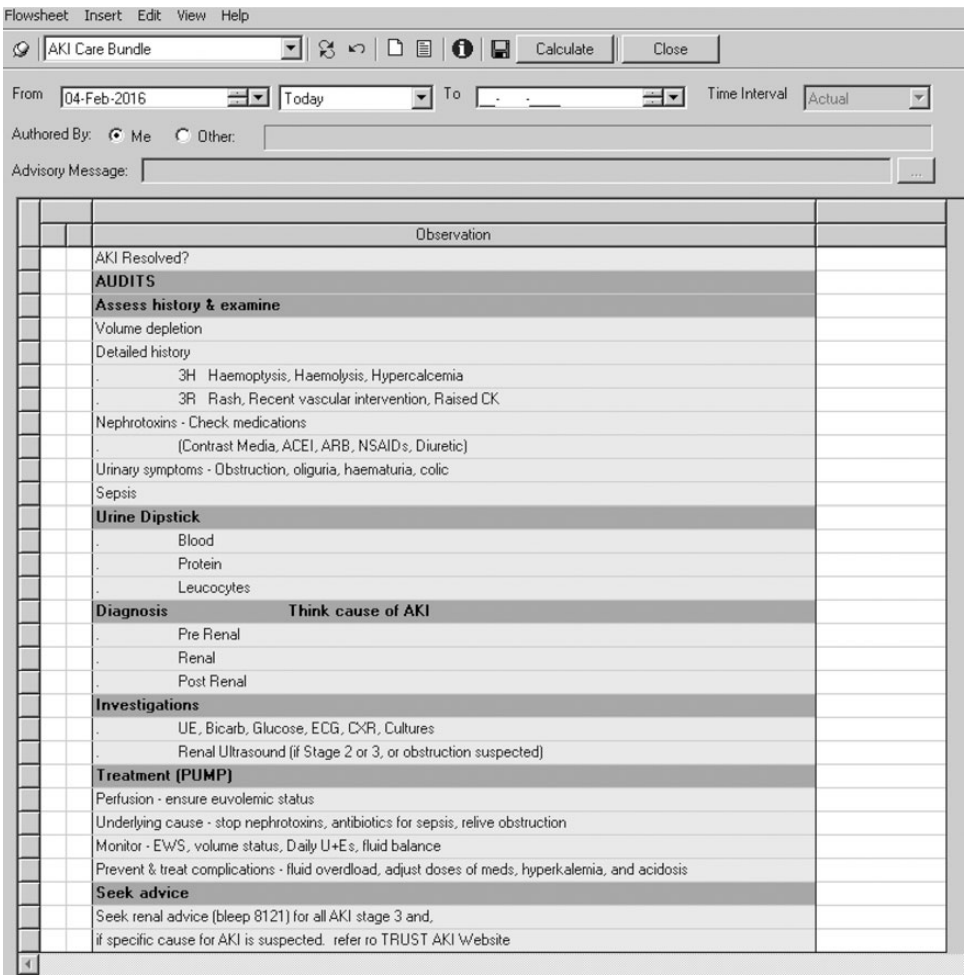


**FIGURE 1:** The electronic AKI-CB. CK, creatine kinase; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NSAID, non-steroidal anti-inflammatory drugs; ECG, electrocardiograph; CXR, chest X-ray; UE, urea and electrolytes; EWS, early warning score; U+E, urea and electrolytes.

Disease, Tenth Revision (ICD-10) codes, as documented on admission [16]. Data from the comprehensive electronic medical record included laboratory data obtained during routine clinical care, first documented AKI stage with date, peak AKI stage with date and last AKI stage with date. Demographic data included age, gender, type of admission, discharge method and destination, length of stay and survival status in February 2015. Date and time of completion of the care bundle was extracted electronically along with each element of the care bundle. Community-acquired AKI was defined as AKI within 24 h of admission.

### Propensity score matching

To recapitulate the design of a randomized trial, patients were assigned a propensity score using a logistic regression model. Model selection was performed using stepwise regression using covariates, age, gender, first AKI stage, site of AKI, admission method, ethnicity and the following comorbidities: acute myocardial infarction, congestive cardiac failure, peripheral vascular disease, peptic ulcer, dementia, diabetes, diabetic complications, liver disease, connective tissue disorders, pulmonary diseases, cirrhosis of liver, cancer, paraplegia, renal disease, metastatic disease and HIV status. Matching was performed using a one to many technique where AKI patients who had the care bundle completed were matched to many AKI patients who did not have care bundle completed and had the most similar estimated propensity score. To ensure good matches, a caliper (maximum allowable difference between two participants) of 0.2 was defined. The model adequacy checks were performed using standardized mean differences and the variance ratio in the group with the AKI-CB completed (intervention group) and not completed (control group) before and after matching (Supplementary data, Figures S2 and S3).

### Outcome measures

The primary outcome was all-cause in-hospital case–fatality. The secondary outcomes were progression of AKI to higher stages, length of stay and survival post-discharge.

### Ethical approval

The study was assessed by the Research and Development Department of Derby Teaching Hospitals NHS Foundation Trust and the National Research Ethics Service Committee, East of England – Cambridge Central and was deemed exempt from the need for ethical approval because it involved audit of improvement in-patient care following introduction of a AKI-CB to standardize care and met the criteria of service evaluation. All authors complied with the principles of Declaration of Helsinki.

### Statistical analysis

The analysis was planned on AKI event or admission as each AKI event was in a separate admission. Continuous variables are described in terms of mean with 95% confidence interval (CI). In the entire cohort and the matched cohort, unadjusted associations between continuous and categorical variables in control and intervention groups were assessed by *t*-test or the $\chi^2$ test as appropriate. Binary logistic regression was used to test significant univariate associations with in-hospital mortality. Age was not normally distributed and was log transformed. To test the linear relation of age to the logit of the dependent variable, a Box–Tidwell procedure was performed. The interaction between age and square root of age was not significant, confirming a linear relationship with the outcome. Results are presented as odds ratios (ORs) and 95% CIs. Data were analysed on each episode of AKI and included patients who had experienced multiple episodes of AKI in separate admission periods. We also performed Cox proportional hazards analysis adjusting for covariates, to assess whether the survival advantage at discharge persisted during follow-up. For Cox proportional hazards analysis, we performed log minus log plot for categorical variables to confirm that there was no violation of the proportional hazards assumption. For numerical variables, we plotted partial residuals against time to confirm there was no trend. All tests were two tailed, and $P < 0.05$ was considered significant. In the sensitivity analysis, we determined whether there was a difference in the effect size after excluding patients who had another AKI episode in a different admission (see Supplementary data). We also performed a second sensitivity analysis to determine the effect size of late completion of AKI-CB. Analysis was performed on IBM SPSS Statistics for Windows, Version 22.0. This study is registered with clinicaltrials.gov NCT02534584.

## RESULTS

### Baseline data before matching

We identified 3717 unique AKI events in separate hospital admissions in 3351 patients in an 18-month period between 1 August 2013 and 31 January 2015. The AKI-CB was completed in 25.6% (939 episodes) of AKI events within 24 h. The overall mean age was 76.1 (95% CI: 75.7–76.6) years, and there was no difference between the two groups. There was a significantly higher proportion of community-acquired AKI, emergency admissions, and AKI stage 2 and 3 in the group with the AKI-CB completed (Table 1). Unadjusted case–fatality was higher in the group that did not have the AKI-CB completed, though this was not statistically significant (23.3 versus 20.2%, P = 0.052).

### Baseline characteristics of matched cohort

Out of 3717 AKI events, 939 AKI events who had the AKI-CB completed were matched with 1823 AKI events where the AKI-CB was not completed (Figure 2). Nine hundred and forty-four AKI events, where the AKI-CB was not completed, were not matched and 11 AKI events were discarded as propensity scores were outside the region of overlap. The standardized mean difference before matching was 0.464 and after matching was 0.034. Table 2 illustrates baseline characteristics of matched cohorts. The mean age of the matched cohort was 76.2 (95% CI: 75.6–76.7) years. The unadjusted case–fatality in the cohort where the AKI-CB was not completed was significantly higher than the cohort with the AKI-CB completed (24.4 versus 20.4%, P = 0.017).

**Table 1. Baseline characteristics and unadjusted analysis of patients as per AKI-CB completion in the entire study cohort**

| | AKI-CB not completed | AKI-CB completed within 24 h | Total | P-value |
|---|---|---|---|---|
| Number of AKI events | 2778 (74.7) | 939 (25.6) | 3717 | |
| Age | 76.1 (75.5, 76.6) | 76.4 (75.5, 77.3) | 76.1 (75.7, 76.6) | 0.53 |
| Gender | | | | |
| Male | 1367 (49.2) | 459 (48.9) | 1826 (49.1) | 0.446 |
| Site of AKI | | | | |
| Community | 1479 (53.2) | 672 (71.6) | 2151 (57.9) | 0.001 |
| Comorbidities | | | | |
| AMI | 256 (9.2) | 85 (9.1) | 341 (9.2) | 0.948 |
| CVA | 68 (2.4) | 22 (2.3) | 90 (2.4) | 0.903 |
| CCF | 406 (14.6) | 122 (13) | 528 (14.2) | 0.234 |
| CTD | 70 (2.5) | 24 (2.6) | 94 (2.5) | 1.000 |
| Dementia | 280 (10.1) | 127 (13.5) | 407 (10.9) | 0.004 |
| Diabetes mellitus | 684 (24.6) | 227 (24.2) | 911 (24.5) | 0.793 |
| Liver disease | 59 (2.1) | 19 (2) | 78 (2.1) | 1.000 |
| Peptic ulcer | 34 (1.2) | 7 (0.7) | 41 (1.1) | 0.279 |
| PVD | 140 (5) | 34 (3.6) | 174 (4.7) | 0.089 |
| Pulmonary disease | 447 (16.1) | 142 (15.1) | 589 (15.8) | 0.502 |
| Cancer | 404 (14.5) | 114 (12.1) | 518 (13.9) | 0.072 |
| Paraplegia | 22 (0.8) | 6 (0.6) | 28 (0.8) | 0.828 |
| Renal disease | 721 (26) | 266 (28.3) | 987 (26.6) | 0.159 |
| HIV | 1 (0) | 0 (0) | 1 (0) | 1.000 |
| Ethnicity | | | | |
| White | 2489 (90.3) | 842 (90.1) | 3331 (90.3) | 0.999 |
| Mixed | 7 (0.3) | 3 (0.3) | 10 (0.3) | |
| Asian | 84 (3) | 30 (3.2) | 114 (3.1) | |
| Black | 29 (1.1) | 10 (1.1) | 39 (1.1) | |
| Any other ethnic group | 19 (0.7) | 7 (0.7) | 26 (0.7) | |
| Not known | 127 (4.6) | 42 (4.5) | 169 (4.6) | |
| Admission method | | | | |
| Emergency | 2525 (90.9) | 875 (93.2) | 3400 (91.5) | 0.049 |
| First AKI result | | | | |
| Stage 1 | 1728 (62.2) | 464 (49.4) | 2192 (59) | <0.001 |
| Stage 2 | 607 (21.9) | 257 (27.4) | 864 (23.2) | |
| Stage 3 | 443 (15.9) | 218 (23.2) | 661 (17.8) | |
| Status | | | | |
| Died | 648 (23.3) | 190 (20.2) | 838 (22.5) | 0.052 |

AMI, acute myocardial infarction; CVA, cerebrovascular accident; CCF, congestive cardiac failure; CTD, connective tissue disorder; PVD, peripheral vascular disease.
Data are presented as *n* (%), except for age, which is given as mean (95% CI).

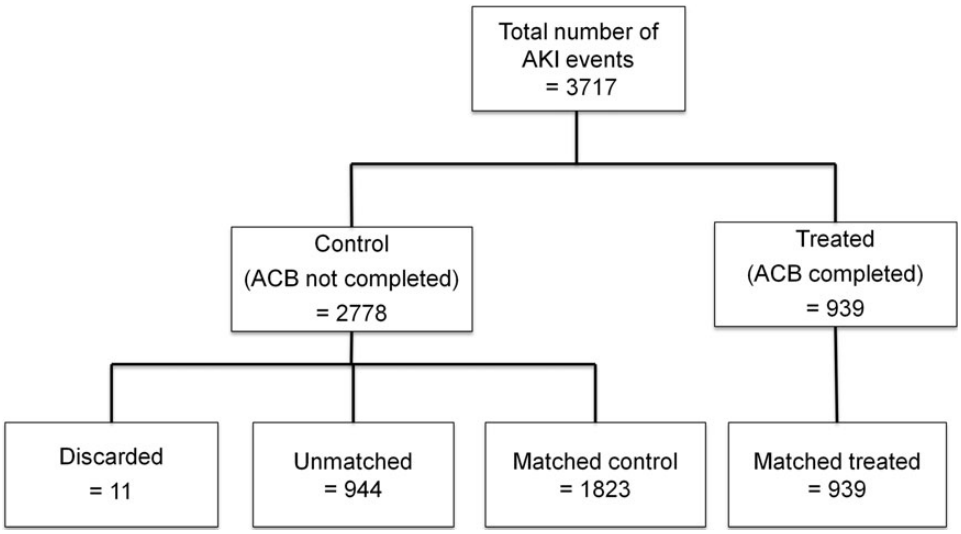


**FIGURE 2:** Study flow chart. ACB, acute kidney injury care bundle.

### Baseline characteristics of unmatched cohort

Patients who were not used for propensity score matching (AKI-CB not completed) evidenced a higher proportion of AKI stage 1, peripheral vascular disease, dementia and cancer when compared with cases and matched controls. However, the unmatched cohort also had significantly higher length of

**Table 2. Baseline characteristics and unadjusted analysis of patients as per AKI-CB completion in the propensity-matched cohort**

| | AKI-CB not completed | AKI-CB completed within 24 h | Total | P-value |
|---|---|---|---|---|
| Number of AKI events | 1823 (66) | 939 (34) | 2762 | – |
| Age | 76.1 (75.4, 76.7) | 76.4 (75.5, 77.3) | 76.2 (75.6, 76.7) | 0.551 |
| Gender | | | | |
| Male | 895 (49.1) | 459 (48.9) | 1354 (49) | 0.936 |
| Site of AKI | | | | |
| Community | 1279 (70.2) | 672 (71.6) | 1951 (9) | 0.454 |
| Comorbidities | | | | |
| AMI | 164 (9) | 85 (9.1) | 249 (9) | 1.000 |
| CVA | 40 (2.2) | 22 (2.3) | 62 (2.2) | 0.788 |
| CCF | 255 (14) | 122 (13) | 377 (13.6) | 0.483 |
| CTD | 46 (2.5) | 24 (2.6) | 70 (2.5) | 1.000 |
| Dementia | 218 (12) | 127 (13.5) | 345 (12.5) | 0.249 |
| Diabetes mellitus | 450 (24.7) | 227 (24.2) | 677 (24.5) | 0.78 |
| Liver disease | 40 (2.2) | 19 (2) | 59 (2.1) | 0.89 |
| Peptic ulcer | 18 (1) | 7 (0.7) | 25 (0.9) | 0.673 |
| PVD | 71 (3.9) | 34 (3.6) | 105 (3.8) | 0.754 |
| Pulmonary disease | 285 (15.6) | 142 (15.1) | 427 (15.5) | 0.739 |
| Cancer | 218 (12) | 114 (12.1) | 332 (12) | 0.902 |
| Paraplegia | 11 (0.6) | 6 (0.6) | 17 (0.6) | 1.000 |
| Renal disease | 486 (26.7) | 266 (28.3) | 752 (27.2) | 0.367 |
| Ethnicity | | | | |
| White | 1643 (90.1) | 842 (89.7) | 2485 (90) | 0.961 |
| Mixed | 3 (0.2) | 3 (0.3) | 6 (0.2) | |
| Asian | 54 (3) | 30 (3.2) | 84 (3) | |
| Black | 17 (0.9) | 10 (1.1) | 27 (1) | |
| Any other ethnic group | 12 (0.7) | 7 (0.7) | 19 (0.7) | |
| Not known | 94 (5.2) | 47 (5) | 141 (5.1) | |
| Admission method | | | | |
| Emergency | 1696 (93) | 875 (93.2) | 2571 (93.1) | 0.461 |
| Elective | 124 (6.8) | 64 (6.8) | 188 (6.8) | |
| Day case | 3 (0.2) | 0 (0) | 3 (0.1) | |
| First AKI result | | | | |
| Stage 1 | 953 (52.3) | 464 (49.4) | 1417 (51.3) | |
| Stage 2 | 471 (25.8) | 257 (27.4) | 728 (26.4) | |
| Stage 3 | 399 (21.9) | 218 (23.2) | 617 (22.3) | 0.902 |
| Status at discharge | | | | |
| Died | 443 (24.4) | 190 (20.4) | 633 (23.1) | 0.017 |

AMI, acute myocardial infarction; CVA, cerebrovascular accident; CCF, congestive cardiac failure; CTD, connective tissue disorder; PVD, peripheral vascular disease.
Data are presented as *n* (%), except for age, which is given as mean (95% CI).





stay of 14.6 (95% CI: 13.7–15.5) days versus 10.9 (95% CI: 10.1–11.7) days (P < 0.001) and mortality (44.6 versus 39.8%, P = 0.034) when compared with AKI events where the AKI-CB was completed (Supplementary data, Table S1).

### Determinants of case–fatality

We analysed key covariates that were selected *a priori* as possible effect modifiers of the relationship between AKI-CB completion and all-cause mortality in the propensity-matched cohort. Logistic regression analysis was performed to investigate the effects of the following covariates in addition to AKI-CB completion: age, gender, ethnicity, admission method, Charlson's comorbidity index (CCI), first AKI stage and site of AKI onset (community versus hospital acquired) on the likelihood of in-hospital all-cause mortality. In multivariable analysis, patients who had the AKI-CB completed within 24 h (OR: 0.76; 95% CI: 0.62–0.92) or were admitted electively (OR: 0.29; 95% CI: 0.16–0.52) had lower odds for death, whereas increasing age and hospital-acquired AKI had higher odds for death (Table 3). AKI stage 2 and stage 3 were associated with higher odds for death than stage 1 (OR: 1.91; 95% CI: 1.53–2.39 and OR: 1.74; 95% CI: 1.38–2.21). The OR increased with increasing CCI and a score of five or more had an OR of 3.31 (95% CI: 2.37–4.64) compared with a CCI of zero.

### Progression of AKI to higher stages, length of stay and long-term mortality

Progression was defined as increase in AKI stage from 1 to 3 within a period of 7 days. In the matched cohort, after excluding AKI stage 3 at presentation, overall 7.4% of people with AKI progressed to one stage higher. The proportion progressing to a higher stage was greater in the group without AKI-CB completion (8.1%) versus AKI-CB completion (6.0%, P = 0.042) (Table 4), but there was no difference in the proportion of patients progressing two AKI stages. There was also no difference in the requirement of renal replacement therapy between the two groups (2 versus 2.4%, P = 0.433). The uptake of AKI-CB was poor in the intensive care unit (Supplementary data, Table S2). There was no difference in length of stay between the two groups.

**Table 3. Univariate and multivariable adjusted determinants of case–fatality in the matched cohort**

| Determinants of case–fatality | Univariate OR (95% CI) | Multivariable[a] OR (95% CI) |
|---|---|---|
| Age | **1.04 (1.03, 1.04)** | **1.04 (1.03, 1.05)** |
| Gender | | |
| Male | 1 (Ref) | 1 (Ref) |
| Female | 0.92 (0.77, 1.09) | 0.88 (0.73, 1.07) |
| CCI | | |
| CCI = 0 | 1 (Ref) | 1 (Ref) |
| CCI = 1 | **1.38 (1.04, 1.83)** | 1.25 (0.93, 1.67) |
| CCI = 2 | **1.86 (1.40, 2.47)** | **1.52 (1.13, 2.03)** |
| CCI = 3 | **2.13 (1.58, 2.288)** | **1.75 (1.28, 2.38)** |
| CCI = 4 | **2.87 (2.04, 4.04)** | **2.55 (1.79, 3.64)** |
| CCI ≥ 5 | **3.71 (2.69, 5.13)** | **3.31 (2.37, 4.64)** |
| Ethnicity | | |
| White | 1 (Ref) | 1 (Ref) |
| Mixed | 0.65 (0.08, 5.53) | 0.74 (0.08, 6.54) |
| Asian | 0.65 (0.36, 1.15) | 0.73 (0.39, 1.33) |
| Black | 0.71 (0.28, 1.94) | 1.19 (0.42, 3.35) |
| Any other ethnic group | 0.38 (0.09, 1.65) | 0.59 (0.13, 2.63) |
| Not known | **0.63 (0.40, 0.99)** | 0.71 (0.44, 1.15) |
| First AKI result | | |
| Stage 1 | 1 (Ref) | 1 (Ref) |
| Stage 2 | **1.65 (1.34, 2.04)** | **1.91 (1.53, 2.39)** |
| Stage 3 | **1.59 (1.28, 1.99)** | **1.74 (1.38, 2.21)** |
| Admission method | | |
| Emergency | 1 (Ref) | 1 (Ref) |
| Elective | **0.23 (0.13, 0.41)** | **0.29 (0.16, 0.52)** |
| AKI-CB completion | | |
| AKI-CB not completed | 1 (Ref) | 1 (Ref) |
| AKI-CB completed in 24 h | **0.79 (0.65, 0.96)** | **0.76 (0.62, 0.92)** |
| Site of AKI onset | | |
| Community | 1 (Ref) | 1 (Ref) |
| Hospital | 1.07 (0.88, 1.30) | **1.28 (1.04, 1.58)** |

Bold ORs and CI are statistically significant.
[a]Adjusted for age, gender, CCI, ethnicity, first AKI stage, admission method, AKI-CB completion and site of AKI.

**Table 4. Length of stay and progression of AKI as per AKI-CB completion**

| | AKI-CB not completed | AKI-CB completed within 24 h | Total | P-value |
|---|---|---|---|---|
| Length of stay in days[a] | 11.5 (10.9, 12.1) | 10.9 (10.1, 11.7) | 11.3 (10.8, 11.8) | 0.254 |
| No progression (%) | 1309 (91.9) | 678 (94) | 1987 (92.6) | 0.042 |
| Progressed 1 stage (%) | 96 (6.7) | 30 (4.2) | 126 (5.9) | |
| Progressed 2 stages (%) | 19 (1.3) | 13 (1.8) | 32 (1.5) | |
| Renal replacement therapy (%) | 56 (2) | 23 (2.4) | 79 (2.1) | |

[a]Mean with 95% CIs.

Cox proportional hazards models were used to investigate mortality after a mean follow-up of 171 days [interquartile range (24, 302.25) 278.3 days]. Completion of the care bundle within 24 h of admission was associated with a hazard ratio for death of 0.878 (95% CI: 0.776–0.993) when compared with patients who did not have the care bundle completed within 24 h (P = 0.039) (Figure 3).

### Sensitivity analysis

Two sensitivity analyses were performed. First, we determined whether there was a difference in the effect size between AKI events where AKI-CB was not completed and completed after 24 h (Supplementary data, Table S3). In the second sensitivity analysis, we excluded all second AKI admissions to determine whether there was a difference in the effect size between AKI events where AKI-CB was not completed against those where AKI-CB was completed within 24 h (Supplementary data, Table S4). The results of the two sensitivity analysis confirmed the robustness of the primary analysis.

### Findings associated with each element in patients who had the AKI-CB completed

Compliance with completion of the AKI-CB was excellent, with all fields completed in all cases except for urinalysis. The findings associated with each element of the care bundle are summarized in Figure 4. In patients who had the AKI-CB completed as part of their management, volume depletion was present in 52.8%, while history specific to renal cause for AKI was present in only 18.2%. A total of 34.8% of patients had nephrotoxins in their medication list. Obstructive symptoms were present in 15% of patients, while sepsis was present in 28.3%. Urinalysis was recorded in <8% of patients. AKI was classed as pre-renal in 56.8%, renal in 11.1% and post-renal in 8.1% of patients. Ultrasonography of kidneys was requested in 19.4% of AKI stage 2 or 3 or if urinary tract obstruction was suspected. Specific interventions were required in 60.4% of patients (stopping nephrotoxic medications, antibiotics for sepsis or relieving urinary tract obstruction). Monitoring of fluid volume, blood tests and early warning sore was assessed to be required in 62% of patients. Nephrology advice was obtained in 14.5% of patients and only 2.4% of doctors documented that they had referred to the AKI guidelines on the hospital website.

## DISCUSSION

This study, using more robust methodology, confirms our previous finding from a prospective pilot study in a different cohort of patients that compliance with the AKI-CB is associated with lower in-hospital case–fatality. In addition, hazard for death was lower after a mean follow-up of 171 days. In the current study, fewer patients progressed to a higher AKI stage when the AKI-CB was completed within 24 h, but there was no difference in progression by more than two stages. Lack of difference in renal replacement therapy requirement also points to the importance of early AKI-CB completion, as once AKI progresses to stage 3, it becomes difficult to halt progression. Our findings are clinically significant because of the simplicity of the AKI-CB and absence of any data to support the use of other therapeutic interventions to prevent AKI progression or to lower in-hospital case–fatality. In this study, we matched important covariates that have been shown to be associated with mortality in AKI patients to reduce the chance of residual confounding. Clearly, an RCT, which can adjust for unknown

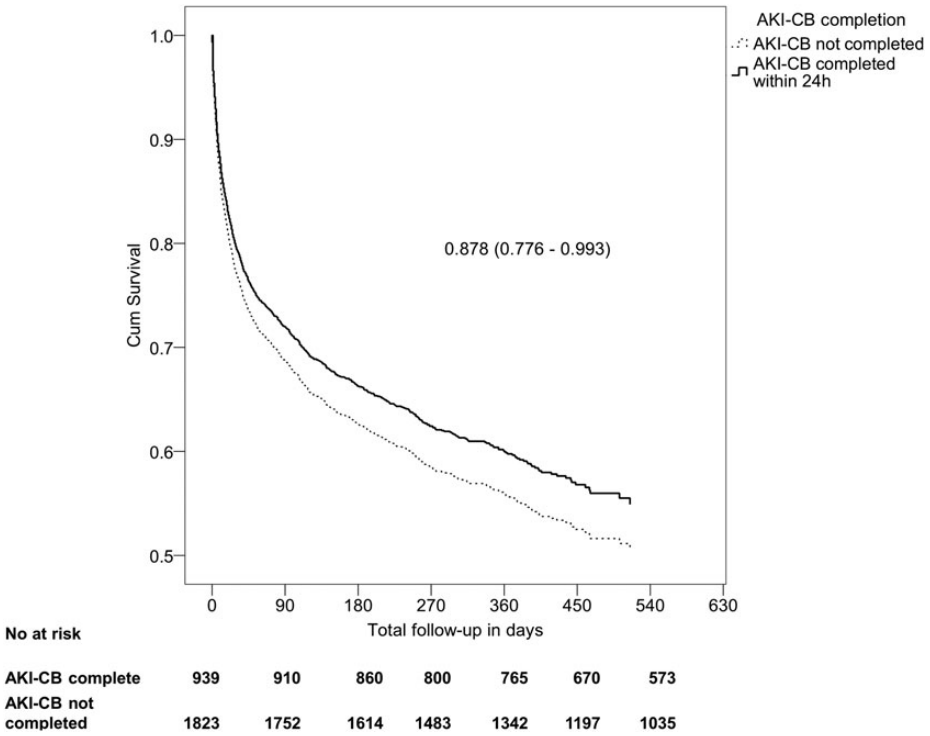


**FIGURE 3:** Adjusted survival curve stratified by timing of completion of the AKI-CB.

confounders, could be useful, but this would present the dilemma of whether it is ethical to randomly assign people to suboptimal care as well as the practical challenge of obtaining informed consent in the setting of an acute illness that may in turn introduce selection bias. In the absence of an RCT, this analysis using propensity score matching provides the most robust evidence to date of the benefit of a care bundle when applied to the management of AKI.

Previous studies have investigated the potential of several different information technology-based interventions to improve outcomes in AKI. In a study conducted in intensive care, a real-time electronic AKI alert was associated with an increase in therapeutic interventions in the form of fluid therapy, diuretics or vasopressors when compared with the pre-alert and post-alert phases [17]. Although a higher proportion of AKI patients in the alert phase returned to baseline renal function, there was no significant difference in intensive care or hospital mortality at 28 days. One possible reason for failure to show improvement in outcome was that the alert was primarily based on urine output criteria. Another reason could be the lack of associated use of guidelines in the form of a clinical decision support system. This is supported by the findings of a recent cluster-randomized trial of electronic AKI alerts that found no improvement in clinical outcomes in hospitals randomized to introduce the alerting system [10]. The most likely reason for this disappointing finding was lack of targeted education to accompany the electronic alert and absence of a clinical decision support system that resulted in no more preventive or therapeutic measures being instituted in the hospitals with alerts compared with those without alerts. Lack of AKI stages, admission method and site of onset of AKI at randomization, all of which are known to influence mortality, are also limitations of this study.

Our studies are the first to demonstrate the effectiveness of a care bundle in the setting of AKI. Nevertheless, use of a care bundle is not unique to AKI and has been previously used in sepsis, stroke, ventilator-associated pneumonia, community-acquired pneumonia (CAP) and acute exacerbation of chronic obstructive pulmonary disease (COPD) [18–21]. In the British Thoracic Society (BTS) Care Bundle project, review of patient-level data showed that use of a care bundle was associated with a reduction in 30-day in-patient mortality from CAP from 13.6 to 8.8% [19]. In addition, there was a statistically significant reduction in mortality from acute exacerbation of COPD in patients in whom oxygen was prescribed at admission (OR: 0.22; 95% CI: 0.05–0.88) and in patients in whom care was delivered within 4 h of admission (OR: 0.60; 95% CI: 0.42–0.87) [20]. The reason for the success of this project was education and support provided through a series of face-to-face and WebEx meetings throughout the study period [22].

During the study period, we stressed the importance of compliance with the AKI-CB at induction of junior doctors and made education an integral part of AKI service improvement [23]. This was reflected in an increase in compliance with AKI-CB completion from 12.5% in the previous study to 25% in in the present study, but we concede that 25% is still unacceptably low. Studies of other care bundles have reported similarly disappointing completion rates. In the sepsis care bundle study, the compliance rate with 6- and 24-h sepsis care bundle was only 52 and 30%, respectively [12]. In the BTS Care Bundle project, the rate of completion of COPD care bundle gradually increased from 1.8 to 15.6% over a

| Observation | |
|---|---|
| AUDITS | |
| **Assess History and Examine (VENUS)** | % |
| Volume depletion | 52.8 |
| Detailed history | 18.2 |
| 3H Haemoptysis, Haemolysis, Hypercalcemia | 3.3 |
| 3R Rash, Recent vascular intervention, Raised CK | 2.3 |
| Nephrotoxins - Check medications | 34.8 |
| (Contrast Media, ACEI, ARB, NSAIDs, Diuretic) | 15.3 |
| Urinary symptoms - Obstruction, oliguria, haematuria, colic | 15 |
| Sepsis | 28.3 |
| **Urine Dipstick** | |
| Blood | 7.6 |
| Protein | 7.1 |
| Leucocytes | 6.6 |
| **Diagnosis** **Think cause of AKI** | |
| Pre Renal | 56.8 |
| Renal | 11.1 |
| Post Renal | 8.1 |
| **Investigations** | |
| UE, Bicarb, Glucose, ECG, CXR, Cultures | 56.6 |
| Renal Ultrasound (if Stage 2 or 3, or obstruction suspected) | 19.4 |
| **Treatment (PUMP)** | |
| Perfusion - ensure euvolemic status | 61 |
| Underlying cause - stop nephrotoxins, antibiotics for sepsis, relive obstructio | 60.4 |
| Monitor - EWS, volume status, Daily U+Es, fluid balance | 62 |
| Prevent & treat complications - fluid overdload, adjust doses of meds, hyper | 49.5 |
| **Seek advice** | |
| Seek renal advice (bleep 8121) for all AKI stage 3 and, | 14.5 |
| if specific cause for AKI is suspected. refer ro TRUST AKI Website | 2.4 |

**FIGURE 4:** Findings associated with each element in patients who had the AKI-CB completed. CK, creatine kinase; ACEI, angiotensin-converting enzyme inhibitor; ARB, angiotensin receptor blocker; NSAID, non-steroidal anti-inflammatory drugs; ECG, electrocardiograph; CXR, chest X-ray; UE, urea and electrolytes; EWS, early warning score; U+E, urea and electrolytes.

12-month period [22]. It has been shown in other studies that compliance with acute myocardial infarction guidelines reduces 1-year mortality; however, compliance with guidelines remained a concern [24].

### Strengths and limitations

The main limitation of this observational study is potential unmeasured confounders, which cannot be completely excluded even in a propensity score-matched study. There were 331 doctors of various grades who completed the AKI-CB over a period of 15 months. In our institute, mostly junior doctors do the initial clerking of patients and another team of doctors performs subsequent management. Doctors' work shifts and teams therefore change from day to day. This would tend to dilute out any effect of more or less diligent individual doctors reducing bias. Moreover, management by constantly changing teams makes it extremely important that the junior doctor clerking the patient initiates initial appropriate care, and this is what the AKI-CB is designed to achieve. Although there was no statistical difference in comorbidities between the two groups, lack of data on the severity of illness at presentation remains an important limitation. In addition, we were unable to match reason for admission to the hospital. We found a significantly greater proportion of dementia, cancer and peripheral vascular disease in patients who were not used in propensity score matching and who did not have the AKI-CB completed. This cohort also had greater proportion of AKI stage 1, but higher mortality. One possible explanation for this observation is that the higher mortality in the unmatched group may have been due to comorbid factors and this illustrates the value of propensity score matching. Another limitation is that this is a single centre study and although we have shown previously that compliance with the AKI-CB is associated with lower mortality, these findings need to be confirmed in other centres using a similar AKI-CB. In addition, we were unable to collect data from patients in whom the AKI-CB was not completed on investigations performed including blood tests, electrocardiograph, ultrasound and X-rays or management actions performed including fluid administration and medication review.

## CONCLUSIONS

The use of a simple AKI-CB was associated with reduced progression of AKI to higher stages and decreased in-hospital mortality. More effort, both in the form of education and information technology measures, is needed to increase compliance from the current rate of 25%. Implementation of an AKI-CB may assist in improving outcomes in all healthcare settings and should be considered as part of the International Society of Nephrology's campaign to eliminate all avoidable deaths from AKI by 2025.

## SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

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## AUTHORS' CONTRIBUTIONS

N.V.K. developed the AKI-CB and the study design. T.R. and K.E.S. undertook data extraction. N.V.K. analysed the data. All authors contributed to the interpretation of the data and revision of the manuscript. Transparency statement: N.V.K. (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. As an observational study, we adhered to the principles of the STROBE statement and have reported this article in keeping with the recommended guidance.

## CONFLICT OF INTEREST STATEMENT

None declared. The results presented in this paper have not been published previously in whole or part, except in abstract form.

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