A Multicentre, Stepped-Wedge Cluster Randomised Trial of a Complex Intervention to Reduce Harm Associated with Acute Kidney Injury

Selby NM[1,2], Casula A[3], Lamming L[4], Stoves J[5], Samarasinghe Y[6], Lewington AL[7], Roberts R[5], Shah N[8], Fluck RJ[2], Johnson M[9], Jackson N[9], Jones C[8], Mohammed MA[4], Caskey FJ[3]

[1] Centre for Kidney Research and Innovation University of Nottingham, [2]Department of Renal Medicine Royal Derby Hospital, [3]UK Renal Registry, [4]University of Bradford, [5]Bradford Teaching Hospitals, [6]Frimley Park Hospital, [7]Leeds Teaching Hospitals, [8]Ashford and St Peter's Hospital, [9]Bradford Improvement Academy

Contact: nicholas.selby@nottingham.ac.uk

Introduction

Acute kidney injury (AKI) is common and associated with poor outcomes. AKI management requires methodical delivery of basic elements of care but variations in standards of AKI care are commonplace. It has been suggested that strategies to address these gaps in care may translate into improved patient outcomes. We sought to test this hypothesis by evaluating the effectiveness, at the hospital level, of a package of measures to reduce harm associated with AKI.

Methods

- **Study design**: Multi-centre, pragmatic, stepped-wedge cluster randomised trial (SWCRT), summarised in figure 1.
- **Study setting**: Five UK hospitals, including teaching and non-teaching centres. Differences between centres included size (range 593 to 2061 beds); number of emergency admssions (23k to 83k per annum); and pre-existing quality improvement infrastructure.
- **Intervention**: AKI alerts, a care bundle and an educational program, introduced sequentially at an organisation-level across fixed three month periods until all hospitals were exposed to the intervention.
- **Randomisation**: Hospitals were randomly allocated to the order in which they introduced the intervention.
- **Patients**: All patients with AKI aged ≥18 years hospitalised for >1day. Chronic dialysis was the only exclusion criterion.
- **Data collection**: In 3 month periods, with a minimum of two pre-exposure (control), one transition and at least one post-implementation (intervention) periods per site. AKI episodes were identified as per a modified KDIGO definition using the NHS England AKI detection algorithm. Patient demographics, comorbidity and outcome data were collected from hospital episode statistics. A nested evaluation of the effect on processes of care was by case-note audit.
- **Outcome measures**: The primary outcome was 30-day mortality associated with AKI. Secondary endpoints included AKI incidence, AKI progression, hospital length of stay (LoS) and effects of the intervention on process of care.
- **Sample size**: With a trial duration of two years, 10,850 AKI episodes would be required to detect a decrease in mortality from 16% to 12.8% with 80% power.

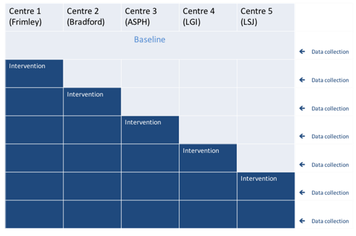

Figure 1. Schematic of stepped wedge design. The SWCRT design involved pre-intervention data collection, followed by sequential implementation of the intervention across fixed 3 month periods until all centres were exposed. Data collection occurred at each step of the wedge including in the post intervention period. Randomisation occurred at the hospital level to avoid contamination between control and intervention groups. Other advantages of SWCRT design include avoidance of ethical concerns regarding withholding an intervention that could be considered in line with minimum care standards and allows differentiation of time-related factors in a way that before-after comparisons cannot. The SWCRT is also particularly suited to interventions that require a quality improvement approach so that centres can benefit from the experience of those that have implemented before them in the stepped wedge.
ASPH Ashford and St Peters Hospital; LGI Leeds General Infirmary; LSJ Leeds St James Hospital

Results

24,059 AKI episodes were studied (unadjusted incidence 7.6 cases/100 admissions) in 20,719 patients. Patient details in control and intervention periods are shown in table 1.

	Control period	Intervention period	p value
Number of admissions	14042	10017	
% Male	50%	48%	0.007
Age	71.2 ± 18	72.4 ± 17	<0.001
Charlson comorbidity score (percentage per group)	Score 0: 16.4% Score 1: 20.3% Score 2: 20.2% Score 3+: 43.1%	Score 0: 18.8% Score 1: 21.0% Score 2: 19.4% Score 3+: 40.9%	<0.001
Ethnicity	86.1% Caucasian	85.3% Caucasian	0.8
Deprivation score (percentage per quintile: 1 least deprived, 5 the most)	(Grp 1) 23%; 18%; 16%; 16%; 27% (Grp 5)	(Grp 1) 36%; 17%; 16%; 13%; 17% (Grp 5)	<0.001
Peak AKI stage	Stage 1: 60.6% Stage 2: 21.4% Stage 3: 18.0%	Stage 1: 64.5% Stage 2: 19.8% Stage 3: 15.7%	<0.001
% hospital acquired AKI (onset >24hrs post admission)	53.8%	49.4%	<0.001
% of admissions in winter	37%	45%	<0.001

Table 1. Characteristics of patients in control and intervention periods. Note that hospitals contributed different proportions of patients to control/intervention periods due to SWCRT design so that unadjusted differences between the groups may reflect centre differences, time and seasonal effects as well as intervention effects.

Primary outcome

- Overall 30d mortality was 24.5%, with no difference between control and intervention periods (OR 1.07, 95% CI 0.93-1.24).

Secondary outcomes

- Hospital length of stay (LoS) was reduced in the intervention period. Results from quantile regression analysis are shown in figure 2A.

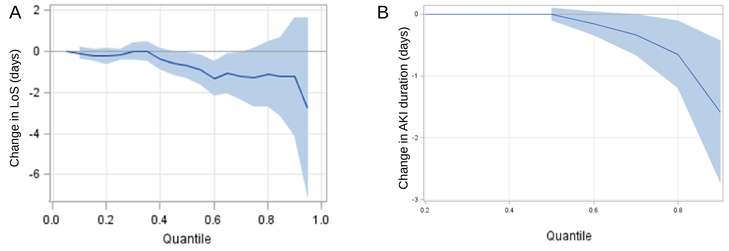

Figure 2A. Quantile regression analysis of hospital length of stay (LoS), allowing comparison across the whole distribution, rather than only a comparison of means. Change in hospital length of stay is shown on the y-axis at different quantiles of the distribution, comparing the effect of the intervention against control period. The solid blue line represents the average change in hospital LoS in the intervention period. Results show significant reduction in LoS at 60th percentile with an effect size of -0.7 days (95% CI -1.3 to -0.1), and a trend for reduction in LoS at higher percentiles.
Figure 2B. Quantile regression analysis of AKI duration. Results show significant reduction in AKI duration at 80th and 90th percentiles with an effect size of -0.7 days (95% CI -1.2 to -0.1) and -1.6 days (95% CI -2.7 to -0.4) respectively.

- Duration of AKI was shorter in the intervention period. Quantile regression showed that the effect was seen in 80-90th percentiles i.e. those patients with a longer AKI duration (≥5 days). These results are shown in figure 2B.
- The incidence of AKI increased in the intervention period (crude incidence 7.3/100 admissions vs. 8.0/100 admissions). After adjustment for age, gender, time, season and centre the rate of AKI was 11.6% higher in the intervention period (p<0.001).
- There was no difference in the rate of AKI progression between control and intervention periods after adjustment for age, gender, comorbidity and time (OR 0.97, 95% CI 0.83 to 1.14).

Results

Process measures were assessed in 1042 patients. In the intervention period, improvements were seen in several metrics including AKI recognition, medication optimization, fluid assessment and urinalysis; care bundle usage was 40% with variation between centres (range 15-68%). These data are shown in figure 3.

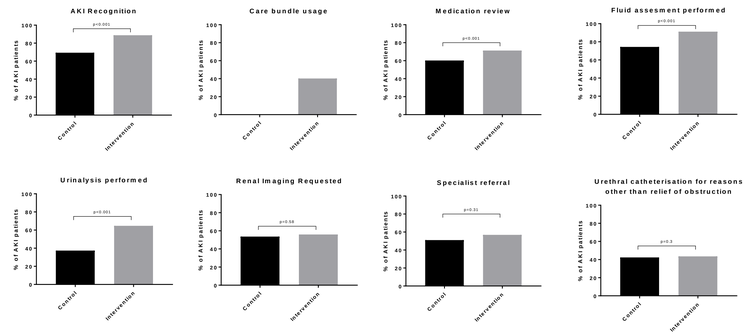

Figure 3. Comparison of processes of care between control and intervention periods. For each audit measure, results are compared using Chi-squared analysis. Urethral catheterisation for reasons other than relief of obstruction was included as a balancing measure to survey unintended consequences.

Conclusions

A complex, hospital-wide intervention to reduce harm associated with AKI resulted in improvements in delivery of care, improved AKI detection, shorter duration of AKI and a modest reduction in LoS, but did not alter 30-day AKI mortality.

- The effect of the intervention on LoS was not apparent in those with a short hospital stay, but became significant in those that stay in hospital for five days or longer. A similar effect was seen with AKI duration, possibly reflecting limited potential for improvement in those with very short LoS or AKI duration.
- Although modest on an individual patient level, the reduction in LoS has a potentially significant health economic impact in view of the large numbers of hospitalised patients who sustain AKI.
- Possible explanations for why the intervention did not affect 30d mortality include: lack of effect of intervention on this outcome; or that failure to achieve complete hospital-wide spread led to dilution of effect at an organisational level. Further insights into the fidelity of the intervention and the variation in improvement in process measures between centres are currently being explored in a qualitative analysis.
- The increase in incidence of AKI during the intervention likely reflects better testing and detection of AKI. This is supported by the increase in AKI recognition seen in the audit of processes of care.

The University of Nottingham UNITED KINGDOM · CHINA · MALAYSIA
Derby Teaching Hospitals NHS Foundation Trust
University of Bradford
Tackling Acute Kidney Injury
The Health Foundation