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Design and Rationale of 'Tackling Acute Kidney Injury', a Multicentre Quality Improvement Study

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Abstract
Acute kidney injury (AKI) is common and associated with extremely poor outcomes. While strategies to tackle deficiencies in basic care delivery are advocated, robust testing of their effectiveness is also needed. The Tackling AKI study was designed to test whether a complex intervention (consisting of an e-alert, care bundle and education programme) can be successfully implemented across a range of UK hospitals, and whether this will deliver improved patient outcomes. This multicentre, pragmatic clinical trial will employ a cluster randomised stepped wedge design to study this in all adult patients who sustain AKI in the 5 participating hospitals over a 2-year period. The intervention will be supported by a comprehensive change management framework. Data collection will include patient outcomes, process measures and a qualitative assessment of barriers and enablers to implementation. This article describes the rationale and design behind the Tackling AKI study.

Background and Rationale

The high incidence and poor outcomes of patients with acute kidney injury (AKI) represent major challenges [1, 2]. In the absence of specific pharmacotherapies, AKI management requires methodical delivery of basic elements of care, as recommended in national and international guidelines [3]. However, several studies encompassing a variety of health care systems have demonstrated that deficiencies in AKI care are all too common and contribute directly to poor outcomes [4–9]. Commonly reported deficiencies include delayed AKI recognition, inconsistent investigation, omissions in fluid/medication management and inadequate senior clinician review [4]. Efforts to address these care gaps are increasingly gaining attention and although initial reports are encouraging [10–12], fur-

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ther robust evidence is required. Over the last 6 years, we have introduced and reported a number of interventions at the Royal Derby Hospital to address care gaps in patients with AKI. These comprise an electronic AKI detection and alerting system [13], a tailor-made education package [14] and an AKI care bundle [11]. Early data suggest that this combined approach has improved delivery of basic care and reduced hospital mortality rates [11, 12]. More recently, similar findings from another UK hospital have been reported in the abstract form [15]. Conversely, a randomised controlled trial of an e-alert for AKI that was introduced into a US hospital in isolation without any improvement framework showed no impact on either the physicians' behaviour or patient outcomes [16].

In 2014, the Health Foundation released a call for proposals for their Scaling Up Improvement programme (www.health.org.uk/programmes/scaling-improvement), to test how interventions with proof of principle can be delivered at a larger scale. In response to this call, the Tackling AKI study was conceived to definitively test the effectiveness of the approach to AKI developed in Derby, and this study was selected for the Scaling Up Programme after a competitive peer-review process. The overall aims of Tackling AKI are to:

- test the effectiveness of a complex intervention to improve basic standards of care for patients with AKI, and to measure the effects on patient outcomes;
- describe the processes, barriers and enablers that allow successful adoption of the intervention across a range of secondary and tertiary care hospitals in the United Kingdom.

Study Organisation

Tackling AKI consists of a lead organisation (Royal Derby Hospital) partnered with 5 National Health Service (NHS) hospital sites in which the intervention will be tested (Leeds General Infirmary, St. James's University Hospital, Bradford Teaching Hospitals NHS Foundation Trust, Frimley Health NHS Foundation Trust and Ashford and St. Peters NHS Foundation Trust, the latter 2 supported by Surrey Pathology Services). These sites represent academic and non-academic centres as well as those with and without onsite nephology services. Quantitative data collection and analysis will be performed independently by the UK Renal Registry and for qualitative data by the University of Bradford. The NHS England AKI programme (part of the Think Kidneys initiative) provides executive partnership.

The Intervention

The intervention has 3 components:

- An AKI electronic detection and alerting system within pathology laboratory software
- An educational program to raise awareness and knowledge of AKI in care workers at hospital
- An AKI care bundle, with individual elements pertaining to assessment, investigation and basic management (fluid therapy, medication management) of AKI.

At each site, the AKI electronic detection system will be identical, conforming with a nationally mandated specification based on the KDIGO classification [17]. This will provide the mechanism of identifying AKI cases on a hospital-wide basis as well as forming a basis for alert generation. The detection algorithm will run at all sites throughout the study period, with alerts becoming visible to clinicians at the point at which the centre is randomised to introduce the intervention. The education programme and care bundle will be adapted to meet the needs of individual hospitals but based on national guidance [2] and materials developed in Derby.

Introduction of the intervention will be supported by a structured approach to change management. This will be tailored to each participating partner organisation and arrangements for joint learning will be made. A number of principles will be adhered to, including engaging and maintaining senior executive support; site-specific assessment of context and planning at baseline; team building incorporating defined roles and responsibilities; and sustainability and spread planning. In addition, there will be 2 core strategies to support implementation of the intervention. First, a peer-assist and review programme will allow learning to be captured at each step of study design and then passed on to the next centre to implement. Second, measurement for improvement will be employed to support care bundle usage, with results fed back to frontline staff to promote uptake.

Study Design

Tackling AKI is a multi-centre, pragmatic clinical trial employing a stepped-wedge cluster randomised trial (SWCRT) design [18]. The SWCRT design was based on several considerations. First, the intervention requires hospital-wide implementation, and randomisation within a single centre would almost certainly result in contamination of control groups. In addition, the nature of the intervention is aimed at reducing care gaps, as opposed to

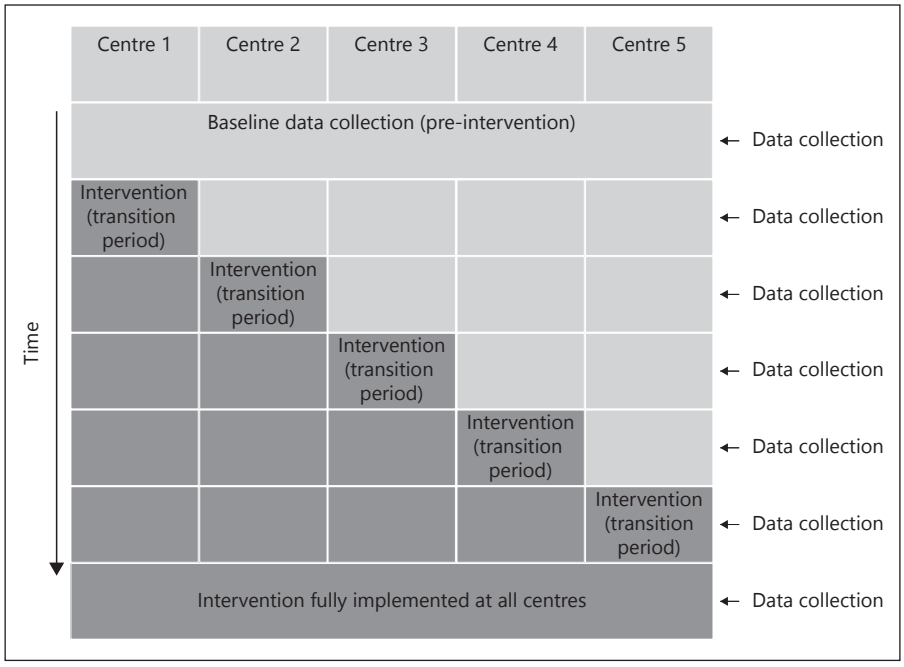

Fig. 1. Schematic of stepped wedge design. After a period of baseline data collection, the intervention is sequentially introduced to participating centres across fixed periods of time (each time period will be 3 months in Tackling AKI excepting the baseline period that will comprise 6 months), until all centres are exposed to the intervention. Data collection takes place at each step of the wedge, including in the post intervention period. The complex intervention being tested in Tackling AKI cannot be implemented immediately, so the first 3 months of implementation at each centre are designated a 'transition period' to allow time for roll-out; the transition periods will not be included in the primary analyses.

testing a new therapy. A SWCRT, with the intervention applied at a cluster level, overcomes ethical concerns around withholding treatment that could be considered in line with minimum care standards because the entire population recruited will receive the treatment by the end of the study. This approach also allows for differentiation between the effect of the intervention and potential independent time-related factors, something not possible with simple time-series (before-after) comparisons.

A SWCRT involves the delivery of the intervention in sequential steps to one or more units of randomisation per time-period and delivered to all the units of randomisation by the end of the study (schematic shown in figure 1). This design is particularly suited to quality improvement or pragmatic trials. A baseline (control) period prior to any of the centres introducing the intervention will be followed by 5 randomisation steps (1 hospital per step). The time-period immediately after a site introduces the intervention, when it is expected not to have reached full effect on outcomes is considered a transition period and excluded from analyses. There will be a total of 8 time-periods, each of 3 months in length (24 months in total). There are no reporting guidelines specific to SWCRTs, so the study's Statistical Analysis Plan (SAP) has been designed to be consistent with the extension to cluster randomised trials of the CONSORT 2010 document [19] and further suggestions recently published for SWCRT [18].

Participants

All patients aged ≥18 years who are hospitalised for at least 24 h and who sustain AKI during the study period will be included. Patients will be defined as having AKI if they have an inpatient serum creatinine result consistent with KDIGO definitions of AKI, as identified by the NHS England algorithm [17]. The algorithm selects baseline serum creatinine results from 1 to 7 and 8–365 days prior to the index result. Patients who do not have baseline creatinine measurements in this period will not be included, as extending baseline criteria back longer than this may result in deterioration of algorithm performance [20]. Urine output criteria will not be used to detect AKI; while of clear value in intensive care settings, there are limited data currently to inform the practicality and utility of their use in general hospitalised patients [21]. Patients on chronic dialysis will be excluded. The study was submitted to Derbyshire Research Ethics committee who designated the study as service improvement and waived the requirement for individual patient consent.

Outcome Measures and Data Collection

The primary outcome will be 30-day mortality after an episode of AKI. A number of pre-defined secondary outcomes include incidence of hospital-acquired AKI; AKI

progression (defined as AKI that increases by at least one stage of AKI from AKI-stage at time of first detection); incidence of individual AKI stages; length of hospital stay; number of critical care bed days used by patients with AKI; and renal recovery by time of hospital discharge. Patient outcome data will be collected using biochemical data to identify cases, and then linked to hospital stay databases to determine patient demographics, co-morbidity (ICD-10 coding) and outcome measures.

Process Measures

The proportion of patients receiving elements of basic care (AKI recognition, fluid assessment, medication review, investigation and senior clinician/speciality review) will be determined by repeated cycles of clinical audit that will be completed in each centre. Thirty sequential patients from each stage of AKI will be selected at each step of the study design, giving a total sample of 1,050 case notes evenly distributed across AKI stages 1, 2 and 3. A comprehensive data specification has been developed to standardise data collection. The audit will also include measures of care bundle usage and compliance.

Qualitative Evaluation

The qualitative evaluation aims to develop an understanding of how the package of AKI interventions works (or not) from the perspectives of key stakeholders involved in the design, implementation and delivery of the package of interventions. The shared learning, which results from scaling-up across multiple centres, will also be considered. The evaluation findings will be fed-back at various points during the course of the project within the step-wedge design and at the end with a collective look back at the common themes across all centres. A 'realist evaluation' perspective [22] will be incorporated that asks the question: in what circumstances, and in what ways does the package of AKI interventions impact on outcomes (or not)? A multimethods approach will be used for data collection incorporating key informant interviews, peer assist/review meeting notes, questionnaires (to determine barriers/enablers) and documentation from change management processes.

Statistical Plan

A comprehensive SAP has been developed, particularly to account for the clustered nature of the design and the confounding effect of time. In summary, analysis of 30-day mortality will be undertaken using a mixed-effects logistic regression model with hospital in the model as a random effect. If a non-insignificant proportion of episodes of AKI should be multiple episodes in same patients, we will also account for the correlation between episodes in the same patient by fitting a second random effect for patient in the analysis. The primary outcome response will be binary and the OR estimate of the mortality risk for the treatment effect (intervention vs. control) with 95% CI will be calculated. Analysis will be adjusted by time-period (step) and individual patients' characteristics (age, gender, Charlson comorbidity score). The impact of the intervention on outcomes could potentially change over time, so possible interactions between time and treatment effect will be explored. Similar principles will be utilised for secondary outcomes.

Sample Size Calculation

The total annual number of hospital admissions across the 5 centres (~434,000) was taken from the Health and Social Care Information Centre (www.hscic.gov.uk). The most conservative published rates were used for assumptions of AKI incidence (2.5% of admissions [23]) and 30-day mortality (16% [13]). Power was set at 80%, alpha at 0.05 and a range of values for inter class correlation between 0.01 and 0.2 was considered. For the sample size calculations we used Stata accommodating for the transition periods [24]. With a trial study-time of 2 years, with 5 participating centres (one unit per randomisation step) and with one transition period (fig. 1), we would be able to detect a decrease in mortality from 16 to 12.8%. This corresponds to a reduction of about 20% in 30-day mortality, which is both clinically relevant and plausible.

Summary

There is a pressing need to develop ways to improve the basic care of AKI. We must focus on both the nature of interventions but also how best to implement them on a hospital wide basis. Tackling AKI is a well-positioned study to provide evidence in these areas, in addition to generating valuable information on the merits of the chosen study design in this context.

Collaborators/Contributors of the Tackling AKI Investigators

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Hospital; Ashley Garner: Leeds Teaching Hospitals NHS trust; Natalie Jackson: Improvement Academy, Bradford Institute for Health Research; Melanie Johnson: Improvement Academy, Bradford Institute for Health Research; Carol Jones: Ashford and St. Peters NHS Foundation Trust; Craig McKibben: Surrey Pathology Services; Andrew J. Lewington: Leeds Teaching Hospitals NHS trust; Russell Roberts: Bradford Teaching Hospitals NHS Foundation Trust; Yohan Samarasinghe: Frimley Health NHS Foundation Trust; John Stoves: Bradford Teaching Hospitals NHS Foundation Trust; Ian White: Ashford and St. Peters NHS Foundation Trust.

Disclosure Statement

The authors have no conflicts of interest to declare.

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Erratum

In the article by Selby et al., entitled 'Design and rationale of 'tackling acute kidney injury', a multicentre quality improvement study' [Nephron 2016;134:200–204, DOI: 10.1159/000447675], the following acknowledgement needs to be added: The authors gratefully acknowledge the contribution of Eileen McDonach in the design and production of the qualitative evaluation plan.