

# Development of risk models for the prediction of new or worsening acute kidney injury on or during hospital admission: a cohort and nested study

Michael Bedford,<sup>1\*</sup> Paul Stevens,<sup>1</sup> Simon Coulton,<sup>2</sup>  
Jenny Billings,<sup>2</sup> Marc Farr,<sup>3</sup> Toby Wheeler,<sup>1</sup>  
Maria Kalli,<sup>4</sup> Tim Mottishaw<sup>5</sup> and Chris Farmer<sup>1</sup>

<sup>1</sup>Kent Kidney Research Group, Kent and Canterbury Hospital, East Kent Hospitals University NHS Foundation Trust, Canterbury, UK

<sup>2</sup>Centre for Health Services Studies, University of Kent, Canterbury, UK

<sup>3</sup>Department of Information, Kent and Canterbury Hospital, East Kent Hospitals University NHS Foundation Trust, Canterbury, UK

<sup>4</sup>Canterbury Christ Church University Business School, Canterbury Christ Church University, Canterbury, UK

<sup>5</sup>Strategic Development, Royal Victoria Hospital, East Kent Hospitals University NHS Foundation Trust, Canterbury, UK

\*Corresponding author

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## Scientific summary

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# Scientific summary

## Background

Acute kidney injury (AKI) is a global health issue and is a common clinical problem characterised by an acute decline in renal function, the results of which range from small changes in serum creatinine to anuric renal failure requiring renal replacement therapy. Its prevalence (5–7% among inpatients) is increasing, associated with an ageing population and increasing comorbidity. Patients with AKI have significantly increased in-hospital and 12-month mortality, length of stay, admission to intensive therapy unit, 30-day readmission and increase in care on discharge. All hospitalised patients are at risk of AKI, resulting from their presenting disease or subsequent iatrogenic injury. AKI is often preventable and reversible; however, the 2009 National Confidential Enquiry into Patient Outcome and Death [Stewart J, Findlay G, Smith N, Kelly K, Mason M. *Adding Insult to Injury. A Review of the Care of Patients Who Died in Hospital with a Primary Diagnosis of Acute Kidney Injury (Acute Renal Failure)*. London: National Confidential Enquiry into Patient Outcome and Death; 2009] highlighted systematic failings of identification and management, and recommended risk assessment of all emergency admissions. The National Institute for Health and Care Excellence (NICE) clinical guideline 169 (NICE. *Acute Kidney Injury: Prevention, Detection and Management of Acute Kidney Injury up to the Point of Renal Replacement Therapy. Clinical Guideline 169*. London: NICE; 2013) recommends research to assess the risk of AKI to drive prevention and early recognition.

## Objectives

1. Identification of AKI: accurately identify and report patients with AKI.
2. Develop predictive models: based on factors identified in primary and secondary care records and the admission characteristics of each patient, develop three predictive models to stratify the risk of (1) AKI on arrival in hospital; (2) developing AKI during the admission; and (3) worsening AKI if it is already present.
3. Produce a clinical algorithm: use the predictive model to develop an algorithm for all patients admitted to hospital to stratify them according to risk of developing AKI.
4. Integration into clinical practice: define the most effective way to incorporate the risk model into a clinical decision support system (CDSS) that can be integrated into everyday clinical practice. This will inform the follow-on study from this project.

## Study design

This study involved both quantitative and qualitative methodology. Quantitative methodology was used to (1) formulate the predictive risk model and (2) validate the risk model in the East Kent population and a second population and NHS trust (Medway NHS Foundation Trust). Qualitative methodology was employed to plan CDSS development and effectively integrate it into everyday clinical care.

## Setting

The study population comprised all patients presenting to the three acute hospitals of East Kent Hospitals University NHS Foundation Trust (EKHUFT) (Kent and Canterbury Hospital in Canterbury, William Harvey Hospital in Ashford and Queen Elizabeth the Queen Mother Hospital in Margate) in the calendar year 2011. The renal tertiary referral centre is based at Kent and Canterbury Hospital. The secondary validation population included all patients presenting to Medway NHS Foundation Trust.

## Participants

### Quantitative analysis

For risk model development and validation in the first population, the study included hospital admissions to EKHUFT during 2011, excluding maternity admissions and elective admissions. For validation in the second population, the study included hospital admission to Medway NHS Foundation Trust over the same time period and with the same exclusions.

### Qualitative analysis

The sample consisted of six renal consultants for the individual interviews and six outreach nurses who attended the focus group. All consultants worked across the three hospitals within the trust and there was representation from all hospitals from the outreach nurses.

## Data collection

Data were extracted from four primary databases at EKHUFT: the hospital episode database (age, sex, comorbidities, hospital admission and outpatient history); the pathology database (relevant pathology tests, e.g. C-reactive protein (CRP) levels, white blood cell count (WBC), microbiology tests, proteinuria testing, and including level of creatinine to define AKI and chronic kidney disease stage); the electronic discharge notification database (drug history); and the operation database (operative procedures).

## Data analysis

### Quantitative

We investigated the use of both Bayesian and traditional regression methods to develop the risk models. In the Bayesian methods we worked out the likelihood function of the data, placed a prior distribution over all of the unknown parameters and used the Bayes theorem to calculate the posterior distribution over all parameters. We selected a normal distribution prior for the unknown coefficients, and within that incorporated the stochastic search variable selection approach described in George and McCulloch (George CI, McCulloch RE. Variable selection via Gibbs sampling. *J Am Stat Assoc* 1993;**88**:88–9). To proceed to the calculation of the posterior and to inference we used Markov chain Monte Carlo methods and coded/constructed a Gibbs sampler. We ran the sampler for 200,000 iterations, with the first 10,000 iterations as burn-in.

The traditional methods were performed using ordinal logistic regression and employed a robust standard error to account for multiple admissions for some patients. Initially, the individual association between each factor and AKI stage was examined individually in a series of univariable analyses. Subsequently, the joint association between the factors and AKI stage was examined in a multivariable analysis. A backwards selection procedure was used to retain only the statistically significant variables in the final models.

The developed models were validated in both the EKHUFT data set and a second population data set at Medway NHS Foundation Trust. The first approach split the validation data set into risk groups based on the predicted probabilities. Within each risk category, the actual occurrence of AKI was assessed and compared with the predictions. This method assesses both the discrimination and calibration of the model. Second, we assessed the discrimination between high- and low-risk cases by calculating the area under the receiver operating characteristic (ROC) curve. A final set of analyses examined the difference in the observed outcome and that predicted by the model using the Hosmer–Lemeshow test.

### Qualitative

The analytical approach taken for the focus group and interviews was that of Flick's content analysis (Flick U. *Introduction to Qualitative Research*. Thousand Oaks, CA: Sage Publications; 1998), whereby themes and subthemes are categorised within a pre-existing template (usually the instrumentation).

## Findings

### Quantitative

We have defined a clear clinical practice algorithm for risk assessment within the first 24 hours of hospital admission. Quantitative analysis has identified key variables from a large data set which would be useful for predicting AKI in patients admitted to hospital. Bayesian methodology enabled prediction of those at low risk of AKI on admission but could not reliably identify high-risk patients. Traditional methods to assess risk at admission (model 1) and at 24 hours (model 2) identified a number of key variables which predict AKI at both 24 hours and 72 hours post admission. Subsequent validation demonstrated areas under the ROC of 0.75 and 0.68, respectively. However, modelling was unable to reliably predict those with worsening AKI (ROC of 0.53).

The predictive variables included in the first model for the prediction of AKI at the point of admission to hospital were age, previous hospital admissions, primary diagnosis, Charlson Comorbidity Index score and laboratory variables, including levels of CRP, haemoglobin (Hb), glycated haemoglobin and troponin, proteinuria and baseline estimated glomerular filtration rate. Other variables included medications and microbiology, including blood culture and mid-stream specimen urine or catheter specimen urine. For the second model predicting new AKI at 72 hours, the results were similar; however, Hb was not a significant predictor, but levels of potassium or magnesium and WBCs were. In the second model, microbiology and medications were not significant.

### Qualitative

The qualitative analysis gave valuable insights into the use of a clinical alerting system for AKI already in operation in clinical practice in the hospitals. The analysis suggested that initial responses to the system appeared encouraging; however, there were some issues highlighted with regard to the user-friendliness of the system and the advantages and disadvantages of the timing of access to clinical alerts. The users also voiced concerns with regard to clinical communication and clinical responsibility. Despite being of small scale, which may limit its generalisability, this work has informed the development of a new alerting system and pathway of care for AKI at the trust, which will be employed to deliver the risk modelling from this study into clinical practice.

## Conclusion

In our studies we have been able to demonstrate that routinely available data can be used to highlight patients at risk of AKI both at the point of admission to hospital and following admission. However, the methodology used has its limitations, and further analysis and testing, including continuous modelling, non-linear modelling and interaction exploration, may refine the model further. This study provides valuable evidence of the relationships between key variables available from hospital electronic records and AKI. Some of the models may be refined further once physiological data become more commonly available across the NHS. We have provided a clear clinical algorithm for risk assessment within the first 24 hours of hospital admission and thereafter. The clinical algorithm includes a decision matrix and the application of the multivariable analysis to patient data. The qualitative element of this study has also highlighted the complexity of the implementation and delivery of alerting systems to the clinical front line.

## Recommendations for future research

The next stage of this work is to test these risk models in terms of their clinical, logistic and economic impact in routine clinical practice in a clinical intervention pilot study.

There should also be further work to investigate the development of clinical risk models in different settings (e.g. elective surgery or radiocontrast investigations) within clinical practice, as we believe that a number of risk models need be employed across the different settings within the secondary care environment. There should also be work to investigate the development of risk models to predict the presence of AKI in patients presenting to their general practitioner in primary care to guide testing in this setting.

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