

This is an Open Access document downloaded from ORCA, Cardiff University's institutional repository:<https://orca.cardiff.ac.uk/id/eprint/111077/>

This is the author's version of a work that was submitted to / accepted for publication.

Citation for final published version:

Holmes, J., Rainer, Timothy H. , Geen, J., Williams, J. D. and Phillips, A. O. 2018. Adding a new dimension to the weekend effect: an analysis of a national data set of electronic AKI alerts. *QJM: An International Journal of Medicine* 111 (4) , pp. 249-255. 10.1093/qjmed/hcy012

Publishers page: <http://dx.doi.org/10.1093/qjmed/hcy012>

Please note:

Changes made as a result of publishing processes such as copy-editing, formatting and page numbers may not be reflected in this version. For the definitive version of this publication, please refer to the published source. You are advised to consult the publisher's version if you wish to cite this paper.

This version is being made available in accordance with publisher policies. See <http://orca.cf.ac.uk/policies.html> for usage policies. Copyright and moral rights for publications made available in ORCA are retained by the copyright holders.



Hunting for the weekend effect in Acute Kidney Injury: an analysis of a national data set of electronic AKI alerts.

Jennifer Holmes (Welsh AKI Network Data analyst) *, Timothy Rainer (Professor of Emergency Medicine)§, John Geen (Professor of Clinical Science) ¸, John D Williams (Emeritus Professor of Nephrology) †, and Aled O Phillips (Professor of Nephrology) †

On behalf of the Welsh AKI steering group.

*Welsh Renal Clinical Network, Cwm Taf University Health Board.

§Department of Emergency Medicine, University of Cardiff School of Medicine.

¸Department of Clinical Biochemistry, Cwm Taf University Health Board and Faculty of Life Sciences and Education, University of South Wales.

†Institute of Nephrology, Cardiff University School of Medicine.

Corresponding Author;
Professor Aled Phillips
Institute of Nephrology
Cardiff University School of Medicine
University Hospital
Heath Park
Cardiff, CF14 4XN
Tel: +44 2920 748467
E-mail: Phillipsao@cf.ac.uk

Abstract

Objective: To compare weekday and weekend mortality following detection of AKI.

Design: A prospective national cohort study, with AKI identified using the Welsh National electronic AKI reporting system.

Setting: Data was collected for all cases of adult AKI in Wales between 1st November 2013 and 31st January 2017.

Participants: Data from 107 298 episodes of AKI was obtained in 77 795 patients.

Main outcome measures: The primary outcome measure was death within 90 days of AKI detection.

Results: 26 439 (28.8%) patients in whom AKI was detected on a weekday died within 90 days of the AKI episode, compared to 4551 (31.9%) patients in whom AKI was detected on a weekend (RR 1.11, 95% CI 1.08-1.14, $p < 0.001$, HR 1.16 95% CI 1.12-1.20 $p < 0.001$). There was no “weekend effect” for mortality associated with hospital-acquired AKI (HA-AKI). In contrast, weekday detection of community-acquired AKI (CA-AKI) was associated with a 22.6% (10 356) mortality compared with weekend detection of CA-AKI, which was associated with a 28.6% (1619) mortality (RR 1.26 95% CI 1.21 -1.32, $p < 0.001$, HR 1.34 95% CI 1.28 – 1.42, $p < 0.001$). The excess mortality in weekend CA-AKI was driven by CA-AKI detected at the weekend that was not admitted to hospital compared with CA-AKI detected on weekdays which was admitted to hospital (34.5% vs. 19.1%, RR 1.8, 95% CI 1.69-1.91 $p < 0.001$, HR 1.03 95% CI 1.88-2.19, $p < 0.001$). Mortality for CA-AKI detected at the weekend and subsequently admitted to hospital was associated with lower 90-day mortality (24.8%) than CA-AKI detected during the week (28%) and admitted to hospital (RR 1.14 95% CI 1.07-1.21, $P < 0.001$).

Conclusions: The “weekend effect” in AKI relates not to the quality of medical care but rather access to in-patient care for patients presenting predominantly to hospital emergency departments with AKI at the weekend, a disproportionate amount of which are discharged with severe AKI.

What this study adds

Section 1: What is already known on this subject

Data describing the weekend effect reflect an excess mortality in patients admitted to hospital at the weekend. The cause of this effect remains the subject of debate and controversy. To date it is not clear if a weekend effect extends beyond hospitalised patients.

Section 2: What this study adds

Acute kidney injury in the majority of cases occurs secondary to significant systemic illness and its severity is easily quantified by the magnitude of increase in serum creatinine. Using a data set of over 100 000 episodes of AKI we have described the variation in mortality across both hospital and community based services. Whilst AKI is associated with a “weekend effect” this is primarily driven by a cohort of community acquired AKI, which present to emergency departments at the weekend with severe AKI (Stage 2/3) but who are not admitted to hospital. The data suggest that access to in-patient services at the weekend may contribute to weekend associated excess mortality.

Introduction

Concern about increased mortality related to weekend hospital admission is currently the subject of much debate. The so called 'weekend effect' describes a greater mortality for patients admitted to hospital at the weekend than patients admitted on weekdays. This effect has been described in large national and international studies of elective ¹, emergency ^{2,3} and all admissions to hospital ^{4,5}, although there is evidence to suggest that the weekend effect might be specific to some diagnoses and procedure groups only ⁶. An assumption that excess weekend deaths are the direct result of current patterns of work have fuelled political debate and the argument for the need for organisational change to increase service provision on weekends, and provide "expanded seven day services". Recent studies however have suggested that the interpretation of the weekend effect are at least in some part explained by data artefact resultant from inconsistent coding and associated weaknesses in administrative data which cast doubt on the use of measures such as hospital standardised mortality rates ^{7,8}. A second concern is the weekend effect may also in part reflect failure to consider the severity of acuity of patients' illness ⁹. Finally studies describing stroke outcome, using sophisticated adjustment for case mix found no weekend effect, suggesting insufficient consideration of comorbidity may have contributed to previously reported weekend effects in stroke outcome ¹⁰, and cast doubt that the effect is directly related to medical staffing levels ¹¹. Of note, studies using specialist clinical databases for specific diseases or clinical departments, which include clinical and physiological data, have found little or no significant difference by day of admission^{10,12}.

Acute kidney injury (AKI) is a clinical syndrome characterised by rapid loss of kidney function, and is associated with adverse patient outcomes ¹³⁻¹⁷. AKI may arise as an isolated problem related to intrinsic kidney disease, however in the majority of cases it occurs in the setting of circulatory disturbance associated with severe illness, trauma or surgery. AKI therefore represents a complication of a wide spectrum of acute illness. AKI is estimated to occur in up to 15% of hospitalised patients and up to 60% of critically ill patients ^{14,15,18}. Based on a presumption that early identification may facilitate appropriate of care and improve patient outcomes, an automated real time e-alert system for AKI based on the Kidney Disease: Improving Global Outcomes (KDIGO) change in creatinine diagnostic criteria has been

established and implemented nationally across all areas of the National Health Service in Wales, and the other home countries of the United Kingdom. Using the electronic AKI alert, we have developed a centralised data collection system to provide a comprehensive characterisation of the incidence of AKI identified by an electronic alert, and its outcome in Wales¹⁹⁻²¹.

In this manuscript we have used this data set to evaluate the “weekend effect” and AKI associated mortality for all cases of biochemically defined AKI across both hospital and community settings. The use of a creatinine-based definition therefore avoids inconsistencies related to coding and also allows a subjective measure of diseases severity using agreed AKI staging criteria.

Methods

The study was approved under Service Evaluation Project Registration.

Electronic Reporting of AKI:

The previously described (and validated) Welsh electronic AKI reporting system^{19 22}, utilises the Welsh Laboratory Information Management System (WLIMS), (InterSystems TrakCare Lab) to automatically compare in real time measured creatinine values on an individual patient against previous results. This generates electronic AKI alerts, derived from a nationally agreed algorithm based on KDIGO AKI criteria²³.

Data Collection:

Data was collected for all cases of adult (≥ 18 yrs of age) AKI in Wales between 1st November 2013 and the 31st January 2017, and organised into day of the week. The days of the week were divided into two groups: Weekdays (Monday to Friday), and Weekends (Saturday and Sunday). All bank holidays were excluded from analysis. Clinical location, patient age, AKI stage and the rule under which the AKI alert was generated was collected together with all measurements of renal function for up to 30 days following the AKI alert. To prevent inclusion of known patients receiving renal replacement therapy, alerts transmitted by patients from a renal, renal transplant, or dialysis setting, and by patients who had a previous blood test in a dialysis unit were excluded.

Mortality data were collected from the Welsh Demographic Service²⁴.

Data analysis:

All patients for which the first alert was issued during a hospital admission who also had a normal serum creatinine (SCr) value generated in a hospital setting within the preceding seven days were defined as Hospital acquired (HA)-AKI. Patients alerting in a non-inpatient setting (including Accident and Emergency/Acute assessment units) and not alerting in primary care were classified as non-primary care community acquired (CA)-AKI. Primary care and non-primary care CA-AKI therefore collectively represent CA-AKI. Hospitalisation of CA-AKI (Admitted CA-AKI) was defined as a measurement of renal function in a hospital setting within 7 days following the AKI e-alert. 13478 (12.6%) patients whilst alerting in an in-patient setting had no results for the previous 7 days. As these patients did not therefore fall into either CA- or HA- definitions, they were excluded from the subgroup analysis.

An incident AKI episode was defined as 30 days i.e. any AKI e-alert for the same patient within 30 days the incident alert was not considered a new episode. Progression of AKI was defined as a peak AKI stage higher than that associated with incident e-alert or for stage 3 alerts an increase $\geq 50\%$ from the SCr generating the alert. Pre-existing chronic kidney disease was defined as an eGFR (calculated by CKDEpi eGFR formula²⁵) $< 60 \text{ ml/min/1.73m}^2$ derived from the baseline SCr. Admission to ICU was defined as a blood test taken in an ICU setting within 7 days of the alert.

Statistical significance was determined by one-way ANOVA, student t test and Chi² test as appropriate. The influence of age, sex and pre-existing CKD on AKI incidence was assessed by Cox logistic regression. P values less than 0.05 were considered statistically significant.

Results

Analyses included a total of 107 298 episodes of AKI in 77 795 patients. Substantially fewer episodes of AKI were detected on weekends than on weekdays. Average daily weekday AKI incidence represented 17.3% of the weekly total compared to the average daily weekend incidence of 6.7% ($p < 0.001$). Mortality data was available for 106 227 AKI episodes, in which there were 30 990 (29.2%) deaths within 90 days of the AKI episode. 26 439 (28.8%) patients in whom AKI was detected on a weekday died within 90 days of the AKI episode, compared to 4551 (31.9%) patients in whom AKI was detected on a weekend (RR 1.11, 95% CI 1.08-1.14, $p < 0.001$, by linear regression HR 1.16 95% CI 1.12-1.20 $p < 0.001$). There was no difference in patient demographics in terms of sex or pre-existing CKD between the weekday and weekend groups, although the weekend cohort was marginally younger.

Severity of AKI as assessed by AKI stage at detection was no different between the two groups.

AKI may present either in patients who are already in a hospital setting, Hospital acquired (HA-AKI) or in patients outside a hospital setting, Community acquired (CA-AKI). 41 794 episodes (39.0%) of AKI represented HA-AKI and 52 016 (48.5%) episodes represented CA-AKI. 13 704 AKI episodes occurred in an inpatient setting but as no results were available for the previous 7 days it was not possible to confidently classify these as either CA- or HA-AKI and these were excluded from the subgroup analyses.

For HA-AKI the average daily weekday AKI incidence represented 17.0% of the weekly total compared to the average daily weekend incidence of 7.5% of the weekly incidence ($p < 0.001$). There was no “weekend effect” for mortality associated with HA-AKI. 90-day mortality associated with HA-AKI detected on the weekend represents 2131 patient deaths (34.4%) compared with 12 523 deaths (35.5%) in HA-AKI detected on a weekday. There was no difference in patient demographics in terms of sex or pre-existing CKD between the weekday and weekend HA-AKI groups, although the weekend cohort was significantly younger. Severity of illness at presentation as assessed by AKI stage at presentation was no different in those presenting on a weekend (AKI1: 83.9%, AKI2/3; 16.1%) compared to a weekday (AKI1: 82.7%, AKI2; 17.3%).

CA-AKI detected at the weekend was associated with a significantly higher 90-day mortality. Weekday detection of AKI was associated with a 22.6% (10 356) mortality compared with weekend detection of AKI which was associated with a 28.6% (1619) mortality (RR 1.26 95% CI 1.21 -1.32, $p < 0.001$, by regression HR 1.34 95% 1.28 – 1.42, $p < 0.001$). There was no difference in patient demographics in terms of age, sex or pre-existing CKD between the weekday and weekend CA-AKI groups. At the weekend there was a significantly higher proportion of AKI 2/3 (28.5%) compared to weekdays (15.6%, $P < 0.001$). By Cox regression AKI stage 2/3 was associated with higher hazard of death (AKI 2/3 *versus* AKI 1; HR 2.15, 95% CI, 2.07-2.23, $p < 0.001$). Weekend CA-AKI associated mortality adjusted for AKI stage remained associated with a higher hazard of death compared to weekday CA-AKI (HR 1.31, 95% CI, 1.25-1.38, $p < 0.001$).

We have previously demonstrated that the majority of CA-AKI is not admitted to hospital¹⁹
^{20 26}. In order to further understand the weekend effect in AKI we examined the influence of hospital admission on mortality in CA-AKI. CA-AKI was associated with hospital admission in 42% of episodes.

Mortality for CA-AKI detected during the week and subsequently admitted to hospital was associated with a higher 90-day mortality (28%) than CA-AKI detected during the weekend (24.8%) and admitted to hospital (RR week vs weekend: 1.14 95% CI 1.07-1.21, $P < 0.001$). Severity of illness assessed by AKI stage at presentation was greater for admitted CA-AKI detected on weekdays (AKI1: 63.6%, AKI2/3; 36.4%) compared to admitted CA-AKI detected at the weekend (AKI1: 68.2%, AKI2/3 31.8%, $p < 0.001$). By Cox regression weekday CA-AKI associated mortality in the admitted cohort, adjusted for AKI stage remained weakly associated with a higher hazard of death (HR week vs weekend: 1.08, 95% CI, 1.01-1.15, $p = 0.02$).

CA-AKI may be detected in either primary care or at the hospital front door (Accident & Emergency or Acute Assessment units). On weekend days 96.2% of CA-AKI was detected at the hospital. Within this group for those admitted 98% had a repeat measurement of renal function in a ward setting within an average of 36 hours suggesting that these patients were admitted on the day of AKI detection (i.e. weekend admission).

Non admission of CA-AKI detected at the weekend was associated with a significantly higher mortality than non-admission of CA-AKI detected on weekdays (34.5% vs. 19.1%, RR 1.8, 95% CI 1.69-1.91 $p < 0.001$, HR 2.07 95% CI 1.92-2.24, $p < 0.001$). The proportion of all CA-AKI detected at hospital, increased at the weekend (96.2% vs. 64.8%, $p < 0.001$). At the weekend the proportion of CA-AKI admitted to hospital was also significantly higher compared to weekday AKI (61.3% vs. 39.9%, $p < 0.001$). There was however a greater proportion of AKI stage 2 and 3 in the CA-AKI non-admitted patients in whom AKI was detected at the weekend (weekend AKI 2/3; 23.2% vs. weekday AKI 2/3, 10.0%, $p < 0.001$). Weekend AKI associated mortality, adjusted for AKI stage, in non-admitted CA-AKI however remained

associated with a higher hazard of death compared to the weekday group of CA-AKI who were not admitted (HR 2.03, 95% CI, 1.88-2.19, $p < 0.001$).

For CA-AKI patients who are not admitted to hospital we have previously reported that a significant proportion of patients have no repeat measurement of renal function and that the time to repeat for those who do have a check of renal function is significantly delayed. The adverse effects of weekend detected CA-AKI in the non admitted group could not however be explained by differences in follow up care. The proportion of those with repeat blood test was significantly higher in non-admitted CA-AKI weekend AKI to the non-admitted CA-AKI weekday patients (34.3% vs. 31.3%, $p = 0.004$). In addition, for those who did have a repeat measurement of renal function the time to repeat was significantly less in the weekend CA-AKI non-admitted group (5.7 ± 7.2 days vs. 8.8 ± 7.7 days, $p < 0.001$).

Discussion

Principal findings

This study demonstrates that AKI detected at the weekend is associated with increased risk of death within 90 day of the AKI episode. Whilst this effect is apparent across all cases of AKI closer scrutiny of the data demonstrates that this effect is driven by the excess mortality associated with AKI detected in the community which is not admitted to hospital. Within this cohort it is significant that there is a higher proportion of AKI stage 2 and 3 which predominantly present to hospital emergency departments where their AKI is highlighted by an electronic alert, but who are subsequently discharged to the community. Previously we have demonstrated that poor outcome for non-admitted CA-AKI is associated with inadequate follow up in terms of measuring renal function^{19 20}. This study confirms that a significant proportion of CA-AKI who are not admitted to hospital have no further measurement of renal function and for those who do have a subsequent measure of renal function following reporting of AKI, there is a significant delay. These deficiencies however, apply equally to non-admitted CA-AKI detected on weekdays and weekends.

It is of note that at the weekend a greater proportion of CA-AKI presents to the hospital and whilst a greater proportion of this is admitted at the weekend there is a cohort of patients

with significant AKI (stage 2/3) which are not being admitted. The weekend associated mortality therefore reflects a cohort of patients with more severe AKI whom are discharged to the community.

In contrast AKI acquired in hospital or in the community and admitted to hospital does not demonstrate this “weekend effect” of excess mortality. Furthermore, for patients with CA-AKI who are admitted, weekend detection and admission of AKI is associated with improved mortality. These data therefore demonstrate that a weekend effect in AKI is not a reflection of the quality of in-hospital care.

Collectively the data suggests that the weekend effect in AKI relates not to the quality of medical care but rather the access to in-patient care for patients presenting predominantly to hospital emergency departments with AKI at the weekend, a disproportionate amount of which are discharged with severe AKI.

Strengths and Weaknesses and relation to other studies

Whilst many studies have confirmed excess mortality associated with the “weekend effect”, concern has been expressed regarding interpretation of the cause of these reported observations^{27 28}. Criticism of interpretation of previous published studies describing the “weekend effect” highlight issues related to coding inaccuracies and objective measures of disease severity. A strength of our study is its accuracy is not dependent on coding but rather on objective measureable changes in serum creatinine. The diagnostic criteria for AKI is based on internationally accepted definitions which also allows staging of AKI severity based on the magnitude of the changes in creatinine thus providing a direct and objective measure of disease severity.

The use of a national data set which collects data on every episode also allows capture of data across the whole of the health community and therefore includes information on both hospitalised and patients “managed” in the community. This approach therefore allows us to examine the interface between community and hospital services. This approach highlights a novel aspect of the “weekend effect” as the disparity in patient mortality is

highest in patients diagnosed with AKI predominantly at the hospital “front door” at the weekend but who are not admitted to hospital.

Although this study uses a novel approach to address the “weekend effect” it is limited by the use of a biochemistry based data set. The data therefore lacks clinical context beyond the presence of pre-existing CKD, the detail of the cause of AKI and the cause of death. In addition, there is no linkage to primary care data sets and therefore the clinical response cannot be captured. Finally, the diagnosis of AKI is made by comparing measured creatinine values on an individual patient against the patients’ previous results, to generate alerts. This approach does consequently preclude the inclusion of the first presentation of AKI in a patient with no previous blood test on the system.

Implications for clinicians and policymakers

The results suggest that the “weekend effect” in AKI not associated with quality of care but access to care. The lack of effect of weekend detection of AKI on patient mortality for admitted CA-AKI and improved outcome for HA-AKI suggest no inequity of hospital based care at the weekend, and therefore unlikely to be related to current models of medical staffing. In contrast the study suggests that AKI associated weekend effect relate to changing patterns of admission for CA-AKI at the weekend. This is consistent with previous studies which suggest a higher Accident and Emergency admission threshold at weekends⁹. Possible explanations for this include an inappropriate delay in hospital discharge at weekends leading to pressure on in-patient beds²⁹ and reduced availability of primary care services⁹ resulting in a greater proportion of CA-AKI presenting directly to hospitals at the weekend. Recent data suggest that a 7-day team-based model of care improves patient flow and weekend discharges³⁰ and increased access to primary care which significantly reduces the weekend workload in A&E departments³¹.

Unanswered questions and future research

Whilst the data suggests that improvement in availability of primary care and increasing 7-day access to the services required to facilitate safe discharge, more research is needed to assess the impact of such radical and costly measures. In addition, the explanation for the

observed failure to admit patients with significant AKI disproportionately at the weekend remains speculative. Introduction of electronic AKI alerts was proposed as a means of highlighting high risk patients to clinicians based on a presumption that early identification may help raise standards of care and improve patient outcomes. Despite this we have highlighted that a significant cohort of patients with severe AKI were discharged with no appropriate follow up care in place, and that this was more apparent at the weekend. Although automated alerts have recently emerged as a major instrument to influence clinician behaviour our findings are consistent with previous data suggesting an electronic alert system for acute kidney injury did not improve clinical outcomes among patients in hospital³². Further work is therefore required to develop strategies which reinforce the alert to change clinician behaviour.

In conclusion we suggest that inequity of access to appropriate in-patient health care services at the weekend underlies AKI associated weekend effect on patient mortality, and this should therefore be taken into account by academics and policy makers when designing and testing proposed equitable care delivery models throughout the week and weekend.

Acknowledgements

JH designed the study, collected and analysed the data and produced the figures. JDW, TR and JG interpreted the data and wrote the report. AOP set up the program of work, designed the study, interpreted the data and wrote the report.

Funding: The work was carried out under the auspices of the Welsh AKI steering group which is sponsored by the Welsh Renal Clinical Network and Welsh Government

Disclosures: There are no competing interests

Data sharing: Anonymised patient level data are available from the corresponding author at The Institute of Nephrology, Cardiff University School of Medicine.

Transparency declaration: The lead author (AOP) 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 discrepancy from the study as planned has been explained.

References:

1. Aylin P, Alexandrescu R, Jen MH, et al. Day of week of procedure and 30 day mortality for elective surgery: retrospective analysis of hospital episode statistics. *BMJ* 2013;**346**:f2424.
2. Barba R, Losa JE, Velasco M, et al. Mortality among adult patients admitted to the hospital on weekends. *Eur J Intern Med* 2006;**17**(5):322-4.
3. Handel AE, Patel SV, Skingsley A, et al. Weekend admissions as an independent predictor of mortality: an analysis of Scottish hospital admissions. *BMJ Open* 2012;**2**(6).
4. Freemantle N, Ray D, McNulty D, et al. Increased mortality associated with weekend hospital admission: a case for expanded seven day services? *BMJ* 2015;**351**:h4596.
5. Ruiz M, Bottle A, Aylin PP. The Global Comparators project: international comparison of 30-day in-hospital mortality by day of the week. *BMJ Qual Saf* 2015;**24**(8):492-504.
6. Concha OP, Gallego B, Hillman K, et al. Do variations in hospital mortality patterns after weekend admission reflect reduced quality of care or different patient cohorts? A population-based study. *BMJ Qual Saf* 2014;**23**(3):215-22.
7. Li L, Rothwell PM, Oxford Vascular S. Biases in detection of apparent "weekend effect" on outcome with administrative coding data: population based study of stroke. *BMJ* 2016;**353**:i2648.
8. Hogan H, Zipfel R, Neuburger J, et al. Avoidability of hospital deaths and association with hospital-wide mortality ratios: retrospective case record review and regression analysis. *BMJ* 2015;**351**:h3239.
9. Meacock R, Anselmi L, Kristensen SR, et al. Higher mortality rates amongst emergency patients admitted to hospital at weekends reflect a lower probability of admission. *J Health Serv Res Policy* 2017;**22**(1):12-19.
10. Bray BD, Cloud GC, James MA, et al. Weekly variation in health-care quality by day and time of admission: a nationwide, registry-based, prospective cohort study of acute stroke care. *Lancet* 2016;**388**(10040):170-7.
11. Bray BD, Ayis S, Campbell J, et al. Associations between stroke mortality and weekend working by stroke specialist physicians and registered nurses: prospective multicentre cohort study. *PLoS Med* 2014;**11**(8):e1001705.
12. Wunsch H, Mapstone J, Brady T, et al. Hospital mortality associated with day and time of admission to intensive care units. *Intensive Care Med* 2004;**30**(5):895-901.
13. Ali T, Khan I, Simpson W, et al. Incidence and outcomes in acute kidney injury: a comprehensive population-based study. *J Am Soc Nephrol* 2007;**18**(4):1292-8.
14. Bagshaw SM, Laupland KB, Doig CJ, et al. Prognosis for long-term survival and renal recovery in critically ill patients with severe acute renal failure: a population-based study. *Crit Care* 2005;**9**(6):R700-9.
15. Lo LJ, Go AS, Chertow GM, et al. Dialysis-requiring acute renal failure increases the risk of progressive chronic kidney disease. *Kidney Int* 2009;**76**(8):893-9.
16. Pannu N, James M, Hemmelgarn B, et al. Association between AKI, recovery of renal function, and long-term outcomes after hospital discharge. *Clin J Am Soc Nephrol* 2013;**8**(2):194-202.
17. Wald R, Quinn RR, Adhikari NK, et al. Risk of chronic dialysis and death following acute kidney injury. *Am J Med* 2012;**125**(6):585-93.
18. Waikar SS, Wald R, Chertow GM, et al. Validity of International Classification of Diseases, Ninth Revision, Clinical Modification Codes for Acute Renal Failure. *J Am Soc Nephrol* 2006;**17**(6):1688-94.

19. Holmes J, Rainer T, Geen J, et al. Acute Kidney Injury in the Era of the AKI E-Alert. *Clin J Am Soc Nephrol* 2016;**11**(12):2123-31.
20. Holmes J, Allen N, Roberts G, et al. Acute Kidney Injury Electronic alerts in Primary Care - Findings from a large population cohort. *QJM* 2017.
21. Holmes J, Roberts G, May K, et al. The incidence of pediatric acute kidney injury is increased when identified by a change in a creatinine-based electronic alert. *Kidney Int* 2017;**92**(2):432-39.
22. Holmes J, Roberts G, Meran S, et al. Understanding Electronic AKI Alerts: Characterization by Definitional Rules. . *Kidney International Reports* 2016;Published online: December 8, 2016.
23. NHS England. Acute Kidney Injury (AKI) Algorithm 2014 [Available from: <https://www.england.nhs.uk/akiprogramme/aki-algorithm/>].
24. NHS Wales Informatics Service. Welsh Demographic Services 2016 [Available from: <http://www.wales.nhs.uk/nwis/page/52552>].
25. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med* 2009;**150**(9):604-12.
26. Talabani B, Zouwail S, Pyart RD, et al. Epidemiology and outcome of community-acquired acute kidney injury. *Nephrology (Carlton)* 2014;**19**(5):282-7.
27. McKee M. The weekend effect: now you see it, now you don't. *BMJ* 2016;**353**:i2750.
28. Black N. Higher Mortality in Weekend Admissions to the Hospital: True, False, or Uncertain? *JAMA* 2016;**316**(24):2593-94.
29. Varnava AM, Sedgwick JE, Deaner A, et al. Restricted weekend service inappropriately delays discharge after acute myocardial infarction. *Heart* 2002;**87**(3):216-9.
30. Gilfillan C, Newnham E, Nagappan R, et al. A 7-day team-based model of care in general medicine: implementation and outcomes at 12 months. *Intern Med J* 2016;**46**(1):79-85.
31. Dolton P, Pathania V. Can increased primary care access reduce demand for emergency care? Evidence from England's 7-day GP opening. *J Health Econ* 2016;**49**:193-208.
32. Wilson FP, Shashaty M, Testani J, et al. Automated, electronic alerts for acute kidney injury: a single-blind, parallel-group, randomised controlled trial. *Lancet* 2015;**385**(9981):1966-74.