Acute Kidney Injury Electronic alerts in Primary Care - Findings from a large population cohort.

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Abstract

Background: Electronic reporting of AKI has been used to aid early AKI recognition although its relevance to CA-AKI and primary care has not been described.

Aims: We described the characteristics and clinical outcomes of patients with CA-AKI, and AKI identified in primary care (PC-AKI) through AKI e-Alerts.

Design: A prospective national cohort study was undertaken to collect data on all e-alerts representing adult CA-AKI.

Method: The study utilised the biochemistry based AKI electronic (e)-alert system that is established across the Welsh National Health Service.

Results: 28.8% of the 22,723 CA-AKI e-alerts were classified as PC-AKI. Ninety-day mortality was 24.0% and lower for PC-AKI vs. non-primary care (non-PC) CA-AKI. Hospitalisation was 22.3% for PC-AKI and associated with greater disease severity, higher mortality, but better renal outcomes (non-recovery: 18.1% vs. 21.6%; progression of pre-existing CKD: 40.5% vs. 58.3%). 49.1% of PC-AKI had a repeat test within seven days, 42.5% between seven and ninety days, and 8.4% was not repeated within ninety days. There was significantly more non-recovery (24.0% vs. 17.9%) and progression of pre-existing CKD (63.3% vs. 47.0%) in patients with late repeated measurement of renal function compared to those with early repeated measurement of renal function.

Conclusion: The data demonstrate the clinical utility of AKI e-alerts in primary care. We recommend that a clinical review, or referral together with a repeat measurement of renal function within seven days should be considered an appropriate response to AKI e-alerts in primary care.

Introduction

It is well established that AKI requiring renal replacement therapy is associated with a high rate of in-hospital mortality (1). Less severe degrees of renal injury, have also been associated with increased mortality, prolonged in-patient hospital stay and increased costs (2, 3). In addition, AKI has long-lasting detrimental effects on a patient's health, with an increased incidence of subsequent Chronic Kidney Disease (CKD) and higher mortality (4-7). The reported incidence of AKI varies depending on its definition, the clinical setting in which it is detected, and the population studied.

Based on a presumption that early identification may help raise standards of care and improve patient outcomes, an automated real time electronic (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 (8). Agreed criteria to define AKI are based on changes in creatinine which are presumed to have occurred within the preceding 7 days (9). Many patients, especially in primary care, will have no test results within a week. The AKI e-alert therefore utilises a pragmatic adaptation of this definition using three different look-back periods to compare creatinine results (10)

In contrasts to studies of AKI in hospitalised patients **(7, 11-16)**, little data is available on the patterns of community acquired AKI, AKI in primary care and AKI which may not be associated with hospitalisation **(17-21)**. As a result, there remains limited research focused on the role of general practice in prevention and management of AKI. **Recent data however, suggest clinical outcomes in patients with acute elevations of serum creatinine in primary care, who are not admitted to hospital are significantly worse than those with stable kidney function (22)**. To highlight AKI in the community, electronic AKI alerts are currently being issued to Primary Care in the UK. The aim is to encourage early clinical assessment of acute illness and volume status, prompt review of medications with temporary cessation of nephrotoxic medications where appropriate. Although electronic reporting of AKI has been advocated, its relevance to CA-AKI and primary care has not been described. Consequently, there is no specific guidance on the appropriate response to an AKI e-alert in this setting.

Methods

Setting

Data was collected across the National Health Service in Wales which serves a population of 3.06 million. The study was approved under "Service Evaluation Project Registration".

Development of Electronic Reporting System

The previously described (and validated) Welsh electronic AKI reporting system (23) utilises the all Wales Laboratory Information Management System (LIMS), (InterSystems TrakCare Lab) which in real time automatically compares measured serum creatinine (SCr) values on an individual patient against previous results, to generate alerts using an algorithm based on changes in SCr level and KDIGO AKI staging criteria (Supplementary Figure). Three "rules" are applied to generate alerts differing in the time period from which the baseline

creatinine is obtained. Rule 1 alerts represent a >26μmol/l increase in SCr within the previous 48 hours and are issued only if rule 2 and rule 3 are not satisfied. Rule 2 alerts represent a ≥50% increase in SCr within the previous 7 days, and a rule 3 alert represents a ≥50% increase in SCr from the median of results from the previous 8 to 365 days. Creatinine is measured using kinetic Jaffe methodology on various analytical platforms across Wales.

Data Collection

Prospective data was collected for all cases of adult (≥18yrs of age) community acquired (CA)-AKI in Wales between November 2013 and April 2016. We defined an incident episode of AKI as 90 days, i.e. any AKI e-alert for the same patient within 90 days of a previous alert was not considered a new episode. **The Medical Record Number (MRN) was used as the patient identifier. This is an unique reference number allocated to each patient registered in the National Laboratory Information Management System (LIMS) and allows for multiple visits/blood test requests across all locations in Wales to be linked.**

CA-AKI was classified as patients with an e-alert generated in a non-inpatient setting. We further defined these groups as Primary Care acquired AKI (PC-AKI) and non-Primary Care acquired AKI (non-PC CA-AKI). 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 ≥50% from the SCr generating the alert. Hospitalisation was defined as a measurement of renal function in a hospital setting within 7 days following the AKI e-alert.

Mortality data were collected from the Welsh Demographic Service (24). Renal outcome analysis required patients to have 90 day follow up data available. Non-recovery was defined as achievement of a SCr value closest to and within 90 days still in keeping with the definition of AKI in comparisons to baseline SCr values. Pre-existing chronic kidney disease (PeCKD) was defined as an eGFR (calculated by CKDEpi eGFR formula) <60ml/min/1.73m^2 derived from the baseline SCr. A worsening eGFR was calculated using the eGFR value closest to and within 90 days and was defined by a decline from baseline eGFR of >15% or >5ml/min/1.73m^2.

Statistical analysis was carried out using SPSS software, version 20 (SPSS, Inc., Chicago, IL). Student's t test was used for analysis of normally distributed data. Categorical data were compared using a Pearson chi-squared test. P values less than 0.05 were considered statistically significant differences.

Results

Comparison of Primary care and non-primary care community acquired AKI.

There were 22,723 CA-AKI alerts **in a total of 21,093 patients**, of which 6534 (28.8%) were generated by tests requested in Primary care (PC-AKI). Of the non-primary care community alerts (non-PC CA-AKI) 69% were generated at the hospital front door (Accident & Emergency and Acute assessment units) 19% in outpatient settings and the remainder in day case units. **37.6% of CA-AKI episodes included multiple alerts (Mean number of repeat**

alerts during episode = 2.1). For comparison over the same time period there were 19,314 incident episodes of HA-AKI.

There was a higher proportion of females and patients with pre-existing CKD for PC-AKI compared to non-PC CA-AKI. For both groups, the majority of alerts were AKI stage 1. There was however a greater proportion of PC-AKI of AKI stage 1 and less AKI 2/3 compared to non-PC CA-AKI. The proportion of those progressing to a worse stage of AKI following the alert was not significantly different between the two groups.

In PC-AKI a higher proportion of alerts were based on rule 3 with a higher proportion of non-PC CA-AKI based on a baseline renal function derived from a more recent test results (rules 1 and 2). For PC-AKI and non-PC CA-AKI patients 4.6% and 7.7% had a blood test result requested in primary care in the preceding 7 days.

Overall 90-day mortality for all CA-AKI was 24.0% and was lower for PC-AKI (15.4%) compared to non-PC CA-AKI (27.5%, $p<0.001$) (Table 1). In contrast in the surviving group renal outcome was worse following PC-AKI with a higher proportion of 'non-recovery' and a greater proportion of those with pre-existing CKD with a significant decline in renal function at 90 days. For patients surviving to 90 days, the time to repeat renal function test after the incident alert (taken as a surrogate marker of action/recognition of the alert) was shorter for those who recovered renal function to baseline both for PC-AKI (12.9 ±16.9 recovered vs. 16.8 ±21.6 days, non-recovered, $p<0.001$) and non-PC CA-AKI (6.8 ±14.2 vs. 11.0 ±14.8, $p<0.001$) although for both outcome groups the time to repeat was significantly longer for PC-AKI compared to non-PC CA-AKI ($p<0.001$ for all).

Relationship between AKI alert and hospital admission in primary care

Of all patients with an AKI alert in primary care only 22.3% were admitted to hospital within 7 days of the alert. A comparison of patients with an alert in primary care who were admitted and those not admitted within 7 days of the alert is shown in Table 2. PC-AKI patients admitted were significantly older than those not admitted and there was a higher proportion of male patients and patients with pre-existing CKD.

Hospitalisation was associated with a higher proportion AKI stage 2 and 3 and a higher proportion of patients progressing to a higher AKI stage than the stage associated with the alert (Table 2). Reflecting the greater disease severity hospitalisation was associated with a higher mortality. Although non-admission was associated with lower mortality, in the surviving patients, non-admission was associated with worse renal outcomes (Table 2) compared to surviving patients admitted following an AKI alert (non-recovery 21.6% vs. 18.1%, $p=0.01$, progression of pre-existing CKD 58.3% vs. 40.5%, $p<0.001$).

Responses to an AKI alert in primary care

For PC-AKI, 49.1% had a repeat test requested within 7 days (Table 3). 23.5% of repeat bloods were requested in primary care within 7 days of the incident alert, following which 10.8% were admitted within 7 days of the repeat (representing 8.6% of all PC-AKI leading to

admission). 18.5% of results from tests repeated in primary care within 7 days demonstrated deterioration in renal function compared to the alerting result.

For PC-AKI, 25.6% had a repeat measurement of renal function within 7 days, but not in primary care (47.6% as hospital in-patients, 41.1% in A&E, and the remainder in a day case or hospital outpatient setting). These had a greater proportion of stage AKI stage 2 and 3 than the incident alert than the group repeated in primary care. In this group 43.2% demonstrated further deterioration and 83.0% were admitted within 7 days of repeat. This accounts for 71.9% of all PC-AKI admitted, and 89.3% of all PC-AKI admitted within 7 days of alerting.

A further 31.6% of PC-AKI had a repeat in primary care beyond 7 days of the alert. Mean time to repeat for this group was 21.9 ±17.9 days. Of these a further deterioration was reported in 17.4%, and admission within 7 days of this repeat occurred in only 4.0%. For 10.8% of PC-AKI a repeat was carried out beyond 7 days but not in primary care (34.8% in A&E, 28.9% as hospital outpatients, 19.5% as hospital in-patient, and the remainder in a day case setting). Of these 28.7% of the repeated demonstrated a further deterioration in renal function and admission (within 7 days) followed the repeated measurement in 41.7% of cases.

8.4% of PC-AKI had no recorded repeated measurement of renal function (within 90 days of alerting). 90-day mortality for this group was 13.9%.

In the surviving cohorts those with late repeated measurement of renal function (repeat >7 days) there was significantly more non-recovery (24.0% vs. 17.9% $p<0.001$) and more progression in those with pre-existing CKD at 90 days (63.3% vs. 47.0%, $p<0.001$) than in patients who had an early repeat measurement of renal function.

Discussion

Whilst AKI is recognised as being associated with increased healthcare utilization and poor health outcomes in the context of hospital settings, currently there is very little information focused on the detection and management of AKI in general practice. Although use of creatinine based definitions of AKI has limitations, the introduction of a national algorithm provides a means of alerting clinicians of significant changes in renal function indicative of AKI. Very little information is however available regarding the significance of AKI e-alerts in primary care, **although implementation of automated primary care alerts has been demonstrated to be both technically feasible and influence primary care clinicians behaviour (17).**

The data demonstrate that roughly two thirds of all community acquired AKI alerting patients, present directly to the hospital front door. The role of primary care in the identification of acute illness and referral of these patients to the hospital is not apparent from our data, and they likely represent a mixture of self referrals and GP referrals to the hospital front door without a blood test. It is however of note that very few patients with non–PC CA-AKI have a blood test in primary care in the 7 days preceding the alert. 66% of CA-AKI patients were admitted directly to an in-patient setting which represents 88% of all CA-AKI admitted to

hospital within 7 days. The remaining third of CA-AKI was generated following a blood test requested in primary care. Whilst these patients have lower 90-day mortality than the non-PC CA-AKI group, renal outcome in the surviving cohort was significantly worse.

For the alerting patients identified in primary care, within the hospitalised group there were a higher proportion of patients with AKI stage 2 and 3, and a higher proportion of patients with a serum creatinine which continued to rise following the incident alert. This suggests that that most severely ill are identified and admitted appropriately. For these patients there are two routes for admission related to an "action" within 7 days, either an alert in primary care followed by attendance at A&E, or a second blood test in primary care within 7 days of an alert followed by hospital admission. Whilst the vast majority of PC-AKI related admissions occur following a repeat check of renal function at the hospital front door, this may represent an appropriate response with the alert triggering referral to the hospital front door.

Whilst those with the most severe illness seemingly are admitted to hospital, of concern is the significantly worse renal outcome in the PC-AKI group who survive the acute episode compared to non-PC CA-AKI cohort. In this study we selected an arbitrary cut off of a repeat measurement of renal function within 7 days (in any setting) as an indication of early "response" to AKI e-alerts transmitted in a General Practice setting. For all PC-AKI a worse renal outcome was seen in those retested later than 7 days following the alert compared to those retested within 7 days. This is despite a higher admission rate in patients who have a repeated blood test within 7 days and a higher proportion of more severe AKI stage at presentation. For PC-AKI, renal outcome was worse for those not admitted to hospital, in which there were significantly fewer patients retested within 7 days of the alert (13.6% vs. 48.5%). Similarly, significantly fewer PC-AKI are retested within 7 days than non-PC CA-AKI, with a better renal outcome seen in the latter group (49.1% vs. 78.0%). Late response as measured by a delay beyond 7 days for a repeat measurement of renal function was therefore an indicator of worse renal outcome in patients surviving an episode of AKI highlighted by an e-alert.

Currently there are no specific guidelines on the management of AKI patients in the community nor the appropriate response to an electronic AKI alert in this setting. For AKI, the National Institute for Health and Care Excellence (NICE) guidelines recommend that a repeat blood sample is taken within 2 weeks to exclude AKI with new fall in glomerular filtration rate is detected (25). Our data would suggest that 7 days would be a more appropriate response time, with early "response" (either a repeat measurement of renal function or referral for review within 7 days), being associated with improved renal outcome. **A key consideration for primary care is the method of communication of the alert to the requesting clinician, as the introduction of e-alerts' in isolation are unlikely to improve outcomes (26). Recent research suggests that delivery of an AKI warning stage results results through interruptive methods is appropriate and acceptable to clinicians (27). Our current practice is that all AKI's are telephoned to primary Care, unless passed 18.30pm, when only stage 2 and 3 are phoned (as per request and agreement by Primary care colleagues). In this situation AKI stage 1 will be phoned the next morning.**

Agreed definitions define AKI based on changes in creatinine that are presumed to have occurred within the preceding 7 days (9). Not all patients have had blood tests within the last week, which is a particular issue in the community and primary care. The national algorithm has adopted a pragmatic approach to generate e-alerts which utilises look-back periods as long as one year. Our data highlight that in a community setting the vast majority of electronic alerts are based on a baseline derived from the median creatinine from the preceding 365 days (Rule 3). The data show significant adverse outcomes both in terms of patient mortality and renal outcome which suggest that his approach offers and acceptable trade–off between identifying all clinical relevant AKI patients and misclassifying patients to generate and alert which is useful and clinically relevant**. It should be notted that any patient presenting with AKI but with no measurement of renal function in the previous 365 days will not be identified by our current alogithim. An alternative suggestion has been the use of population based estimated reference creatinine measures (28), however currently in our clinical setting for these patients when a creatinine value is above the reference range, no AKI alert is issued but a message to highlight the rasied value accompanies the result report.**

Although this study is the first to describe AKI highlighted by an automated electronic alert within primary care, it is important emphasise that our intention is not to characterise AKI but rather to delineate the significance of an electronic alert. The data lacks clinical context, race, 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. Despite these limitations our study provides the first large scale description of the significance of AKI e-alerts in primary care.

The data demonstrate the clinical utility of AKI e-alerts in primary care and also identifies potential deficiencies in care. Although patients with the most severe degree of renal injury are admitted to hospital, patients in which AKI is highlighted by a test requested in primary care have worse renal outcomes. It is of note that less than half of patients highlighted by alerts in primary care are retested within 7 days of alerting. Furthermore, delayed response to the alert is associated with a significantly worse renal outcome. In conclusion we recommend that a clinical review, or referral together with a repeat measurement of renal function within 7 days should be considered an appropriate response to AKI e-alerts in primary care.

Table 1. Characteristics of PC-AKI cohort vs. non-PC CA-AKI and HA-AKI cohorts.

	PC-AKI	**Non-PC CA-AKI**	**p value**
n (% of incident episodes)	6534 (13.9)	16189 (34.4)	
Mean age ±SD (yr)	72.2 ±23.9	70.3 ±24.9	
Male % (n)	41.7 (2725)	47.9 (7749)	P<0.001
Pre-existing CKD, % (n)	43.2 (2816)	34.6 (5588)	P<0.001
Mean baseline SCr ±SD (μmol/L)	95.8 ±51.4	92.1 ±54.6	
Mean alert SCr ±SD (μmol/L)	182.2 ±130.3	185.2 ±142.2	
Subsequent test in Primary Care, % (n)	55.2 (3604)	6.9 (1111)	P<0.001
% repeat measurement <7days	49.1%	78.0%	P<0.001
Hospitalisation within 7 days of alert, % (n)	22.3 (1459)	66.2 (10713)	P<0.001
90-day mortality, n (%)	878 (15.4)	3861 (27.5)	P<0.001
Non-recovery, n (%)	1076 (20.9)	1768 (15.2)	P<0.001
Worsening eGFR among patients with PeCKD, n (%)	1220 (53.4)	1567 (40.6)	P<0.001
AKI Severity, % (n)			
Stage 1	78.3 (5119)	70.9 (11478)	P<0.001
Stage 2	12.5 (818)	17.7 (2873)	
Stage 3	9.1 (597)	11.4 (1838)	
Progression of AKI, % (n)	17.8 (1161)	19.0 (3082)	n/s
Mean peak SCr ±SD (μmol/L)	209.0 ±160.1	212.2 ±167.1	
Peak AKI Stage, % (n)			
Stage 1	63.9 (4177)	55.8 (9034)	P<0.001
Stage 2	19.6 (1281)	23.8 (3850)	
Stage 3	16.5 (1076)	20.4 (3305)	
AKI rule, % (n)			
Rule 1	1.1 (69)	4.8 (775)	P<0.001
Rule 2	3.8 (247)	12.5 (2020)	
Rule 3	95.2 (6218)	82.7 (13394)	

Data on patient sex were missing for 4 episodes of the non-PC CA-AKI cohort and excluded from analysis of the sex variable. Baseline eGFR data were missing for 138 episodes (18, PC-AKI; 120, Non-PC CA-AKI) and excluded from analysis of the Pre-existing CKD variable. Mortality data was available for 19753 episodes (5709, PC-AKI; 14044, Non-PC CA-AKI). SCr follow up data was available for 16824 episodes (5161, PC-AKI; 11663, Non-PC CA-AKI) and included in analysis of the non-recovery variable. eGFR follow up data was available for 6148 episodes by patients with pre existing CKD (2285, PC-AKI; 3863, Non-PC CA-AKI) and included in analysis of the worsening eGFR variable. PC-AKI, Primary Care acquired AKI; Non-PC CA-AKI, Non-Primary Care Community acquired AKI; PeCKD, pre existing chronic kidney disease; SCr, Serum creatinine.

Table 2. Characteristics of Hospitalised PC-AKI cohort vs. non-hospitalised PC-AKI cohort.

	Hosp. PC-AKI	**Non-hosp. PC-AKI**	
n (% of AKI incident alerts)	1459 (22.3)	5075 (77.7)	
Mean age ±SD (yr)	74.8 ±13.5	71.5 ±16.6	
Male % (n)	49.3 (719)	39.5 (2006)	P<0.001
Pre-existing CKD, % (n)	59.7 (869)	38.5 (1947)	P<0.001
Mean baseline SCr ±SD (μmol/L)	114.5 ±57.9	90.4 ±48.0	
Mean baseline eGFR ±SD (ml/min/1.73m^2)	56.8 ±25.3	71.3 ±29.2	
Mean alert SCr ±SD (μmol/L)	263.5 ±181.8	158.9 ±99.5	
% repeat measurement <7days	48.5%	13.6%	P<0.001
90-day mortality, n (%)	391 (30.3)	487 (11.0)	P<0.001
Non-recovery, n (%)	192 (18.1)	884 (21.6)	P=0.01
Worsening eGFR among patients with PeCKD, n (%)	257 (40.5)	963 (58.3)	P<0.001
AKI Severity, % (n)			
Stage 1	54.8 (800)	85.1 (4319)	P<0.001
Stage 2	20.3 (296)	10.3 (522)	
Stage 3	24.9 (363)	4.6 (234)	
Progression of AKI, % (n)	28.9 (422)	14.6 (739)	P<0.001
Mean peak SCr ±SD (μmol/L)	312.0 ±207.6	179.5 ±129.3	
Peak AKI Stage, % (n)			
Stage 1	34.0 (497)	72.5 (3680)	P<0.001
Stage 2	28.0 (408)	17.2 (873)	
Stage 3	38.0 (554)	10.3 (522)	
AKI rule, % (n)			
Rule 1	0.8 (12)	1.1 (57)	n/s
Rule 2	4.1 (60)	3.7 (187)	
Rule 3	95.1 (1387)	95.2 (4831)	

Baseline eGFR data were missing for 18 episodes (4, Hosp. PC-AKI; 14, Non-hosp. PC-AKI) and excluded from analysis of the Pre-existing CKD variable. Mortality data was available for 5709 episodes (1292, Hosp. PC-AKI; 4417, Non-hosp. PC-AKI). SCr follow up data was available for 16824 episodes (1292, Hosp. PC-AKI; 4417, Non-hosp. PC-AKI) and included in analysis of the non-recovery variable. eGFR follow up data was available for 6148 episodes by patients with PeCKD (1292, Hosp. PC-AKI; 4417, Non-hosp. PC-AKI) and included in analysis of the worsening eGFR variable. Hosp. PC-AKI, Hospitalised Primary Care acquired AKI; Non-hosp. PC-AKI, non-hospitalised Primary Care acquired AKI; PeCKD, pre existing chronic kidney disease; SCr, Serum creatinine.

Table 3. Characteristics of PC-AKI subcategories by time and place of repeat measurement of renal function.

	PC <7d	**Non-PC <7d**	**PC ≥7d**	**Non-PC ≥7d**	**No repeat**
n (% of PC-AKI incident episodes)	1536 (23.5)	1675 (25.6)	2068 (31.7)	707 (10.8)	548 (8.4)
Mean age ±SD (yr)	74.2 ±14.3	74.4 ±13.9	72.4 ±15.5	70.2 ±16.8	61.6 ±22.2
Male,% (n)	40.4 (620)	48.6 (814)	39.7 (821)	42.0 (297)	31.6 (173)
Pre-existing CKD, % (n)	51.1 (783)	58.0 (968)	35.7 (738)	33.4 (235)	16.9 (92)
AKI Severity, % (n)					
Stage 1	79.7 (1224)	57.8 (968)	89.4 (1849)	84.9 (600)	87.2 (478)
Stage 2	15.4 (237)	18.7 (313)	8.8 (182)	6.8 (48)	6.9 (38)
Stage 3	4.9 (75)	23.5 (394)	1.8 (37)	8.3 (59)	5.8 (32)
Mean time to repeat ±SD (days)	3.9 ±1.9	1.8 ±1.7	21.9 ±17.9	31.0 ±22.2	
Repeat SCr > than Alert SCr, % (n)	18.5 (284)	43.2 (724)	17.4 (359)	28.7 (203)	
Hospitalisation within 7 days of repeat, % (n)	10.8 (166)	83.0 (1391)	4.0 (83)	41.7 (295)	
90-day mortality, n (%)	153 (11.3)	441 (29.9)	119 (6.6)	97 (16.1)	68 (13.9)

Baseline eGFR data were missing for 18 episodes (3, PC <7d; 6, Non-PC <7d; 2, PC ≥7d; 3, Non-PC ≥7d; 4, No repeat) and excluded from analysis of the Pre-existing CKD variable. Mortality data was available for 5709 episodes (1355, PC <7d; 1475, Non-PC <7d; 1790, PC ≥7d; 601, Non-PC ≥7d; 488, No repeat). PC <7d, Repeat measurement of renal function within 7 days in Primary Care; Non-PC <7d, Repeat measurement of renal function within 7 days not in Primary Care; PC ≥7d, Repeat measurement of renal function within between 7 and 90 days in Primary Care; Non-PC ≥7d, Repeat measurement of renal function within between 7 and 90 days not in Primary Care; No repeat, No repeat measurement of renal function during 90 day episode; PC-AKI, Primary Care acquired AKI; PeCKD, pre existing chronic kidney disease; SCr, Serum creatinine.

Supplementary Figure Legend

Supplementary Figure 1: Algorithm for generating e-alerts for Acute Kidney Injury based on serum creatinine (SCr) changes with time. RV, Reference value, defined as the SCr value with which the index SCr value is compared; D, difference between current and lowest previous result within 48 hours; RI, Population reference interval.

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