Swansea University
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Acute Kidney Injury in Wales

Does the introduction of electronic alerts for Acute Kidney Injury in Welsh NHS hospitals influence morbidity, mortality or primary care reviews and prescriptions?

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Summary

Background

Acute kidney injury (AKI) is a common condition with poor outcomes. Deficiencies in care are well described, so clinician-facing electronic AKI alerts (eAlert) were attached to blood test results in Wales with the aims of improving recognition and clinical outcomes.

Aims

Create an AKI cohort through replicating eAlerts in the secure anonymised information linkage databank (SAIL), allowing for the validation of the eAlerts sent in practice.

Assess the effect of eAlerts on hospital coding, recovery from AKI, need for dialysis, mortality and changes in primary care prescriptions and reviews.

Method

An AKI cohort was created within SAIL by recreating the NHS England eAlert algorithm. Using our renal dataset, we identified patients undergoing dialysis who do not have AKI. Using this cohort as a comparator, we validated the Welsh eAlerts seen in clinical practice, and assessed their effect on mortality, recovery, hospital coding, need for dialysis and primary care Read code entries.

Results

Only two thirds of AKI recognised by our methodology had an eAlert sent. This is because Welsh eAlerts had a modification applied to it, making it different to the eAlerts used elsewhere in the UK, which was previously unknown to researchers and clinicians. 1 in 12 eAlerts seen by clinicians were false positives (dialysis patients). eAlerts improve recovery from AKI but do not improve the need for dialysis, primary care medication reviews and, in all bar one health board, they do not reduce mortality at 30-days or 1-year. We did not observe an increase in primary care medication reviews, nor did we see changes in many important medication prescriptions following the introduction of eAlerts.

Conclusions

Welsh eAlerts alone are not enough to improve AKI outcomes in Wales and standardising alerts with those sent throughout the rest of the United Kingdom is now being adopted.

Declarations and Statements

Word Count body (Contents to Glossary inclusive) = 68,717 words

DECLARATION

This work has not previously been accepted in substance for any degree and is not being concurrently submitted in candidature for any degree.

Signed .....[redacted].Dr T M Scale .....

Date .....29th September 2022.....

STATEMENT 1

This thesis is the result of my own investigations, except where otherwise stated. Where correction services have been used, the extent and nature of the correction is clearly marked in a footnote(s).

Other sources are acknowledged by footnotes giving explicit references. A bibliography is appended.

Signed .....[redacted]Dr T M Scale.....

Date ..... 29th September 2022.....

STATEMENT 2

I hereby give consent for my thesis, if accepted, to be available for photocopying and for inter-library loan, and for the title and summary to be made available to outside organisations.

Signed .....[redacted]....Dr T M Scale.....

Date ..... 29th September 2022.....

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Abbreviations

Abbreviations	Meaning
A&E	Accident and Emergency Department
ABMUHB	Abertawe Bro Morgannwg University Health Board
ABUHB	Aneurin Bevan University Health Board
ACEi	Angiotensin converting enzyme inhibitor
ACEi/ARB	Angiotensin converting enzyme inhibitor and angiotensin receptor blocker
ADDE	Office of national statistics death data in SAIL
ADQI	Acute Dialysis Quality Initiative
AKD	Acute Kidney Disease
AKI	Acute Kidney Injury
AKI-D	Acute Kidney Injury Requiring Dialysis treatment
AKIN	Acute Kidney Injury Network
ALF	Anonymous Linking Field
ALF_PE	Anonymous Linking Field Project Encryption
APC	Admitted Patient Care
APD	Automated peritoneal dialysis
ARB	Angiotensin receptor blocker
ARF	Acute Renal Failure
ARI	Acute renal impairment
AWLIMS	All Wales Laboratory Information Management System
AWRD	All Wales Renal Dataset
BCUHB	Betsi Cadwaladr University Health Board
BMA	British Medical Association
BP	Blood Pressure
CA-AKI	Community Acquired AKI
CAPD	Continuous peritoneal dialysis
CCDS	Critical Care dataset
CKD	Chronic Kidney Disease
CPW	Community Pharmacy Wales
CTUHB	Cwm Taf University Health Board

CVUHB	Cardiff and the Vale University Health Board
DAL	Discharge Advice Letter
DBMS	Database Management System
DHCW	Digital Health Care Wales
DMR	Discharge Medication Review
DOB	Date of birth
DOD	Date of death
DOS	Date of Index Sample/Serum Creatinine
eAlert	Electronic alert
EHR	Electronic Health Record
EQACV	External Quality Assurance Creatinine Value
GD	Gareth Davies analyst
GFR	Glomerular Filtration Rate
GP	General Practice
HD	Haemodialysis
HDUHB	Hywel Dda University Health Board
HES	Hospital Episode Statistics for England
HHD	Home haemodialysis
IBM DB2	International Business Machines Database 2
ICD-10	International Classification of Diseases, Tenth Revision
ICU	Intensive Care Unit
IDMS	Isotope dilution mass spectrometry
IGFBP-7	Insulin-like growth factor-binding protein 7
IGRP	independent governance review panel
IT	Information Technology
ITU	Intensive Therapy Unit
KDIGO	Kidney Disease: Improving global outcomes
KIM-1	Kidney Injury Molecule-1
LIMS	Laboratory Information Management System
LOS	Length of stay
LSOA	lower layer super output area codes

Ltd	Limited
LV3	Level 3 care (critical care)
MAU	Medical Admissions unit
MDRD	Modification of diet in renal disease formula
NCEPOD	National Confidential Enquiry into Patient outcomes and deaths
NGAL	Neutrophil Gelatinase-Associated Lipocalin
NHS	National Health Service
NPV	Negative Predictive Value
NRES	National Research Ethics Service
NWIS	National Health Service Wales Informatics Service
ONS	Office of national statistics
PABR	Pathology data from Bridgend TelePath system
PABR	Pathology Bridgend dataset
PAMO	Pathology data from Swansea Masterlab system
PATH	All Wales pathology data from Welsh Results report service
PD	Peritoneal Dialysis
PEDW	Patient Episode Database for Wales
PPV	Positive Predictive Value
PTHB	Powys Teaching Health Board
RCT	Randomised controlled trial
RIFLE	Risk, Injury, Failure, Loss and End stage kidney disease
RR	Renal Registry
RRT	Renal Replacement therapy
RRT1	Renal replacement therapy table 1 - from timeline data
RRT2	Renal replacement therapy table 2 - from dialysis session data
RV1	Baseline creatinine - lowest result in 0 to 7 days
RV2	Baseline creatinine - median value 8 to 365 days
RV3	Baseline creatinine - lowest result in previous 48 hours
SAIL	Secure Anonymised information linkage databank
sARF	Severe Acute Renal Failure
SCr	Serum Creatinine (Blood test)

SQL	Structured Query Language
T/P	Transplant
TMPT-2	Tissue inhibitor of metalloproteinases-2
TMS	Timothy Marcus Scale (author)
Tx	Transplant
UK	United Kingdom
UKKW	United Kingdom Kidney Week
UO	Urine output
USA	United States of America
VEL	Velindre NHS Trust
WCP	Welsh Clinical Portal
WDS	Welsh Demographic Service
WOB	Week of Birth
WRRS	Welsh Results Report Service

Presentations and Publications

Presentations

Defining Acute Kidney Injury Episodes – ADR conference Dec 2019 (Presented by G Davies)

Validation of Acute Kidney Injury e-alert system in Wales – International Population Data Linkage Network Conference – Banff 2018 (Presented by G Davies)

Posters

Scale T, Davies G, Lyon R, Chess J. Medication prescription after admission with hospital coded acute kidney injury in Wales – (UKKW – Harrogate) 2018

Davies G, Scale T, Akbari A, Chess J, Lyons R. Replication of Acute Kidney Injury e-Alerts – (Information Population Data Linkage Newfork Conference - Banff) 2018

Davies G, Scale T, Akbari A, Chess J, Lyons R. Defining Acute Kidney Injury Episodes – (Administrative Data Research Conference – Cardiff) 2019

Scale T, Chess J. Communication with primary care following hospital admission with acute kidney injury – UKKW 2020

Scale T, Davies G, Marks A, Lyons R, Chess J. AKI episodes – do episode definitions impact outcomes reported? UKKW 2020

Davies G, Scale T, Akbari A, Chess J, Lyons R. Methods to accurately exclude renal dialysis patients from the Welsh acute kidney injury e-Alert system – Adelaide 2020

Scale T, Davies G, Lyon R, Chess J. Validation of the Welsh electronic acute kidney injury alerts – (UKKW – Newport) 2023

Scale T, Davies G, Lyon R, Chess J. Do electronic acute kidney injury alerts improve mortality in Wales? – (UKKW – Newport) 2023

Scale T, Davies G, Lyon R, Chess J. Prescriptions and reviews in primary care following AKI – (UKKW – Newport) 2023

Chapter 1 – Acute Kidney Injury; Where are we and how did we get here? Narrative review of literature

There has been a growing interest and experience in using electronic health records (EHR) to study the syndrome of acute kidney injury (AKI), to better identify and understand the condition but also how its recognition has varied over time (1, 2). This review looks at the historical context of AKI and early descriptions of it, leading into the modern definitions widely adapted in contemporary research. It explores the multiple methods of defining AKI, and how they developed into the currently used criteria, exploring the effects that the different definitions have on the prevalence of the condition. It looks at the use of hospital coding to identify AKI for retrospective research and the pros and cons of this method. The review explores the development and use of electronic alerts (eAlerts) in AKI around the World and how they have been adapted in the UK. It also reviews the knowledge and understanding that we have developed of AKI outside the hospital setting in the community.

A broad narrative review of the literature was performed prior to embarking on answering the research question in 2016. The initial approach was a review of the published literature covering the questions described in the next paragraph. This review was crucial to help understand and plan the approach to creating an AKI cohort within the secure anonymised information linkage (SAIL) databank as well as to identify the gaps in research.

Framing the question

1. How is AKI defined?
    a. This review sets out to describe the evolution of the definition of AKI, to help describe and explain the reason for the variations found in incidence of AKI.
    b. How analysis of creatinine levels compares to clinical coding in identification of AKI.

2. What are electronic AKI alerts and what is known of their effect?

a. To explore the literature to explain why Wales and England have introduced electronic alerts in the last few years and what is known about their impact to date.

3. What is known about AKI in primary care?
    a. As part of understanding the impact of the electronic alerts, the changes in practice in primary care are explored. This starts with investigating what is already know about AKI in primary care.

Searches

To review the literature surrounding AKI, eAlerts and community/primary care I carried out an evaluation of the literature using medline (Pubmed) and Embase (OVID) databases. These medical databases were used as they capture many of the nephrology and critical care journals relevant for AKI epidemiology as used by Sawhney et al in their paper "Long-term prognosis after acute kidney injury (AKI): what is the role of baseline kidney function and recovery? A systematic review" (3). Study titles were reviewed and studies involving children were excluded together with publications not available in English language. Those studies not relevant to the above questions based on their titles were also excluded. Following that, the abstracts of the remaining articles were reviewed, and, in most cases, the full publications were evaluated. Using the references of the reviews (narrative and systematic) other related articles not identified by the searches were identified.

The table below includes the search terms used in the review;

Database	Search	Reviewed	Included
Pubmed	Acute Kidney Injury definition	499	183
Pubmed	Acute Kidney Injury eAlerts	6	6
Pubmed	Acute Kidney Injury electronic alerts	27	27
Pubmed	Acute Kidney Injury Community	25	16
Pubmed	Acute Kidney Injury Primary Care	4	4
Pubmed	Acute Kidney Injury Coding	59	41
Pubmed	Acute Kidney Injury/ARF ICD	25	23
OVID	Acute Kidney Injury definition	159	115
OVID	Acute Kidney Injury electronic alerts/eAlerts	57	19
OVID	Acute Kidney Injury Community	280	36
OVID	Acute Kidney Injury Primary Care	43	23
OVID	Acute Kidney Injury Coding	40	28
OVID	Acute Kidney Injury ICD	1	1

Table 1 - Literature Search

Introduction

To understand our current position, it was useful to look back at the origins of the recognition of this condition.

The history of acute renal failure

AKI, previously termed acute renal failure, is increasingly recognised as a syndrome affecting people with acute illness. Over the last 30 years there has been increasing interest in AKI, partly due to the realisation of the significant morbidity and mortality burden associated with this condition.

AKI is heterogenous, caused by many different disease states, some of which as shown below.

Exposures	Susceptibilities
Sepsis	Dehydration or volume depletion
Critical illness	Advanced age
Circulatory shock	Female gender
Burns	Black race
Trauma	CKD
Cardiac surgery (especially with CPB)	Chronic diseases (heart, lung, liver)
Major noncardiac surgery	Diabetes mellitus
Nephrotoxic drugs	Cancer
Radiocontrast agents	Anemia
Poisonous plants and animals	

CKD, chronic kidney disease; CPB, cardiopulmonary bypass.

Table 2 – "Causes of AKI: exposures and susceptibilities for non-specific AKI" taken from KDIGO 2012 Guidelines (4)

Much of the early literature in this area described obstructive (often renal calculi induced) disease. However, there is a description as far back as ancient Greek times of intrinsic renal disease. In the 5th century BC Hippocrates describes;

'*external hurt is causing haemorrhage of capillaries and destruction of renal parenchyma*'

as described in Marketos et al's paper (5, 6). Since then there have been sporadic references to AKI; John Stow describes the death of the 5th Earl of Derby, Ferdinando Stanley in his 1631 publication, he tells us how the Earl develops anuria which led William Jeffcoate to believe the death was caused by acute renal failure with the exact aetiology unclear (6, 7).

At the end of the 18th century, Batista Morgagni coins the term 'ischuria' to describe renal failure (8-10). In 1802, a posthumous publication by William Heberden builds upon this and gives an excellent description of ischuria, comparing obstructive causes to those caused by problems within the kidney,

"…but the most dangerous ischuria is that in which the kidney secretes no urine from the blood" (11).

He also describes a case where;

"A total suspension has lasted seven days, and yet the patient has recovered"

This is a clear description of acute renal failure, possibly due to the underlying condition acute tubular necrosis. John Abercrombie goes on further to describe ischuria renalis in 1821 (8), stating

"The minute relation of these phenomena with probably ever elude our researches"

When Abercrombie described 'Ischuria Renalis' there can be seen clear parallels with modern descriptions of acute renal failure and AKI.

"The disease seems, in general, to come on suddenly……The particular symptom is a sudden diminution of the secretion of urine, which soon amounts to complete suspension." (8)

He goes on further to describe how initially in his patients, he wondered if it was urinary retention but after catheterisation, he found the bladder to be empty. This is a description of how acute renal failure is diagnosed in the period before blood biomarkers of kidney function, such as urea or creatinine.

In the late 19th century, William Osler building upon Richard Bright's description of glomerular disease and defined 'Acute Bright's disease' where he mentioned poisons, toxic agents, pregnancy and acute nephritis amongst the causes in his 1892 first edition of 'The principles and practice of medicine, designed for the use of practitioners and students of medicine' (12). A 9th edition, with Thomas McCrae as a co-author in 1921 goes further to describe anuria(13);

"Total suppression of urine occurs under the following conditions: (a) As an event in the intense congestion of acute nephritis. For a time no urine may be formed; More often the amount is greatly reduced…. (c) Cases occur occasionally in which the cause is prerenal."

The treatment of this, sounded most unpleasant:

"Large hot irrigations, with normal salt solutions, with Kemp's double-current rectal tubes, are stated to stimulate the activity of the kidney in a remarkable way" (13).

This description of renal failure of different aetiology and probably an early description of a form of intestinal dialysis treatment.

In 1917 Davies and Weldon discussed 664 cases of 'War Nephritis' (14) where they describe a case with

"degeneration of the epithelium of the convoluted tubules"

with further descriptions of this in keeping with the histological findings of acute tubular necrosis. Some 24 years later, Beall and Bywater describe crush injuries in 4 patients during the second World War, which resulted in acute renal failure. The authors attributed the renal failure to muscle necrosis (15, 16). In the very same journal Mayon-White and Solandt also described a case report of a 11-year-old girl who had a compression injury and uraemia (17). Bywaters went on to write a review of crush injuries the following year furthering the knowledge around what is now termed rhabdomyolysis and AKI (18).

The term acute renal failure was probably established by Homer Smith in 1951 (19, 20), although it was mentioned in papers as early as 1946 (21, 22). This stayed the term for acute deterioration in renal function until the 21st Century where AKI became the new reference. The first reference of AKI on medline that I can find in a publication title or abstract is by Ronco in a paper on early goal-directed therapies in critically ill patients in 2004 (23). In the latter half of the 20th century until present day, there has been a massive growth in the literature, coinciding with the growth of the internal medical subspecialty of nephrology. This was shown in my figure below which shows medline publications across time.

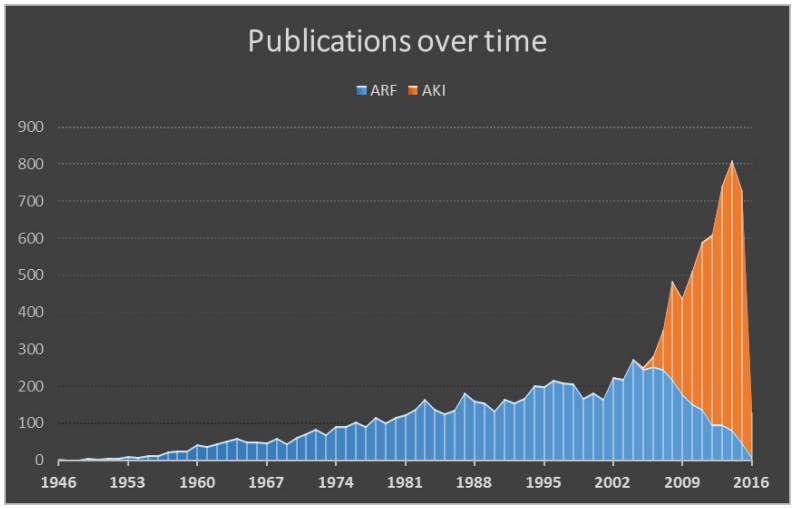


Figure 1 - Comparison of medline publications with Acute Kidney Injury (AKI) or Acute Renal failure (ARF) over time

Definitions of AKI

AKI is an acute deterioration in the ability of the kidney(s) to clear toxins, metabolites and maintain homeostasis. There has been little by way of consensus with regards to the incidence of AKI. The main reason for this is that there have been a multitude of different definitions and methods for studying this condition over time. The most common method used is the blood test serum creatinine (24), sometimes in combinations with urine production (urine output). Creatinine is a protein that is steadily cleared by the kidneys, it is not toxic, but serum levels rise when kidney function is impaired.

In 2005 Glenn Chertow et al highlighted the effect that using different creatinine-based criteria to define AKI have on the incidence of AKI (1). They used several different methods, which resulted in a variation in incidence of AKI from 1% to 44% of hospital admissions, as shown in the graph below (reproduced from a review written by Hoste and Schurgers (25)).

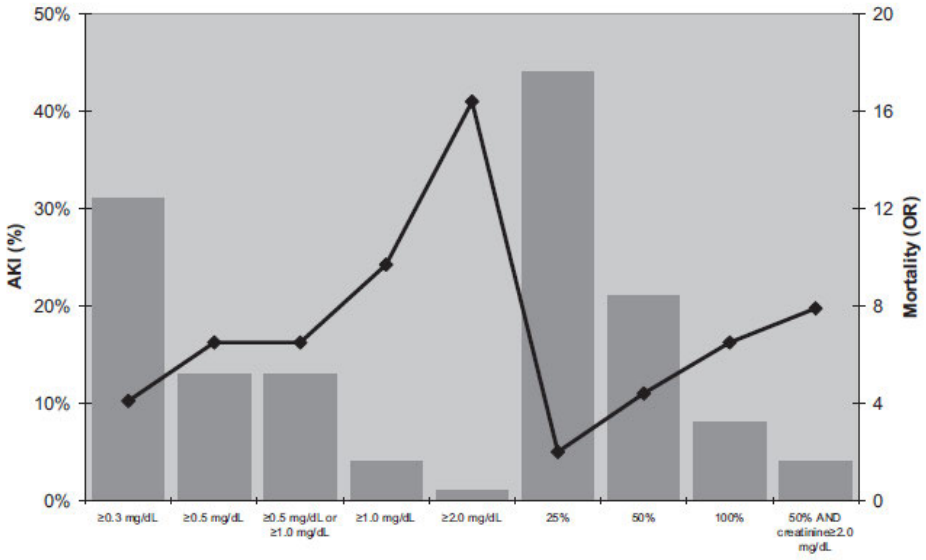


Figure 2 - Definition of AKI, Incidence and Mortality – from Hoste and Schurgers (25)

Before the era of serum markers for AKI, urine output and in particular suspension of urine (anuria)(8, 11) was the main way of defining the condition hence the term 'Ischuria' meaning the retention of urine.

In the 20th century, serum markers of retention of nitrogenous waste (urea and creatinine) were adopted as surrogate serum markers of kidney function and have been used to aid the recognition of AKI or as it was usually called then, acute renal failure (ARF). The most commonly used marker is creatinine (24). Creatinine increases when kidney function deteriorates in a non-linear (exponential) manner. Creatinine is dependent on muscle mass and as such the relationship between this and kidney function required adjustments for sex, and age. Due to this relationship, there is no one cut off of serum creatinine value that defines AKI (24). Even in the early definition of AKI it was described as a sudden deterioration of renal function (20) , as such using a single creatinine value to label AKI may result in the finding of chronic kidney disease instead. As a result of this it has been long recognised that the change in kidney function is the key discriminator. Nevertheless a few studies used a single creatinine cut off as the definition (26, 27). The exact definitions used to identify AKI have lacked consensus until this century. In addition to the threshold for recognising AKI, there have been variations in the definition of what an individual's

usual renal function is (baseline renal function). Differences in these two areas effects the overall incidence of AKI.

One important early study that looked at changes in serum creatinine was by Susan Hou and her group in the United States of America in 1983 (28). Their paper called 'Hospital-acquired renal insufficiency: a prospective study' looked at 2,216 patients admitted under surgical and medical specialities over a 5-month period starting in September 1978. They found 129 episodes of AKI (4.9%) in 109 patients based on a criterion that they developed (Table 3). They felt that 42% of these patients developed acute renal failure due to reduced renal perfusion. They reported crude inpatient mortality rate of 24.8%, however, they based this upon episodes and not individuals, therefore if we say there were 32 deaths in 109 patients then we see a mortality rate of 29%. This study was able to show that the worse the renal impairment the higher the mortality rate was. This was shown by 3.8% of the lowest AKI definition group (serum creatinine increases of 0.5 to 0.9 mg/dl) dying in hospital versus 71% of the patients with a creatinine increase between 3 and 3.9 mg/dl. It also showed a significant difference in in-hospital mortality in those with oliguria (as defined by ≤400ml urine per day), 52% vs 17% in those without oliguria ($p<0.01$). This was an important single centre study for several reasons. One was because it was an early prospective study into AKI, focusing on the frequency of in-hospital AKI. It also attempted to consider the effect that different baseline creatinine values have on the definition of AKI. The other reason is that the criterion that they used went on to be adopted by several different future studies, most importantly by Kevin Nash (29) and his group (including Susan Hou) in 1996 (published in 2002).

Hou Criteria – identifying AKI

Baseline Creatinine mg/dl (µmol/L)	Increase in Creatinine mg/dl (µmol/L)
≤1.9 (168)	0.5 (44)
2-4.9 (177-433)	1 (88)
≥5 (442)	1.5 (133)

Table 3 - Used in Hou et al 1983, Nash et al 2002 (28, 29)

Nash et al looked at 4,622 consecutive patients admitted under medicine and surgery between February and June 1996 (29). They found 332 cases of 'acute renal

insufficiency' in this group, equating to 7.2%, suggesting an increase in the incidence of AKI over the 17 years between the studies. The study found a mortality rate of 19.4% compared to 24.8% in the earlier study, but this was reported as not being statistically significant. Again, there was a correlation between increasing severity of AKI and mortality. The importance of this study is that it suggested an increased incidence of AKI over time based on these prospective studies in America and importantly using the same definitions of AKI. However, it was not the same hospital, or the same region of America, there were potentially differences in admissions and testing practice. This is particularly important, when considering that community-based AKI was not included.

In the 1980's Neil Shusterman and his group used a similar method to Hou, identifying AKI by creatinine rises which varied dependant on the baseline creatinine. This was less sensitive in comparison to our modern definition of AKI (30).

Baseline Creatinine mg/dl (µmol/L)	**Increase in Creatinine mg/dl (µmol/L)**
<2 (177)	0.9 (80)
≥2 (177)	1.5 (133)
SCr to remain elevated for at least 1 additional, consecutive determination	

Table 4 - Shusterman definition(30)

The difference in definition contributed to the different incidence seen in these two studies. In Hou's study, 4.9% of the surgical and medical take had AKI, compared to just 1.9% in Shusterman's study. Although Shusterman's included gynaecology patients which also may have contributed to the lower incidence (i.e. younger patients less likely to develop AKI), along with geographic and hospital-based differences. There were also potentially differences in the definition of the baseline as Hou did not describe the method and Shusterman used the first admission creatinine. I discuss shortly, how this can have a great effect on reported incidences of AKI.

Studies in the 1980s by Ronald Eisenberg et al used similar criteria (31, 32), based on an increase in creatinine of ≥1mg/dl (88µmol/L) or an increase in urea of 50%/

≥20mg/dl (7.1mmol/L). The focus of these studies was patients developing contrast nephropathy from angiography. This was also the focus of Cochran's study in 1983 which looked at ARF within 5 days post renal angiography (33). For this study ARF was defined as an increase in creatinine of more than 0.3mg/dl or 20% during the 5 days. With these criteria, Cochran found that 16.9% of the 266 patients studied developed ARF (800 patients originally in the study, but only 266 had sufficient data for the analysis).

Another criterion used as definition of ARF in studies examining contrast nephropathy was an increase of SCr of 0.5mg/dl (44µmol/L) within 48 hours. The first reference of this use that I could find was by Schwab et al in 1989 in a randomised trial of two contrast agents (34); it was later used by Solomon et al and Weisberg et al in similar studies in 1994 (35, 36).

In the UK, around the same time as Hou, Wilkins et al (37) looked at AKI incidence, prediction factors and outcomes in an intensive care environment. They did so via a case note review of 475 patients (without a pre-existing renal disorder) and found that 23% of these patients developed ARF defined as a creatinine rise greater than 0.18 mmol/L (180µmol/L) and a urea rise above 8mmol/L for more than 24 hours. The intensive care unit ARF mortality in this cohort was 88% compared to 24% in those without renal failure.

In 1993 Professor Terry Feest published a paper investigating the incidence of ARF in the Devon region in England across two health districts (26). The definition used for 'severe acute renal failure' was a creatinine rising to above 500µmol/L and then subsequently falling below the index value (baseline). His group found that the annual incidence of ARF in adults was 172 per million population (pmp) in adults. This was highest in the very elderly (80-89 year olds) category with an incidence of 949 pmp. This study gave a glimpse of the incidence of ARF, using a definition designed to find cases of severe acute renal impairment. It is likely that there is an over representation of patients with chronic renal failure as the differentiation between

ARF and chronic kidney disease (CKD) was that the creatinine returned below 500µmol/L.

Liano and colleagues (38) found only a slightly higher overall incidence of ARF in the Madrid population of 209 pmp when using a less severe ARF definition. They defined ARF by a creatinine rise >177µmmol/L in those with normal baseline renal function or a rise of creatinine of more than 50% in those with baseline creatinine below 264µmmol/L. They also included those with an improvement (i.e. recovery) of creatinine of 50% from presentation value as ARF.

Baseline Creatinine	**Increase in Creatinine above**
"Normal Renal Function"	To >177µmol/L
Mild to Moderate chronic kidney disease	50% increase
265µmol/L	
Inclusion	**Exclusion**
Normal SCr at admission	Baseline ≥3mg/dl (265µmol/L)
Elevated SCr at admission but "complete recovery"	Myeloma
Elevated SCr at admission but no suggestion of chronic disease, normal sized kidneys	Hydronephrosis (with cortical atrophy)

Table 5 - Liano definition and study criteria(38)

This definition is specific for identifying ARF however it misses patients with acute on chronic renal failure, which is a significant proportion of AKI patients.

Khan et al (27) in Aberdeen (published in 1997), found a much higher incidence of 620pmp when using a rise above 300µmmol/L for the first time as the definition. It is likely that this study is less specific, identifying false positives in people with CKD not ARF.

With the varying definitions, it was often the more severe forms of AKI that were identified. A review in 1994 found 28 studies describing the surgical incidence of AKI,

and reported that all the papers used different definitions of disease (39). Commonly, research was in the intensive care unit (ICU) setting (40-44) or in those requiring dialysis (45, 46). Even within ICU, the findings varied from 1% to 25% of the population (41, 47). Researchers recognised the need for consensus, so a 'call to arms' was placed (48), with a proposed definition. In an unorthodox method, the author of an editorial, Rinaldo Bellomo et al invited readers to e-mail him their opinions directly, in what they termed 'electronic democracy'. They also directly challenged key bodies in the renal and intensive care communities to develop and implement a consensus definition.

Normal	ARI	ARFS	Severe ARFS
Normal [creat] and [urea] and UO > 800 ml/24 h	[creat] > 120 μmol/l and [urea] > 8 mmol/l and/or UO < 800 ml/24 h or UO < 200 ml/6 h	[creat] > 240 μmol/l and [urea] > 16 mmol/l and/or UO < 400 ml/24 h or UO < 100 ml/6 h	Need for RRT and either ARI or ARFS criteria
	If A/C ARI use increase in [creat] of 60 μmol/l or in [urea] of 4 mmol/l and/or UO same as above	If A/C use increase in [creat] of 120 μmol/l or in [urea] of 8 mmol/l and/or UO same as above	Need for RRT and A/C criteria for ARI or ARFS

Table 6 - The proposed Criteria – from Bellomo et al (48)

RIFLE

In 2002, the Acute Dialysis Quality Initiative (ADQI) group met to set about creating a definition in an attempt to remove this ambiguity. It published the results of a conference and the creation of the Risk, Injury, Failure, Loss and End stage kidney disease criteria commonly referred to as the RIFLE criteria (49).

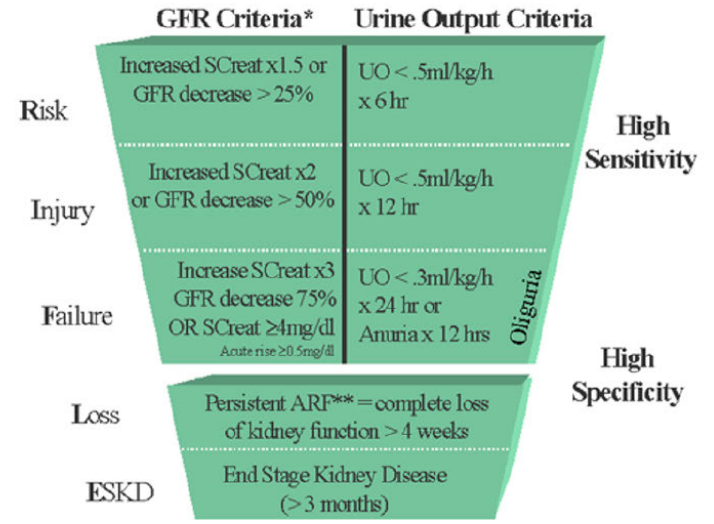
Prior to the publication there were a couple of papers by some of the ADQI attendees who discussed the key issues. The first paper by Kellum et al (50), appealed to the interested community to set up a meeting. One of the observations that he and his co-authors made was;

"The perfect quantitative definition of ARF will never exist, because clinicians will always be Interested in detecting mild forms of the syndrome for some research or clinical questions, where as they will be interested only in more severe forms for others."

In recognising that it would not be perfect, the authors suggested ways of minimising application problems, such as relative increases in creatinine to reduce the effect that pre-existing renal disease would have on interpretation. They also suggested the use

of a combination of ‘creatinine relative increase’ and urine output. In 2003, Mehta and Chertow also discussed the issues around classification of ARF (51). They highlighted the variation used amongst previous authors and how too many studies relied upon serum creatinine alone with no adjustment for age and sex, which are well known to cause variation in the normal ranges. The authors highlighted how this may lead to potential error by discussing one of their previous studies. For example, in a prior paper by Bates, where Chertow et al (52) defined ARF as an increase in SCr by 50% to at least 2mg/dl (177µmol/L) they found that there was a 2-fold increased chance of ARF in men. This RIFLE classification aimed to alleviate these concerns.

The RIFLE criteria considered different stages of renal impairment, using both serum creatinine and urine output which if one is positive, can identify AKI (i.e. it is not necessary to have both). The criterion also included recovery, defining complete recovery as the serum creatinine returning within its baseline classification, whereas in partial recovery a persistent change remains but with improvement in RIFLE staging (49).



Proposed classification scheme for acute renal failure (ARF). The classification system includes separate criteria for creatinine and urine output (UO). A patient can fulfill the criteria through changes in serum creatinine (SCreat) or changes in UO, or both. The criteria that lead to the worst possible classification should be used. Note that the F component of RIFLE (Risk of renal dysfunction, Injury to the kidney, Failure of kidney function, Loss of kidney function and End-stage kidney disease) is present even if the increase in SCreat is under threefold as long as the new SCreat is greater than 4.0 mg/dl (350 μmol/l) in the setting of an acute increase of at least 0.5 mg/dl (44 μmol/l). The designation RIFLE-F_C should be used in this case to denote 'acute-on-chronic' disease. Similarly, when theRIFLE-F classification is achieved by UO criteria, a designation of RIFLE-F_O should be used to denote oliguria. The shape of the figure denotes the fact that more patients (high sensitivity) will be included in the mild category, including some without actually having renal failure (less specificity). In contrast, at the bottom of the figure the criteria are strict and therefore specific, but some patients will be missed. *GFR = Glomerular Filtration Rate; ARF Acute Renal Failure

Table 7 - RIFLE criteria

The criticism

RIFLE was a good start, as it allowed for the identification of ARF and classification based on the severity of the disease. However, with further research it became apparent that it was not sensitive enough to pick up small changes in creatinine which also had an impact on outcomes. This was first shown by a study by Lassnigg et al in 2004 (53) and then further evidence was reported by Chertow and colleagues on 2005 (1), where they found that a small increase in creatinine by 0.3mg/dl to 0.4mg/dl led to an increased risk of mortality (Multivariable Odds Ratio of 1.7, 95% confidence interval CI of 1.2-2.6). In this study a baseline of the lowest creatinine of

the admission was used, and the degree of increase was taken from the peak creatinine.

This table, taken from this paper, shows the odds ratio for mortality split by the different increases in creatinine.

Criterion	Unadjusted OR (95% CI)	Age- and Gender-Adjusted OR (95% CI)	Multivariable OR (95% CI)[b]	Area under ROC Curve
↑ SCr ≥ 0.3 mg/dl	6.9 (5.2 to 9.0)	6.6 (5.0 to 8.7)	4.1 (3.1 to 5.5)	0.84
↑ SCr ≥ 0.5 mg/dl	11.1 (8.7 to 14.2)	10.6 (8.3 to 13.6)	6.5 (5.0 to 8.5)	0.86
↑ SCr ≥ 1.0 mg/dl	19.9 (15.1 to 26.1)	19.0 (14.4 to 25.0)	9.7 (7.1 to 13.2)	0.84
↑ SCr ≥ 2.0 mg/dl	36.4 (24.3 to 54.6)	37.7 (25.0 to 56.9)	16.4 (10.3 to 26.0)	0.83
↑ SCr by 25%	4.0 (3.0 to 5.2)	3.9 (3.0 to 5.2)	2.0 (1.2 to 3.9)	0.83
↑ SCr by 50%	5.9 (4.6 to 7.5)	5.8 (4.6 to 7.5)	4.4 (3.4 to 5.7)	0.84
↑ SCr by 100%	8.9 (6.9 to 11.4)	9.2 (7.1 to 11.8)	6.5 (4.9 to 8.6)	0.84
↑ SCr by 50% to a minimum peak of 2.0 mg/dl	16.9 (12.8 to 22.3)	15.9 (12.0 to 21.0)	7.9 (5.8 to 10.9)	0.84
↑ SCr ≥ 0.5 mg/dl with baseline SCr < 2.0 mg/dl or ↑ SCr ≥ 1.0 mg/dl with baseline SCr ≥ 2.0 and < 5.0 mg/dl	11.0 (8.6 to 14.0)	10.5 (8.2 to 13.4)	6.5 (5.0 to 8.5)	0.86

Table 8 - Mortality related to changes in creatinine values, from Chertow et al(1)

In patients undergoing cardiac surgery, Andrea Lassnigg and her colleagues in 2004, found that 30-day mortality increased with an increase in creatinine following the procedures (53). This prospective study looked at 4,118 patients undergoing cardiac and thoracic aorta operations in 2001. It looked at changes in creatinine from the baseline defined as the creatinine "just" prior to the operation, compared with the creatinine in the first 48 hours after the operation. The figure 3 from the paper shows the effect of changes on 30-day mortality.

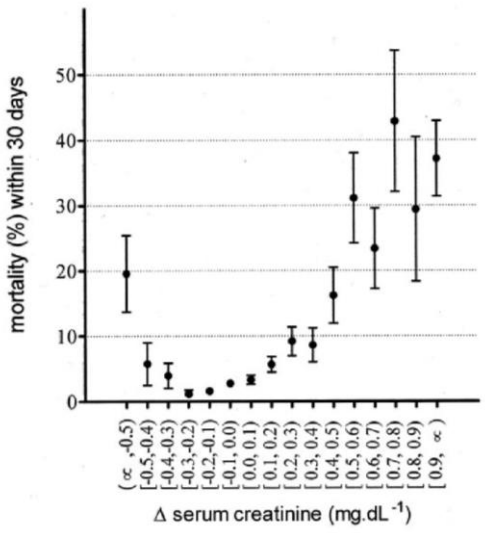


Figure 3 - Change in creatinine effect on mortality – from Lassnigg et al (53)

In a further study, by the same group in 2008, these findings were reproduced in another centre (54). The findings were also corroborated by a review and meta-analysis by Steven Coca et al in 2007 (55). The authors concluded that even 10% to 24% increases and 0.3mg/dl to 0.4mg/dl increases were associated with an approximately 2-fold increased risk of death in the short term. The findings of increased mortality with changes as small as 10% was based on the findings of two studies, one by Thakar et al (56) where 31,677 post cardiac surgery patients were reviewed, and a study by Samuels et al which was presented at the American Society of Nephrology's (ASN) kidney week in 2005 (57). Samuels et al showed an increased mortality associated with a 10% rise in creatinine and found an increased length of intensive care stay as shown below.

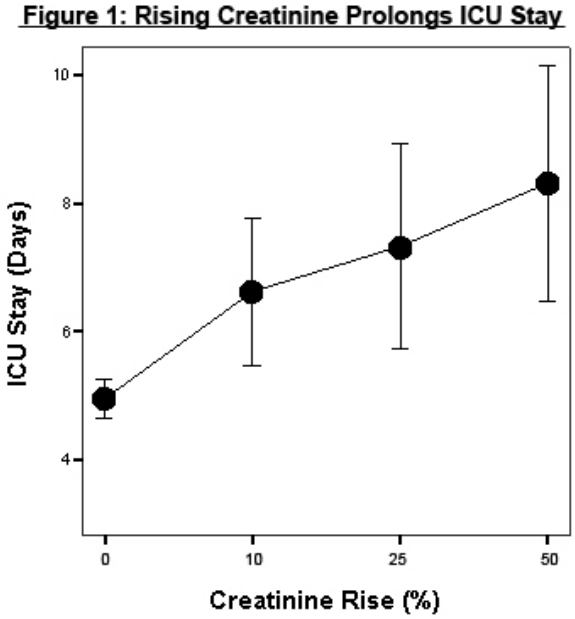


Figure 4 - Creatinine change and mortality, Samuel (57)

Another concern was the use of glomerular filtration rate (GFR), or an estimated version based on the modification of diet in renal disease formula (MDRD), or another formula, as part of the definition of AKI. In the context of acute illness, GFR is well recognised as being unreliable (58, 59). The use of GFR estimates for baseline will also overestimate the incidence of AKI in patients with chronic kidney disease as shown by Bagshaw et al (60).

There was also apprehension that there was not a specific stage for those patients with AKI requiring renal replacement therapy (61).

Based on these pitfalls, there was an effort to further refine the definition of AKI, which was formalised following the creation of the Acute Kidney Injury Network (AKIN) in 2005 and the subsequent AKI definition in 2007.

AKIN

The AKIN classification of AKI builds upon the RIFLE definition but developed a few important changes. The most notable change was the addition of an increase in creatinine by 0.3mg/dl (or 26.4µmol/L) within 48 hours of a previous creatinine value. This potentially facilitates the identification of earlier and clinically significant renal impairment. As previously mentioned, there were many studies in the early 2000s that showed that a small change in creatinine correlates with a significant risk of morbidity and mortality for the patient (1, 53-57).

Following the meeting of the AKIN group, the criteria shown in figure 5 were published in 2007 (62).

Classification/staging system for acute kidney injury[a]

Stage	Serum creatinine criteria	Urine output criteria
1	Increase in serum creatinine of more than or equal to 0.3 mg/dl (≥ 26.4 µmol/l) or increase to more than or equal to 150% to 200% (1.5- to 2-fold) from baseline	Less than 0.5 ml/kg per hour for more than 6 hours
2[b]	Increase in serum creatinine to more than 200% to 300% (> 2- to 3-fold) from baseline	Less than 0.5 ml/kg per hour for more than 12 hours
3[c]	Increase in serum creatinine to more than 300% (> 3-fold) from baseline (or serum creatinine of more than or equal to 4.0 mg/dl [≥ 354 µmol/l] with an acute increase of at least 0.5 mg/dl [44 µmol/l])	Less than 0.3 ml/kg per hour for 24 hours or anuria for 12 hours

Figure 5 - AKIN, if renal replacement therapy required – automatically becomes stage 3

The AKI staging names changed to 1,2,3 with the highest number representing the most severe disease. The use of glomerular filtration rate (GFR) was also removed from AKIN. Again, AKI can be diagnosed by either creatinine-based identification or urine output-based (or both if present).

The criticism

Following the introduction of the AKIN classification, there were a few publications aimed at directly comparing the RIFLE and AKIN criteria. One of the first was by Bagshaw and his group in 2008 (63). This study looked at their retrospective critical care data, with 120,123 intensive care patients. When comparing the two criteria

they found very little by way of difference in the recognition of AKI (<1%). The authors concluded that there was no improvement in 'sensitivity, robustness and predictive ability of the definition and classification of AKI in the first 24 h after admission to ICU' when comparing the two groups.

A slight concern with regards to the AKIN classification was the addition of renal replacement therapy as a guide to diagnosis of AKI stage 3. There was some concern that variability between physicians in the initiation threshold for RRT would lead to some misclassification of stage 3 AKI and therefore could potentially affect studies investigating AKI outcomes (64, 65).

The main concern with regards to the AKIN criteria was the use of a 48-hour baseline definition, the practical application of which is very difficult. One example of the difficulty using this time frame was highlighted by Zappitelli and colleagues, who examined AKI in a paediatric population (66). For the sake of their research, they had to remove this time frame, as simply, non-critical care children are not bled daily and it can be argued that this is the same in some adult populations, especially in community settings. It was hoped that AKIN would improve sensitivity of the detection of AKI, but even in a population with many patients having daily blood tests, such as ICU, this did not seem to be the case within the first 24 hours as shown by Bagshaw et al (63) and in the first 48 hours as found by Joannidis et al (67). Joannidis and colleagues compared the RIFLE and AKIN criteria in ICU patients, and they found that they identified AKI with similar mortality, however RIFLE missed 504 (out of 24,356 patients) cases of AKI picked up by AKIN, most of which were AKI stage 1 (457). AKIN missed three times that, with 1,504 patients identified as AKI by RIFLE being missed by AKIN across all three categories of risk, injury and failure (781, 452 and 271 respectively).

This timeframe of a test within 48 hour could also miss more gradual change, an example of this is shown in a table created by Cruz and colleagues, shown below (59);

Acute Kidney Injury Network and Risk–Injury–Failure–Loss–Endstage renal disease classifications: an illustrative example[a]

ICU day	Creatinine	RIFLE classification	AKIN classification	Comment
1	1	No AKI	No AKI	
2	1.1	No AKI	No AKI	
3	1.2	No AKI	No AKI	
4	1.3	No AKI	No AKI	
5	1.4	No AKI	No AKI	
6	1.5	Risk	No AKI	1.5 × estimated baseline creatinine of 1.0
7	1.6	Risk	No AKI	
8	1.7	Risk	No AKI	
9	1.8	Risk	No AKI	
10	1.9	Risk	No AKI	
11	2	Injury	No AKI	2 × estimated baseline creatinine of 1.0
12	2.1	Injury	No AKI	
13	2.2	Injury	No AKI	
14	2.3	Injury	No AKI	
15	2.4	Injury	No AKI	Reference creatinine for AKIN
16	2.5	Injury	No AKI	
17	3	Failure	Stage 1	Δ >0.3 with respect to ICU days 15 and 16, 3 x estimated baseline creatinine of 1.0
18	3.9	Failure	Stage 1	Not yet 2 × reference creatinine

[a]A 65-year-old white male, baseline creatinine not known but estimated at 1.0 mg/dl with the Modification of Diet in Renal Disease formula, admitted to the intensive care unit (ICU). AKI, acute kidney injury.

Figure 6 - Example of how AKIN can be late in picking up AKI from Cruz et al (59)

Another problem with the AKIN classifications, was the mention of non-specific guidance;

"The above criteria should be used in the context of the clinical presentation and following adequate fluid resuscitation when applicable" (62)

This may lead to heterogenous interpretation as there are going to be different ideas as to what 'adequate fluid resuscitation' entails. It is also very difficult to analyse these practices in retrospective studies. The Cruz article among others called for the development of a new classification for AKI, building upon the work of both RIFLE and AKIN (10, 58, 59, 64, 68, 69). The table below summaries the cons of AKIN and RIFLE Table 9.

RIFLE	AKIN
Use of GFR in definition	48 hour creatinine change
Misses small but significant increases in SCr	Small changes may just be functional (pre-renal)
Diagnosis after significant damage is done	Vague statement – 'adequate fluid resuscitation….'

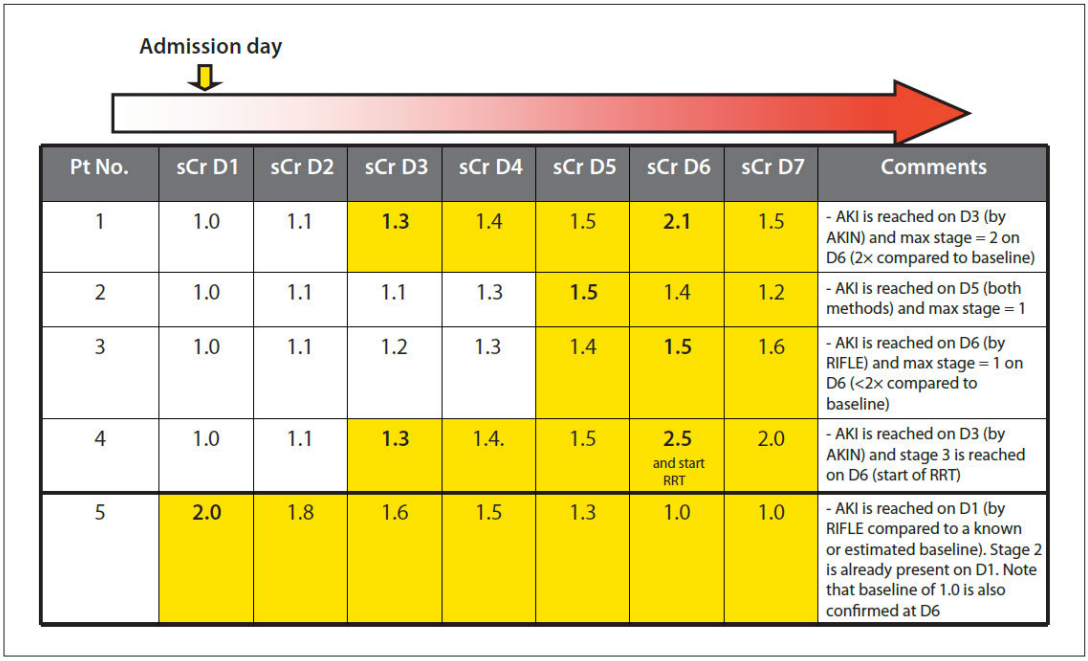
Table 9 - Cons of each method

KDIGO

The next definition was created by the Kidney Disease Improving global outcomes (KDIGO) group. This group refined the definition following some publications which were critical of the preceding definitions.

Srisawat, Hoste and Kellum wrote a paper in 2010 outlining the problems with the then current definitions of AKI (10). A key point that they made was that although AKIN was able to pick up small but significant changes in creatinine as AKI stage 1, it would be potentially slower in the identification of AKI and would not accurately pick up the peak stage of AKI as shown in the table below (10);

In this table, patient 1 shows how recognition of peak AKI stage is different between RIFLE and AKIN. It also shows how RIFLE can identify some AKI where AKIN would not (i.e. Patient 5). The authors comment that there is variability in the degree of AKI missed by AKIN, where even stage 3 AKI patients would not be identified.



Pt No.	sCr D1	sCr D2	sCr D3	sCr D4	sCr D5	sCr D6	sCr D7	Comments
1	1.0	1.1	**1.3**	1.4	1.5	**2.1**	1.5	- AKI is reached on D3 (by AKIN) and max stage = 2 on D6 (2× compared to baseline)
2	1.0	1.1	1.1	1.3	**1.5**	1.4	1.2	- AKI is reached on D5 (both methods) and max stage = 1
3	1.0	1.1	1.2	1.3	1.4	**1.5**	1.6	- AKI is reached on D6 (by RIFLE) and max stage = 1 on D6 (<2× compared to baseline)
4	1.0	1.1	**1.3**	1.4.	1.5	**2.5** and start RRT	2.0	- AKI is reached on D3 (by AKIN) and stage 3 is reached on D6 (start of RRT)
5	**2.0**	1.8	1.6	1.5	1.3	1.0	1.0	- AKI is reached on D1 (by RIFLE compared to a known or estimated baseline). Stage 2 is already present on D1. Note that baseline of 1.0 is also confirmed at D6

Figure 7 - Example of RIFLE and AKIN by Srisawat et al(1)

The problem with the 48 hour rule for AKI in the AKIN criteria was highlighted in a paper by Thakar et al investigating ICU patients (70) where they found an additional 5.7% of the patients they studied had AKI if the definition was extended beyond a 48 hour baseline creatinine. These patients were also found to have a higher odds ratio of death than those diagnosed within 48 hours (OR 2.52 vs 4.66 in <48 vs >48 hours respectively). It was clear from this and the Joannidis et al (67) paper, that a combination of the definition would be required.

Findings like these helped to refine the AKI guidelines in the 2012 KDIGO Acute Kidney injury publication (4). They proposed the following definition;

Stage	Serum creatinine	Urine output
1	1.5–1.9 times baseline or ≥0.3 mg/dl (≥26.5 μmol/l) increase	<0.5 ml/kg/h for 6–12 h
2	2.0–2.9 times baseline	<0.5 ml/kg/h for ≥12 h
3	3 times baseline or ≥4.0 mg/dl (≥353.6 μmol/l) increase or initiation of RRT or in patients <18 years a decrease in eGFR <35 ml/min/1.73 m^2	<0.3 ml/kg/h for ≥24 h or anuria ≥12 h

Table 10 - KDIGO staging criteria (68)

In these criteria, the ≥26.5μmol/L definition related to a creatinine within the first 48 hours. The rest is related to the 'baseline', with the change 'known or presumed to have occurred within the last 7 days'. This definition has been widely validated since its publication. AKI can be diagnosed by either creatinine-based identification or urine output-based (or both if present). One useful study by Zeng et al (71) compared these KDIGO criteria with its predecessors RIFLE, AKIN and another method called creatinine kinetics (CK) which was developed by one of the authors, Waikar and Bonventre (24). The CK criteria used absolute increases in creatinine outlined below;

CK	Increase in SCr ≥0.3 mg/dl within 24 h or ≥0.5 mg/dl within 48 h	1 2 3	Increase in SCr ≥0.3 mg/dl within 24 h or ≥0.5 mg/dl within 48 h Increase in SCr ≥0.5 mg/dl within 24 h or ≥1.0 mg/dl within 48 h Increase in SCr ≥1.0 mg/dl within 24 h or ≥1.5 mg/dl within 48 h

Figure 8 - Creatinine Kinetics(24)

The study was carried out on 31,970 hospital admissions in Brigham and Women's hospital in Boston, USA. It found that the 4 methods behaved differently with 18.3%, 16.6%, 16.1% and 7% of the admissions being diagnosed by AKI by KDIGO, AKIN, RIFLE and CK definitions respectively. Mortality was similar between KDIGO, AKIN and RIFLE (OR 2.8, 2.6, 2.9 – confidence intervals overlap) but CK had a higher OR for in-hospital mortality 5.2.

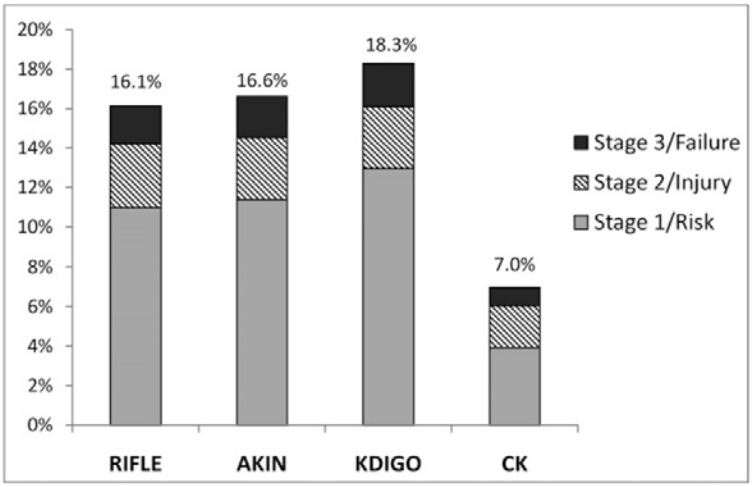


Figure 9 – Percentage of admission with AKI by the different identification methods from Zeng et al (71)

The criticism

Although the criteria have had an overall positive reception (72, 73) there are some weaknesses. Many of the problems with KDIGO are similar to that in AKIN. Someone presenting with AKI without a prior blood test, which then subsequently improves may not be picked up as AKI. The Canadian Society of Nephrology (72) and the Kidney Disease Outcomes Quality Initiative (KDOQI) group (73) expressed some concern about the practical clinical application of the criteria. Some of the concern is regarding other influences on serum creatinine values (73-76), however, it still remains the best widely available marker of kidney disease (77). Another concern was that the criteria did not consider the duration of AKI, however, this is not crucial for prospective use (72-75).

This figure below from Tsai et al (78) summarises the differences between the definitions. It is important to highlight that they all look for AKI using serum creatinine or urine output.

	Serum creatinine			Urine output
	RIFLE	AKIN	KDIGO	
Definition	SCr increase ≧50% within 7 days	SCr increase ≧50% or ≧0.3 mg/dL within 48 h	SCr increase ≧0.3 mg/dL within 48 h or ≧50% within 7 days	UO < 0.5 mL/kg/h for 6 h
Staging	RIFLE	AKIN	KDIGO	
RIFLE-Risk AKIN stage 1 KDIGO stage 1	SCr increase ≧50% or GFR decrease >25%	SCr increase ≧50% or ≧0.3 mg/dL	SCr increase ≧0.3 mg/dL within 48 h or ≧50% within 7 days	UO < 0.5 mL/kg/h for 6 h
RIFLE-Injury AKIN stage 2 RIFLE stage 2	SCr increase ≧100% or GFR decrease >50%	SCr increase ≧100%	SCr increase ≧100%	UO < 0.5 mL/kg/h for 12 h
RIFLE-Failure AKIN stage 3 KDIGO stage 3	SCr increase ≧200% or GFR decrease >75% or SCr ≧ 4 mg/dL (with an acute rise ≧0.5 mg/dL)	SCr increase ≧200% or SCr ≧ 4 mg/dL (with an acute rise ≧0.5 mg/dL) or need RRT	SCr increase ≧200% or SCr ≧ 4 mg/dL or need RRT	UO < 0.3 mL/kg/h for 24 h or anuria for 12 h
RIFLE-Loss	Need RRT for >4 weeks			
RIFLE-End stage	Need RRT for >3 months			

Abbreviation: RIFLE, risk of renal failure, injury to the kidney, failure of kidney function, loss of kidney function, and end-stage renal failure; AKIN, Acute Kidney Injury Network; KDIGO, Kidney Disease Improving Global Outcome; SCr, serum creatinine; UO, urine output; GFR, glomerular filtration rate; RRT, renal replacement therapy.

Figure 10 - Summary of RIFLE, AKIN and KDIGO, Tsai et al (78)

Urine Output

The addition of a urine output (UO) based definition consistently leads to the recognition of more patients with AKI (67, 79-84) than SCr alone. As with much of the retrospective research, the prospective alerts in England and Wales do not use the urine output part of the KDIGO definitions. The main reason for this is that many hospitals in England and Wales do not have electronic observations (85), not to mention the variability and logistical difficulties in keeping accurate urine output measures, particularly in those not yet identified as having AKI (63, 86). As a result of this, the majority of publications utilising the urine output part of the AKI diagnosis (prospectively and retrospectively) have been based in the intensive care environment (63, 67, 79, 86-91) although some have been post-operatively (92-94). As such, the application of the UO criteria has not been as widely validated in hospital in the same way that SCr and has some potential hazards. Palevensky et al (73) pointed that there has been 'poor calibration' between UO and SCr as well as a poor correlation with prognosis (76, 81, 82, 90), however, patients with oliguric AKI do have a higher mortality rate than patients without AKI (84) and this is increases with the duration of oliguria (83, 84). Palevensky also highlights that oliguria can be related to volume depletion and therefore appropriate fluid resuscitation is required, but the kidney is not 'injured' at that point (73, 74). There is also criticism that the use of weight-based criteria for the cut off is inappropriate, given that there is a non-linear relationship between weight and urine output (4, 73-75, 95), and it is not clear

whether actual or ideal body weight should be used (75, 96). Finally, they mention the concern that drugs such as loop diuretics and dopamine can affect urine output, which can affect the recognition but also they worry that urine output can be used as a marker of recovery and this can be manipulated by these medications without benefit to the patient and possibly harm (73, 97, 98). One thing that could be added to that is that not all AKI causes oliguria, such as acute interstitial nephritis (99). The use of urine output as a criterion for AKI potentially gives rise to treatment goals (i.e. aims to improve urine output above threshold); this, however, does not have a clear mortality benefit (100).

In contrast to some of the earlier studies, Ralib et al 2013 did find a correlation between oliguria and mortality (79) emphasising that it still plays an important role in the recognition of early, significant AKI. This is my experience clinically, particularly emphasised by the fact that creatinine takes time to increase (101, 102), whereas urine output may diminish immediately (4), potentially highlighting a need for treatment before it is too late and acute tubular necrosis (where kidney cells necrose and block the tubules preventing urine production) is established.

Other biomarkers

There have been many other biomarkers studied over time including Neutrophil Gelatinase-Associated Lipocalin (NGAL), Kidney Injury Molecule-1 (KIM-1), Cystatin C, tissue inhibitor of metalloproteinases-2 (TMPT-2) and insulin-like growth factor-binding protein 7 (IGFBP-7) (101, 103-107). Although there may still be a role for use of these or other biomarkers in identifying AKI, they are not at this time widely implemented or accepted and are, therefore, not part of the KDIGO guidelines (108). They are also not adopted in Wales outside research or special circumstances, and so will not be available for electronic health record research in Wales.

Baseline kidney function

The definition of a baseline creatinine is a crucial step in the recognition of AKI and changes in this can influence the recognition of AKI (109-111). The KDIGO definition

for AKI does not give clear guidance on this but suggests using estimates of serum creatinine-based on eGFR (108) using the method from RIFLE (49). A reason that this method was seen as an option was because many patients presenting to hospital do not have previous renal function tests (112). However, this method overestimates AKI in the presence of CKD (60, 74, 113, 114). A complicated correction for this estimate was suggested by Siew and colleagues in 2013 using comorbidities as variables (112) but the number of inputs required make it impractical for prospective use. In an attempt to explore the effects of baseline variation, a study by Lafrance et al (110) found that by adjusting the timeframe for using the lowest creatinine value for a patient over a period of a year, the frequency of in hospital AKI varied from 12.5% to 18.3%. Siew and colleagues found that the use of a mean SCr between 7 and 365 days correlated best with the opinion of a group of nephrologists (115). A problem with a mean value is that a previous episode of AKI with resolution would result in a falsely high baseline. This can largely, but not completely avoided by using a median creatinine value (116). The use of a median creatinine for the period of 8 to 365 days has been utilised by the NHS England electronic alert (117). Simon Sawhney and colleagues have taken this a step further, and used a median between 8 and 90 days if available, if not, then a median from 91 to 365 days (118).

Coding

Overview

Many countries use a clinical coder to code primary and secondary diagnoses following hospital admissions (119). This is usually based on the standardised international classification of disease (ICD), which is on its 11th revision. The 10th revision, ICD-10 has been used by several studies investigating hospital coding for AKI (116, 119-124). Other AKI studies have used the 9th revision (ICD-9) (1, 123, 125-133) which is largely equal to ICD-10 (134). Coding practices can vary between hospitals in a city (125) and within a country (135) let alone between countries(136). There may be bias in the coding, particularly when there is an associated financial renumeration, often referred to as ‘code creep’ (137-139). It is likely that this practice is more common in countries where billing is directly related to coding and less likely in

countries with a national health system like the United Kingdom (138). The benefits and the disadvantages of using coding are nicely summarised in this image from the Acute Dialysis Quality initiative (ADQI) group;

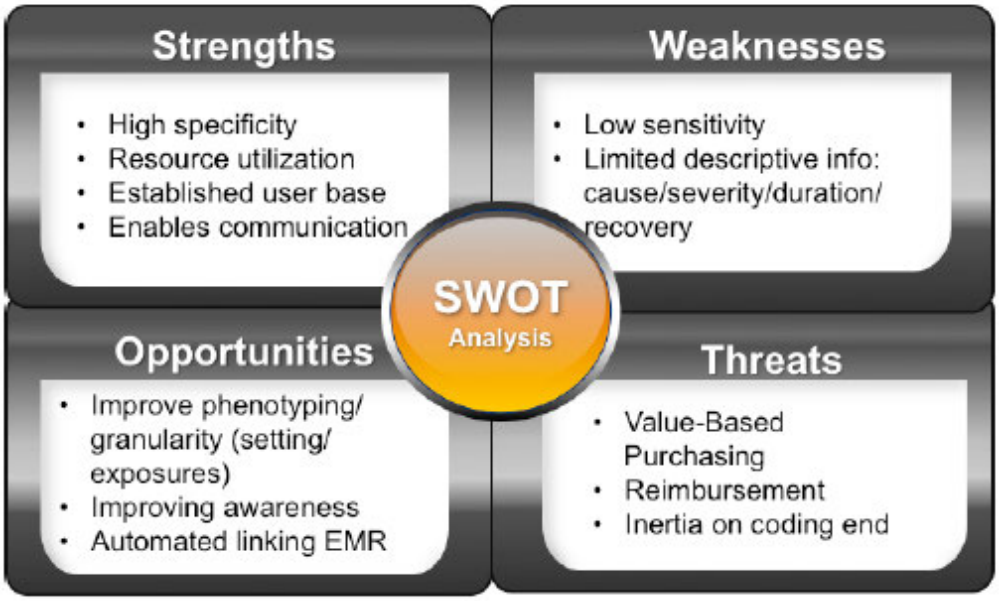


Figure 11 - Figure from Acute Dialysis Quality Initiative 15 www.adqi.org(140, 141)

Coding has been used in several studies in this century to describe the incidence of AKI/ARF (119, 120, 122, 124, 125, 130, 132, 138, 142-145). Many of the studies using coding have been carried out in the United States and Canada (120, 123, 125-133, 142, 145-147) but there is an increasing number of publications from the UK, utilising big datasets (119, 122, 138, 144, 148). Coding has high specificity but low sensitivity in comparison to SCr or SCr and urine output definitions of AKI, as it relies on documentation of the AKI (125, 126, 130, 142, 145). This is a problem as AKI is the result of many different disease processes (140, 149), so someone may have pneumonia clearly documented, but the AKI they have as the result of this might not be clearly documented. The two main markers of coding quality are the completeness (i.e. percentage of admissions with coding) and the depth of coding (i.e. the average number of codes per hospital admission) (135, 150). With a condition like AKI, which is often associated with another illness, depth of coding is particularly important. The sensitivity improves when examining AKI requiring dialysis (AKI-D) (142), although Grams et al found a sensitivity of just 36.5% in AKI-D in their population (specificity

of 99.9%) (145) due to misclassification of end stage renal failure on dialysis instead of AKI-D.

Validation of coding

Some of the key publications came from Boston, USA in 2006 (125, 126, 142). Waikar et al, published a paper using administrative data comparing the patients with ARF coded by ICD-9 coding to those with a blood test diagnosis-based on a 100% increase in creatinine as a definition of ARF. The authors found a low sensitivity (35.4%), and high specificity (97.7%). The sensitivity increased when the renal failure required dialysis treatment to a sensitivity of 90.4% and specificity of 93.8%. Across the three Boston hospitals used in the study, there was some variation in the sensitivity (shown in the table below), but as a whole the findings were similar.

Waikar Hospitals	Definition of AKI	Sensitivity	Specificity	Positive Predictive Value	Negative Predictive Value
BWH	100% Increase	32.2	99.2	79.9	92
MGH	100% Increase	35.1	98.9	81.1	89.6
CSEMC	100% Increase	47.6	99	77.9	91.9
Combined	100% Increase	35.4	99	80.2	91
BWH	Hou Criteria	26.2	98.1	47.4	96.5
MGH	Hou Criteria	29.3	97.2	48.4	95.2
CSEMC	Hou Criteria	30.2	97.7	47.5	97.7
Combined	Hou Criteria	28.3	97.7	47.9	96.1

Table 11 - Sensitivity of coding from Waikar et al 2006 (125) (BWH, Brigham and Women's Hospital; MGH, Massachusetts General Hospital; CSEMC. Caritas-St.Elizabeth's Medical center)

In 2006 there were two other papers, one again by Waikar (142) and one by Liangos (126), both of which showed a low sensitivity and high specificity from coding. The finding of the three papers also shows a relatively low positive predictive value (PPV) for identifying AKI, particularly with smaller increases in creatinine (i.e. with Hou's criteria).

Some recent English studies (119, 138, 144, 151) suggest that sensitivity is better in the UK. The National Confidential Enquiry into Patient Outcomes and Care (NCEPOD) looked at deaths in patients with AKI (138, 151). In these patients, they reported a sensitivity of 74.1%. Since this is a cohort of patients who have died, you may expect

a more severe AKI due to the association between a higher mortality risk and increasing severity of AKI (i.e. AKI stage 3) (61). This coupled with the finding that coding sensitivity improves with increasing severity of AKI (125) might explain the increased sensitivity in the NCEPOD study in comparison to the American studies.

The finding of this report was subsequently used by Kolhe et al (138, 144) which used the English 'Hospital Episodes Statistics' (HES) dataset in the analysis of their findings of incidence of AKI. In both of these studies, there was a clear increase in the number of AKI episodes recognised by coding over time, likely due to the improved recognition of AKI by coding rather than a substantial increase in true AKI, although this may have had some impact.

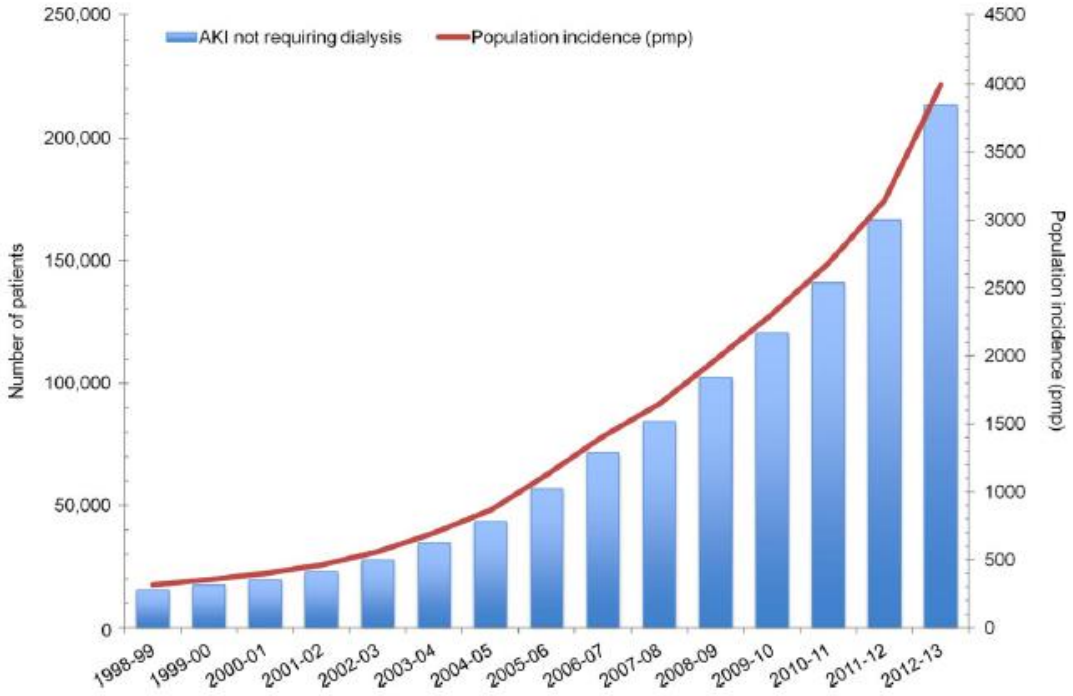


Figure 12 – AKI not requiring dialysis from Kolhe et al (144)

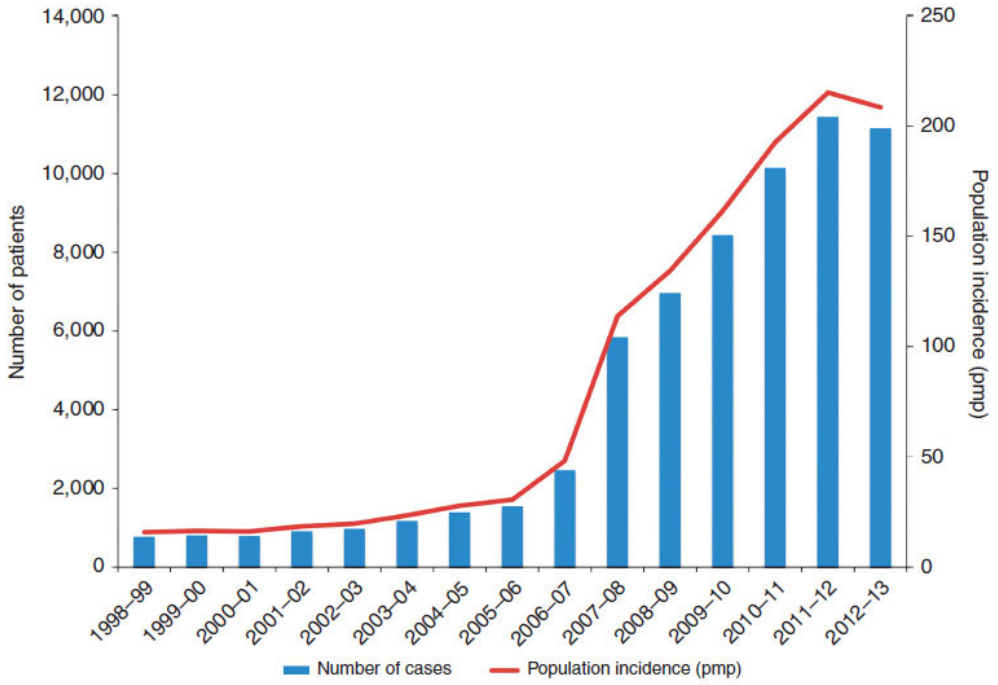


Figure 13 – AKI requiring dialysis patient in England from Kolhe et al (138)

Similarly, Grams et al in 2014 found a change in the validity of coding over time, with a sensitivity of just 9.7% between 1996-2002 versus 24.4% between 2002-2008, when using KDIGO criteria (145).

A single centre English study by Tomlinson et al in 2013 found a high positive predictive value (95%), showing that those with coding for AKI were likely to have AKI (119). This is hardly surprising given that around 50% of the AKI patients in this cohort required renal replacement therapy (i.e. severe AKI). However, we know from SCr-based studies that most cases of AKI are KDIGO stage 1 (116, 152, 153). It is therefore likely that this study, which used coding to identify AKI, underestimated the frequency of AKI.

Marion Kerr et al reviewing the financial implications of AKI, used the HES data for the whole of England and with this, 3.24% of admissions were coded with AKI (ICD-10). This study also had a validation cohort in East Kent Hospital University NHS Foundation Trust (EKHUFT), which found that 16.26% of that population had AKI based on AKIN criteria.

General practice coding for AKI has had little attention. It is felt that it is likely that it follows the trends of hospital coding (154). We may also see a discrepancy between Wales and England because it has become mandatory in England to report AKI on hospital discharge summaries (155); this is not the case in Wales and therefore GPs may not know about the inpatient AKI. There is also the potential that discharge summaries could improve coding for AKI, if summaries are done prior to coding.

In summary, there has been a change in coding practice over time. The effect of this and the impact on the true sensitivity of coding in the UK is not clear. If the accuracy of coding practice has improved over time, then the implications of findings of studies at different points in time may simply reflect the quality of coding for AKI at that point. It is unlikely that the results of American studies are applicable to the UK and vice versa given the differences in hospital coding practices, designs of hospital services and hospital funding. The use of electronic alerts, adoption of consensus definitions and growing attention to AKI will increase the sensitivity of AKI coding. A summary table of the variation in sensitivity of hospital coding is shown on the next page, Table 12.

Studies	Code	Sensitivity – (95% CI)	Specificity – (95% CI)	Positive predictor value – (95% CI)	Negative predictor value- (95% CI)	AKI Definition	Country	Dataset	n	AKI
Waikar et al 2006 (125)	ICD-9	35.4	97.7	47.9	96.1	100% increase	USA	3 Boston, Massachusetts hospitals – 2004	97705	5.80%
Waikar et al 2006 (125)	ICD-9	28.3	99	80.2	91	Hou et al criteria	USA	3 Boston, Massachusetts hospitals – 2004	97705	12%
Waikar et al 2006 (142)	ICD-9	29.3	97.4	59.1	91.5	100% increase	USA	2 Boston teaching hospitals and Nationwide Inpatient Sample – 2002	19206	11.4%
Waikar et al 2006 (142)	ICD-9	17.4	98.7	63.5	89.9	100% increase	USA	2 Boston teaching hospitals and Nationwide Inpatient Sample – 1994	7545	11.5%
Liangos 2006 (126)	ICD-9	19.2	99	87.6	90.1	Hou et al criteria	USA	National Hospital Discharge Database & Caritas St.Elizabeth s Medical center, Boston – 2001	13,237	12%
Parker 2006 (133)	ICD-9	22 (20-25)	98 (98-99)	32 (29-35)	97 (97-98)	SCr ≥2.5mg/dl	USA	California Hospital Discharge Abstract Database	38230	3.30%
Stewart 2009 (151, 156)		74.1	96	90.9	87.2	RIFLE	UK	Across UK- Questionnaire and Case note review – 2007	1045	
Hwang 2012 (120)	ICD-10	21.8 (20.9-22.8)	98.4 (98.2-98.5)	74.2 (72.3-76.1)	85.3 (84.9-85.6)	AKIN stage 1	Canada	Single centre, Ontario, Canada	38566	17.80%
Hwang 2012 (120)	ICD-10	61.6 (57.5-65.5)	95.6 (95.4-95.8)	17.3 (15.7-19)	99.4 (99.3-99.5)	RIFLE Injury	Canada	Single centre, Ontario, Canada	38566	1.50%
Tomlinson 2013 (119)	ICD-10			95% (91-99%)		KDIGO SCr criteria	UK	Single centre, Addenbrooke, Cambridge	690	
Grams 2014 (145)	ICD-9&10	17.2 (13.2-21.2)	98.5 (97.9-99.1)	72.1 (62.4-81.8)	81.8 (76.5-87.2)	KDIGO SCr criteria	USA	Atherosclerotic risk in communities study participants (Washington County cohort)	1970	361
Grams 2014 (145)	ICD-9&10	11.7 (8.8-14.5)	98.9 (98.2-99.5)	83.5 (75.4-91.7)	69.3 (66.9-71.7)	KDIGO SCr and Urine output criteria	USA	Atherosclerotic risk in communities study participants (Washington County cohort)	1839	609

Table 12 – Sensitivity of coding

eAlerts

The RIFLE, AKIN and KDIGO definitions for AKI have been extensively used to understand the condition. In England in 2014 the 'Think Kidneys' group along with NHS England issued a national Patient Safety Alert calling for the implementation of harmonised AKI warning system (117, 157). It was hoped that electronic alerts (eAlerts) can been used to aid the recognition of AKI and potentially to support the decision making of the clinician. With earlier recognition it was hoped that there would be prompt intervention in AKI (151, 158), which could lead to improved outcomes (159). The alerts are made up of two components; the first part is the recognition, which has varied over time depending on the definition of AKI.

The balance between sensitivity and specificity of these alerts is crucial, as poor sensitivity would result in missed patients and poor specificity would potentially result in alert fatigue (160-164). The second element is the way the clinician is informed of the outcome of the recognition. This alert can be passive, such as a note accompanying the blood result, or it could be interruptive, such as a prompt which requires an action for the user such as a pop-up on a computer or mobile device which will not disappear until there is an acknowledgement from the user. Interruptive alerts are felt to be the most effective in highlighting a problem to clinicians (160, 165, 166), particularly those that are outside of the electronic medical record using a pager, e-mail or direct communication (160, 164). Although, interruptive alerts can become burdensome and unpopular (167) if a balance between functionality, practicality and sensitivity are not achieved. The alerts may be well received initially, but support can wane with time (168).

NHS England eAlert in Wales

Following the development of the AKI eAlerts by NHS England, they were adapted and introduced throughout Wales between 2013 and 2015. This has allowed researchers to publish the initial findings of these alerts (153, 169). Although these alerts have been validated in the detection of AKI (116, 159), the implementation of these alerts in different sites has not been validated. Anecdotally, we have seen false positive alerts, issued for dialysis patients and false negatives of suppressed alerts because a patient is under a renal physician. These errors occur due to the reliance on laboratory staff identifying dialysis patients based

on the location of the patient's blood test or the type of clinician requesting the test. From a clinical, patient care point of view, the importance of this is probably minimal as the patients are under the care of the nephrologist who due to the nature of their job are very primed to look for changes in kidney function. However, these errors may impact the research carried out on these alerts. This is because in Wales (153, 169) and England (117, 170) research is carried out on the results of alerts, but only when generated without the ability to cross link or validate with other data sources.

There are other concerns regarding the AKI eAlerts such as 14% of the AKI recognised by the alerts in the hospital setting are in fact chronic kidney disease (154, 171). The algorithm relies on two tests being performed within a year, and as such, it behaves differently in the community compared to hospital setting (172).

Development and Validation

The use of computer based alerts to aid the recognition and management of acute renal injury is not a new concept, having been successfully demonstrated by Rind et al in 1994 (163). This Boston based study looked at the use of an electronic mail (e-mail) based alert to clinicians looking after patients with acute rises in creatinine (rise of 44µmol/L or more) on nephrotoxic or renally excreted medications (50% increase to a creatinine of 177µmol/L or more). The e-mail would give tailored information of the patient's creatinine increase and medication. This e-mail would be cascaded to clinicians who had reviewed the patient's information in the last 3 days, with the options of clicking "taken care of". If medications were not adjusted and the alert not responded to then the e-mail would be sent to further clinicians who looked at results on the patient in the 3 days following the alert. Remarkably, this study found that patient's nephrotoxic medications were stopped 21.6 hours earlier with this intervention and there was a reduction in the relative risk of developing serious renal impairment (RR 0.45 with 95% CI 0.22 to 0.94, p=0.034) as defined by a doubling of SCr or SCr and increase in SCr above 177µmol/L when the baseline is less that 106µmol/L. Unfortunately, in spite of this study being carried out 25 years ago, many places in the UK still do not have electronic prescribing (173).

Thirteen years after this, Colpaert et al (174) in Belgium described the implementation of a eAlert system to help identify AKI in ITU patients and they published data on these alerts (87) in 2012. They implemented an alert based on the full RIFLE criteria (using urine output and serum creatinine changes), which sent out an automated message to the ICU physician looking after the patient. When a patient shifted from one RIFLE classification to another (including improvement) there was a further message. The alerts also instructed doctors to re-evaluate the patient and intervene if appropriate. This study found that the alerts increased the percentage of therapeutic interventions (fluids/ vasopressors/ diuretics) within 60 minutes of the results, when compared to the control group, from 7.9% in the pre group compared to 28.7% in the alert group and then 10.4% in the post group ($p<0.001$). The introduction of an alert, however, did coincide with an education course 1 week before the introduction; this could potentially lead to bias as this teaching would be fresh in the mind of the doctors at the time of the alerts, but this impact may well have waned with time. There was also the potential Hawthorn effect of the participants recognising that they were participating in a trial and therefore affecting the outcome (175).

In 2010 McCoy et al published the outcomes of the introduction of a clinical decision support (CDS) system introduced in a university hospital in Nashville (176). The study compared the adjustment of medications before and after the introduction of an interruptive alert. The authors found a significantly ($p<0.001$) improved rate of intervention in the alert group (52.6 per 100 events) compared to the control group (35.2 per 100 events). These authors then went on to perform a randomised controlled trial (165) investigating pharmacy surveillance and intervention in patients with AKI in reducing adverse drug events. In this study they found no significant difference between the intervention by a pharmacist compared to the control group which had the clinical decision support system. As the authors suggest, these studies were carried out in close proximity, in the same hospital, so the staff were used to the CDS and the alerts they created. Therefore, application of the pharmacy surveillance elsewhere may yield different results.

In 2015 Ahmed et al (177) in Minnesota validated a modified AKIN (baseline involved a median of the creatinine for the last 180 days or an estimate based on a GFR of 60ml/min) based AKI 'sniffer' system which included the urine output aspect of the criteria. When validated

against two clinicians who were blinded to the system, they found a sensitivity and specificity of 88% and 96% respectively.

Also in 2015, Simon Sawhney and colleagues (in Aberdeen, UK) assessed the performance of an automated code, examining definitions of baseline (116). They found that the NHS England AKI algorithm performed well against ICD-10 coding for AKI with a sensitivity of 91.2% (87.6-94). The same group (171) found a similar performance when comparing the algorithm versus a nephrologist using RIFLE AKI criteria diagnosis (sensitivity of 90.5%). They found 14% were false positives, mis-labelling patients with CKD as AKI which fell to 2.1% when using the more severe AKI stages of 2 and 3 (excluding stage 1 AKI), but this missed two-thirds of RIFLE AKI patients.

When the Welsh AKI steering group looked at the effects of different AKI rules on mortality based on the Welsh electronic AKI reporting system, they found that the different rules had different associated mortality rates (169). Rule 1 was based on an increase in creatinine above >26µmol/L in the last 48hours, rule 2 on a ≥50% increase in creatinine in the last 7 days and rule 3 on a ≥50% increase in SCr from the median SCr in 8-365 days. They reported a 90-day mortality of 28.3%, 32.4% and 26.6% respectively.

These studies help to understand how the AKI eAlerts identify AKI, but they do not explore the practical implementation of these alerts and the potential for variation in the real-world application of these alerts across different sites. They do not describe how dialysis patients can be excluded from triggering AKI in prospective, real world clinical AKI eAlerts.

eAlerts in the UK

In 2011, Mark Thomas et al (178) described the findings of the using a simple creatinine-based automatic alert system to identify AKI in Birmingham, England. In this study, they defined AKI as a SCr rise of ≥75% from the previous creatinine. In these patients with AKI, they found an overall mortality of 36% within 6 months. The alert used in this study was passive and they did not analyse the effect of the implementation but used the alert to assess risk factor for poor outcomes.

A year later, Nicholas Selby and colleagues, applied an AKIN based alert system to identify AKI in Derby, England (170). The baseline SCr values in these patients were initially estimated using reverse eGFR, however, they were then adjusted when AKI was recognised, and a more accurate baseline was manually applied by Dr Selby. Using these new baselines, the authors were able to determine that 1.7% of the alerts were false positives. Overall, the rate of AKI was 5.4% of the admissions with a mortality rate of 23.8% in AKI (versus 3.2% in all patients). Again, the alerts in this study were passive, and the outcomes the alerts were not assessed. This study and group of researchers played a key role in the development and implementation of the national eAlert system which was introduced in 2014 (157).

In 2014, Porter et al from Nottingham, published their experience from the introduction of an eAlert system in 2011 (179) which sent out 'real time' statement with the blood results based on a modified RIFLE and AKIN criteria. They published an inpatient incidence of 10.7% as well as mortality rate of 35.7%. They did not assess whether the introduction of this alert made a difference to clinical care or patient outcomes.

Likewise Wallace et al (159) published their experience with the introduction using a modification of the AKIN criteria. This alert required a manual review by the duty biochemist. Baseline creatinine was the most recent creatinine. If there was a rise of 26umol/L or more, or they had a 50% increase, then their results were reviewed by the biochemist. The study states that 'All four duty biochemists used the same criteria' (AKIN), however, there seems to be some element where there was a subjective opinion with regards to the true baseline; 'A stable creatinine level from the last 3 months was used for comparison'. A message was sent out to the user with the blood results to indicate AKI. The impact of the alerts was not assessed.

Flynn and Dawnay developed an eAlert system in University College, London and applied it to real time data (180). Again, they used slightly different definitions and implementation in that they e-mailed the intensive treatment unit outreach team twice a day with a list of inpatients as well as adding a comment to the report. This study did not analyse the impact of the alerts.

In 2016 the Welsh AKI steering group published the finding of the first 6 months of AKI alerts in Wales (153). For 6 months between March 2015 and August 2015 there were 31,601 alerts in 17,689 patients with a 90-days mortality rate of 25.6%.

eAlert impact

A meta-analysis and systematic review released in 2017 concluded that 'e-alerts for AKI do not improve survival or reduce RRT utilization' (181). Despite this, we see some studies investigating AKI alerts seeming to give positive results. Rind et al (163) and McCoy et al (176) found improved adjustments in medications and Colpaert et al reported improved interventions in their critical care patients (87). There may be several reasons for this, but most likely it is the application of these eAlerts in clinical practice. In the papers mentioned above, the alerts were interruptive or in the case of Rind et al they escalated the alerts if there was a lack of response. As such they are different to those alerts introduced in England and Wales. This is further highlighted by the finding that even the systematic reviews do not agree. A German review, also from 2017, concluded that 'Non-randomized controlled trials of electronic alerts for AKI that were coupled with treatment recommendations have yielded evidence of improved care processes' (182).

In 2015, Wilson et al published the finding of the first randomised controlled trial (RCT) into the effects of their alert system (183). The alerts used by this group were based on the KDIGO criteria compared to the lowest creatinine in the last week. Passive alerts were sent out to the clinician (intern, resident or nurse practitioner) and pharmacist looking after the patient by text or mail for the first alert showing AKI for the patients. These alerts contained links to the KDIGO guidelines. The study was a single blinded study in the University of Pennsylvania hospital in USA. 2393 patients were randomised with 1201 in the intervention arm and 1192 in the usual care arm, with equal baseline characteristics. The findings were that there was no difference in the different arms with regards to the primary outcomes of ranked composite scores of the relative maximum change in creatinine value, dialysis and death within 7 days of randomisation. The only difference found was that surgical wards were more likely to request a renal consultation, and their patients were then more likely to have dialysis or die. Although this was a decently implemented RCT, there was potential for some bias that could skew the results. Firstly, it was a single centre meaning that clinicians and pharmacists were

potentially primed toward the recognition of AKI, this could also be compounded by the Hawthorne effect of the individuals knowing they are involved in a study and therefore adjusting their practice (175, 184). Secondly, the use of a single alert only to avoid alert fatigue potentially meant that later stages of AKI were missed, particularly if clinicians/pharmacists were looking out for the alerts and not using their discretion. Thirdly, 44% of the alerts were sent by mail but there are no comments on how long this would take to reach the clinicians/pharmacists, which may result in delayed recognition and action. Fourthly, the use of the KDIGO guidelines attached to the alerts may not be the most practical idea, since the guidelines are 141 pages in length (4) and therefore are impractical for quick reference. Given this, one might expect that the alerts would only change recognition and not practice. Fifthly, the in-hospital mortality rate (9.8% in the alerts and 9.4% in the control) was lower than some other studies (185), for example in-hospital mortality rates were 18.5% and 23.8% in studies by Porter et al (179) and Selby et al (170) respectively. Sixthly, the alerts are only applied to inpatients and not out-patient or primary care, where alerts may make a bigger difference (185) although the baseline definition (lowest SCr within a week) may mean that very few alerts get picked up by this method. This method of AKI detection has been found to be relatively insensitive (116) (due to the reliance on a blood test within the last week) when compared to clinical coding (74.2%) therefore it is likely to have missed many cases of AKI. These eAlerts were passive alerts, and therefore may be less effective than an interruptive alert, however, this is what we have in England and Wales (although some centres may implement the alerts in an interruptive way). Also, the alerts are SCr-based only, so may not be as effective at identifying early AKI, but this is also the case for eAlerts in the UK at present. Another RCT by McCoy et al of pharmacy surveillance and CDS support failed to reduce adverse drug event in AKI (165).

Nitin Kolhe and colleagues assessed the impact of an AKI care bundle introduced alongside an electronic alert in their hospital in Derby (186). In this study, they demonstrated a reduced odds ratio for death at discharge (0.641; 95% CI 0.46, 0.891) and at 30 days (0.707; 95% CI 0.527, 0.950) in the group that had their care bundle completed within 24 hours. This study is promising as it suggests that early and appropriate intervention can improve mortality. The study also found that there was a more than 10-fold increase in the use of a care bundle after the introduction of an interruptive alert.

Similarly, Mark Thomas and his colleagues in Birmingham, used electronic AKI alerts to help identify patients for a team of outreach nurses and nephrologists, who would then phone and give advice to the patient's team (187). In this non-randomised weekday only study with a control group (group prior to introduction of team) they did not find a significant difference in mortality, length of stay or peak creatinine. Due to the size of the study (control n=157, active n=251) an effect on mortality cannot be ruled out, particularly as there was a suggestion of improved mortality. Of note, the study was published in 2015, but the actual study was carried out prospectively in 2009 using RIFLE criteria.

Another English study by Prendecki et al (188) in 2016 found that patients who were seen by a critical care outreach team (CCOT) within 24 hours of AKI had a reduced mortality compared to those seen after 24 hours, 19.4% vs 47.5% (p=0.0085). Importantly, the CCOT review was on the basis of the patient 'physiological decline' and not AKI itself, so the difference in mortality may be related to different factors, but it certainly warrants further study.

The early stages of AKI electronic alerts have been troubled by the same problems that AKI epidemiology was hampered with, in varying definition and implementations (117). In 2015, an attempt was made in England, also adopted in Wales, to minimise this with the introduction of a nationwide alert algorithm following a patient safety alert (117, 157).

In 2018, Al-Jaghbeer et al in the USA published their findings following the implementation of their clinical decision support system (CCDS) for recognising AKI in 528,108 patients. This CCDS used the KDIGO criteria to identify AKI based on changes from the lowest SCr value of the last year. This study looked at the primary outcomes of length of stay and hospital mortality. Mean length of stay in AKI was reduced from 9.3 to 9 days following the alerts ($p<0.001$) and crude mortality was reduced from 10.2% to 9.4% (odds ratio, 0.91: [95% CI] 0.86 to 0.96). Importantly, this study suggested that passive AKI alerts can make a difference in 14 hospitals in the US, but is this the case in Wales within a different health care system?

Primary Care

Whilst AKI in secondary care and in intensive care has had an upsurge in attention, AKI in the community has had minimal consideration (189-191). It has been established that early treatment of AKI improves outcomes (158, 187) and that the majority of AKI begins in the community (152, 170, 192-194). There has also been minimal attention to what happens to patients following AKI, particularly in the context of follow up in the community. Given this, we need to improve our understanding AKI in the community, how it presents, what contact the patients have with the primary care team and likewise what happens after the AKI episode.

Community Acquired AKI

There is a consensus that a large proportion of AKI begins in the community although there is variation about the exact figures (189). This is mainly due to differences in the definition of community acquired AKI (CA-AKI) which varies from community-based blood tests, to tests 'on admission', to tests within 24 or 48 hours of admission. There are also variations based on the datasets studied, in that some will be hospital based cohorts (170, 194) where as others have complete pathology datasets (172, 190). Some UK studies, defining CA-AKI as on day of admission, found that it was the initial AKI in between 57.3 (194) to 60.9% (170) of AKI cases. In both these studies, the population was admitted patients only. In a population study by Sawhney et al in the Grampian region of Scotland, 38.9% of patients developed AKI within 24 hours of admission (172) or in the community. The Grampian study found that 16% of the AKI was acquired in the community in patients that were not admitted within 7 days of the AKI(172), therefore they would be missed by admission-based studies.

In Wales, Holmes et al found 49.3% of the AKI population had AKI on blood tests from primary care, A & E, the acute medical assessment units or in outpatients (153). The same group, using a slightly different definition of CA-AKI of an alert from an non-inpatient setting, looked in more detail at these patients with CA-AKI (190). They found that 46.8% of these patients had blood tests within 30 days prior to the AKI episode, 30.1% of which were from primary care and 24.1% were from inpatient locations (190). Using this same method, they looked specifically at the primary care SCr tests with AKI, comparing them to CA-AKI (195). They

found that 28.8% of CA-AKI was from alerts requested from primary care, with only 22.3% of these patients being admitted within 7 days of the AKI alert (195). Those patients who were admitted had a higher disease severity and mortality, but better renal outcomes (non-recovery: 18.1% vs 21.6% and reduced progression of existing CKD: 40.5% vs 58.3% in the hospitalised patients when compared to non-hospitalised patients respectively) (195). Just less than half (49.1%) of these patients with primary care identified AKI had a repeat SCr test within the next week (195). In Cornwall, Barton et al found that 44%, 60%, 74% and 87% of the primary care based AKI patients had repeat creatinine values at 7,14,28 and 90 days (196). They also observed that 0.4% of SCr tests requested by primary care had elevations in keeping with AKI (196).

If the definition of CA-AKI was extended to a test within the first 48 hours of an admission, then it makes up 67.3% of AKI as found in a cohort study by Wonnacott et al(152).

One reason that there may be such variation may be based on the baseline creatinine values. In some of the studies when there was no baseline value, estimates were based on Modified Diet in Renal Disease (MDRD) Glomerular Filtration Rate (GFR) of 75ml/min per 1.73m^2 where no previous values were available (170, 194) or the upper reference range of normal was used (152), whereas in others, if there were no previous tests then this would not be considered AKI (153, 172, 197). Schissler et al (192) in 2013 used ICD-9 coding to recognise hospital admissions with AKI, then used RIFLE criteria to identify the stages: using this method they found that 79.4% of the AKI were community acquired.

Patients with CA-AKI were generally found to have a lower short-term mortality (152, 153, 170, 172). In the Grampian study, the 30-day mortality was 24.2%, 20.2% and 2.6% in the hospital acquired, community acquired patients admitted within 7 days and the community acquired not admitted within 7 days groups respectively (172). Selby et al had similar results with an in-hospital mortality of 28.9% and 20.6% in HA-AKI and CA-AKI in their inpatient cohort (170). Holmes et al found a CA-AKI 90-day mortality of 22.6% (190), when this AKI defining test was requested from general practice this fell to 18.1% (195). When CA-AKI patients are compared to a non-AKI community SCr tested cohort, they appear to be on average, an older population (70.3 years (95% CI 68.23–72.4) vs 57.1 years (95%CI 54.7–59.8);

P < 0.001) (191), with a higher odds of 30-day mortality compared to non-AKI with an OR of 9.7, 42.9 and 237 in AKI1, AKI2 and AKI3 in non-hospitalised patients (197).

Although there is a lower mortality associated with CA-AKI, it is still significant, and given that a significant proportion of AKI begins in the community, it needs to remain a focus in the attempts to prevent and treat AKI.

Community Interventions

Compared to hospital and intensive care AKI, few studies have attempted to understand AKI in the community. Medications are a frequent cause of AKI (198), commonly in the elderly (199) and nursing home patients (200). Morris et al explored the implementation of 'sick day rules' informing patients to stop certain medications, which have been proposed as a potential method of minimising AKI (201, 202). The idea of sick day rules, in part stems from rules used in the management of diabetes (201, 203). The qualitative study looked at opinions from clinicians (doctors, nurses and pharmacists), they found that following initial enthusiasm, this weakened following difficulties in implementing (201). This was reproduced the following year (204). Since this, the 'Think Kidneys' group have reviewed their guidance and carried out a systematic review of 'sick day rules' in AKI (205, 206). This review found 6 studies, all of which were hospital based that looked at implementation of 'sick day rules' for angiotensin converting enzyme inhibitors (ACEi) or angiotensin receptor blocker (ARB) cessation in at risk patients. The review failed to find convincing evidence that 'sick day rules' improve outcomes in these patients in the hospital, mainly pre-operative studies (205). A study by Mansfield et al, found only a small increased risk of AKI in patients on ACEi/ARB, with a relative risk of 1.17 (95% CI 1.09 to 1.25) (121). There are concerns regarding the potential harm of stopping ACEi/ARB medications (206). An interim report from a group that introduced sick day rules in the Highlands, showed no change in admissions with heart failure, although this was an early report, so may well have been too soon to see an effect. The evidence for non-steroidal anti-inflammatory drug (NSAID) causality with regards to AKI is stronger (189) and the long-term absence is easier to debate. However, a major difficulty with AKI advice and NSAIDs, is that they can be purchased over the counter.

Electronic alerts in Wales, can be viewed by the requesting GP on the bloods reviewing system (varies by location), elsewhere efforts have been made to use other methods to alert primary

care of the AKI (207, 208). In this study carried out in London, the biochemistry laboratory staff phoned through AKI to primary care. 84% of GPs responding to a survey after implementation found this a "useful service that has altered practice" (207, 208). The outcome of these patients was not compared to pre-implementation, but they found that 48% of patients with alerts were admitted to hospital (208). 11% of patients had no action following the alert (208).

Are primary care clinicians informed about inpatient AKI?

After an episode of AKI we see an increased mortality beyond hospital discharge (118), with some studies reporting 1-year mortality at almost 50% (172, 209). What is not clear, is why patients die during this period (210), and how much of this is preventable. Simon Sawhney and the Grampian group looked at hospital readmissions; they found that in a cohort patients discharged following an episode of AKI, of those that were re-admitted (29%) in unscheduled care (emergency admissions) within 90-days, 26.1% were coded with acute pulmonary oedema(210). In Boston (USA) a study from 2015 by Koulouridis et al found that 18% of patients with AKI who were subsequently re-hospitalisations had a primary diagnosis of heart failure on their original admission (211). When the re-hospitalisation primary diagnosis codes were examined, 24% of these patients with a previous admission with AKI were coded for heart failure (211). Acute pulmonary oedema is caused by too much fluid in the lungs, often the result of fluid overload and/or heart failure. The condition can be caused by decompensated heart failure which can be caused by the cessation of heart failure medication (212), it can also be caused by acute (213) and chronic kidney disease (214). There is an emphasis to stop nephrotoxic medications before, during and after an episode of AKI (165, 176, 198), but many of these medications should be considered for restarting after recovery - i.e. diuretics, ACEi and ARBs (206). This area has not been widely studied. From clinical experience, the restarting of medications is often left to the junior ward staff or deferred to the general practitioners who are usually unable to review the clinical notes and are therefore somewhat blinded (215-217). The primary care team may also receive the discharge summaries too late to act as suggested in the content (215). In the UK, discharge summary completion rates are a marker of care quality and should be completed within 24 hours (218-220). The discharge summaries are often split into two sections, the medication changes (often done by pharmacists, doctors or nurse prescribers) and the clinical side containing a

minimum of primary diagnosis, and follow up arrangement (218, 219, 221). A major question with regards to primary care follow up of patients within hospital AKI is, are the primary care providers aware of the AKI? In an attempt to improve communication in discharge summaries to primary care the 'Commissioning for Quality and Innovation' (CQUIN) created a payment target necessitating the inclusion of the diagnosis and severity of AKI to be on the discharge summaries in England (222). Reschen and Vaux in Reading in the UK, found that only 22% of AKI admission discharge summaries had appropriate AKI information in their hospital (223). After they carried out a quality improvement project, they found that by the third quarter completion/compliance was up to 92% (223). In the US, a study investigating the quality of discharge summarise found that <50% of the discharge summaries in patients with AKI documented the condition (224).

AKI community follow up

Referral of patients with AKI to nephrology is infrequent and often related to severity of AKI (27, 151, 152). In a cohort of patients that died with AKI, 30.1% of the patients were referred or discussed with nephrology and for 20.3% of those not referred, it was felt they should have been (151). More recently, Wonnacott et al in East Wales found that 8.3% of their cohort were referred to nephrology, with a more patients with CA-AKI being referred, compared to HA-AKI (10.3% compared to 4.2% respectively, p=0.001) (152). In Scotland, a study by Khan et al from 1997 found that 22% of AKI (defined as a 'temporal' rise in creatinine ≥300µmol/L) patients were referred to nephrology; this increased to 34% if advanced cancer and the elderly (>80) were not included (27). In further analysis, 100% of those patients aged 0-19 were referred, compared to just 5% in those >80 (27).

Given the low frequency of referral to nephrology whilst a patient is an inpatient, it is understandable that most patients do not have nephrology follow up. The United States Renal Data System (USRDS) annual report from 2017 found that only 16% of patients with AKI (based on ICD-9 coding) in the Medicare service had nephrology follow up within 6 months in 2014 (225). This increased to 31% in the diabetic population with AKI. The report also found that the percentage of patients followed up with nephrology was decreasing year on year, but the authors suspect that this is related to 'code creep' resulting in the identification of less severe AKI, and therefore these patients are less likely to be referred (225). A previous

USRDS report from 2007 found that within 30 days of AKI, 74.5%, 11.9% and 29.5% of patients with AKI were seen by their primary physician, nephrologists and cardiologists respectively, in the 30 days following AKI (226, 227). Chawla et al argued, that when you compare this to myocardial infarctions the follow up is 76% versus 11.9% in AKI (227). The group in East Wales found a nephrology follow up of 8.1% after discharge (follow up to 14 months post discharge) with AKIN defined AKI (152). The lower rate here may be related to less severe AKI. This was similar to the findings of Siew et al (8.5%) (228). The lack of follow up is echoed by Kirwan et al who found that only 12% of patients with AKI in the intensive care unit (ICU) requiring renal replacement therapy (RRT) were followed up by nephrology upon discharge from hospital (229). In this cohort there was an increase for 49% of patients with baseline CKD to 70% 3 to 6 months after discharge with mean eGFR changing from 60 to 48ml/min/1.73m^2 respectively (229).

In 2013, Harel et al published the findings from their Ontario cohort, comparing those patients who survived AKI-D admissions with nephrology follow up within 90 days to those without, using a propensity score matching (230). This study found a lower mortality of 8.4 compared with 10.6 per 100-patient years (hazard ratio 0.76, 95% CI: 0.62–0.93) (230).

In primary care, Barton et al found that 51%, 72% and 77% of stage 1,2,3 AKI had repeat creatinine tests within 14 days of recognition (196). One might expect this to be the minimal testing/review following AKI, yet almost 50% of stage 1 and nearly a quarter of severe AKI (stage 3) were not receiving a repeat test (196). The author used the upper reference range where there was no previous creatinine. They queried if they identified more CKD with progression as a result, and not AKI, hence the failure of repeat tests in AKI 1. This may well be the case where there were baselines, as they used an increase of ≥26µmol/L without time restraints but it might not have been as much of a problem with the upper reference range patients, as you may expect people with CKD to have had a blood test in the last year.

Primary care follow up of AKI

AKI care needs to be individualised and this includes in primary care (189), nevertheless there are some simple recommendations for general practitioners following an episode of AKI. These include the avoidance of NSAIDS (155, 201, 231, 232), reviewing medications (155),

monitoring kidney function (155, 222, 233) and coding of AKI (222, 234). The handling of some cardiac medications (such as diuretics and angiotensin converting enzyme inhibitors is less clear, with an individualised approach needed (206).

Summary

AKI is a common condition that has existed as long as humans have. It has many potential causes and the heterogenous nature of this AKI is echoed by the heterogenous nature of its historical definitions. This has resulted in gaps in our knowledge of the epidemiology and management of this condition. Attempts to develop a consensus in the definition of AKI have led to a sharp increase in research. The knowledge of this syndrome is improving but care remains suboptimal. An attempt to address this was made using electronic AKI Alerts based on the KDIGO definition. These were created in the hope that they will improve recognition and management of this condition. We are starting to research these alerts, but our understanding of the effect of eAlerts on morbidity, mortality and recording of AKI (coding) remains incomplete. It is unknown whether alerts are implemented in a uniform manner and whether they behave the same across different sites. We do not know the extent of false positive alerts in patients undergoing chronic haemodialysis treatment. There are also large holes in our knowledge regarding the aftercare of patients following AKI. In particular, what happens in primary care following AKI? In Wales we are fortunate to have data of the AKI eAlert implementation in a large data repository that allows for anonymised research across primary, secondary and tertiary medical care. This study looks to address these aspects and understand if eAlerts are sent correctly, how they compare to hospital coding and what is their effect on mortality, need for dialysis and on primary care interactions?

Chapter 2 - Methodology and data quality check

Background

This research has been carried out within the Secure Anonymised Information Linkage (SAIL) databank at Swansea University. This is a large data safe haven which facilitates linkage of pseudo-anonymised health records. The pseudo-anonymisation is created by giving individuals an encrypted unique identifier which is called Anonymous Linking Field (ALF) within SAIL replacing a person's name and NHS number. This ALF encryption is unique to an individual, maintaining their anonymity and allows for data linkage across datasets from a variety of sources that are housed within the SAIL databank. SAIL also uses week of birth instead of date of births and lower layer super output area codes (LSOA) instead of addresses to minimise the risk of reidentifying people. Through these methods, patient level data can be used by a researcher without being easily able to identify the person. This section explains the datasets used for this research, the methods used to rigorously check the data quality and how improvements to the datasets were made.

Creation of an ALF

The ALF is created by the National Health Service Wales Informatics Service (NWIS). To do this, each dataset supplied to SAIL needs a demographic file to be sent to NWIS by the data provider. This may be the researcher if they have collected their own data outside SAIL, an NHS trust or even NWIS themselves if it is a dataset they house. This file is named 'File 1', and it requires a very specific structure because it is not reviewed by a human eye in NWIS. File 1 contains a linkage field that can join this file with the main body of the dataset which gets sent directly to SAIL. This linkage field is specific for that dataset and cannot be used to link other datasets, for example a specimen number in a blood test dataset. The file 1 also contains patient demographics including name, date of birth, gender, address and National Health Service (NHS) number. This ALF is created by a couple of methods; The main method is by using the patient's NHS number. Where this is missing, it can be created based on the patient's demographics and address (i.e. the combination of surname, forename, postcode, date of birth, gender). Weaker matches are also possible based on a combination of the above and where the forename does not match, using a forename lexicon (i.e. a known variant).

The ALF codes are then supplied to SAIL from NWIS in a demographic file for the individual dataset called 'File 3'. This File 3 also contains the patient's gender, week of birth which is taken from the date of birth and LSOA for each patient which is created from the person's address. This means that the area in which the patient lives can be identified but not the address. The ALF code supplied by NWIS is then encrypted by the SAIL team into a unique alphanumerical code that is distinct for the research proposal (this prevents cross-linking between projects that have not received governance approval for a dataset). This ALF identifies the same person within the various datasets. Where ALF identifiers are not available, cross-linking between datasets such as pathology and primary care is not feasible, therefore an important data quality check for each dataset is the number of entries without corresponding ALF.

Below is a diagram (Figure 14) which display how the demographic (often called the ALF file in SAIL) is created.

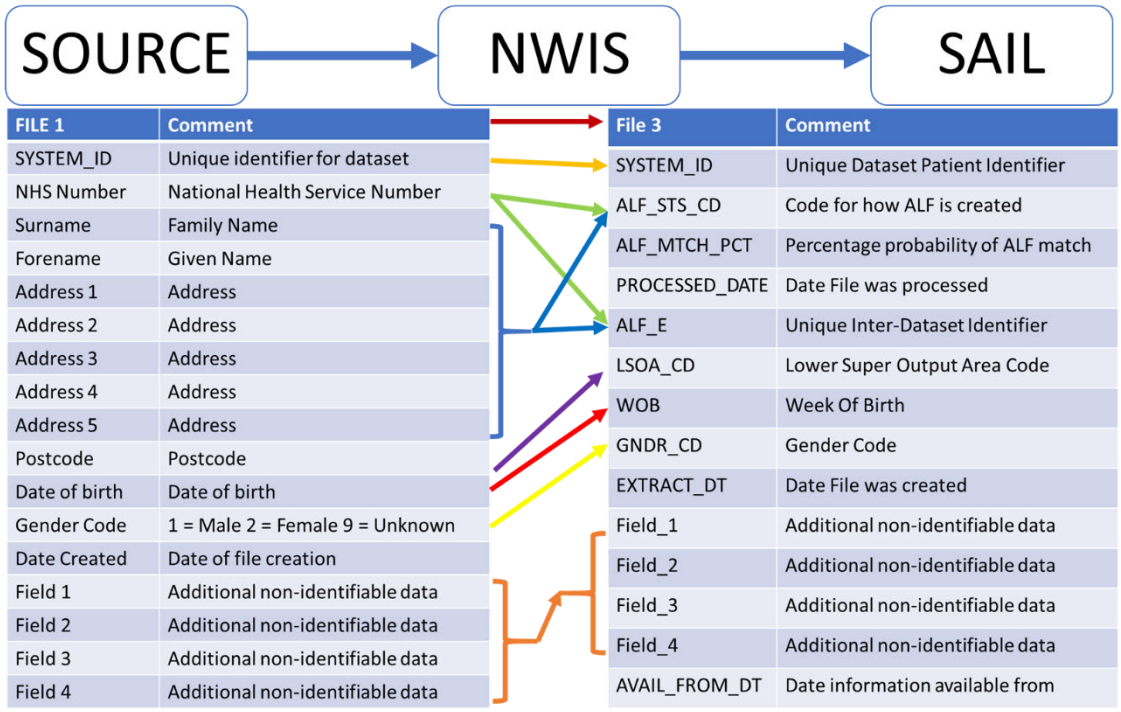


Figure 14 - File 1 to File 3 (Demographics)

In figure 14 we see how the demographic file from a database from a source outside SAIL, such as the from an NHS, is sent to SAIL via NWIS and converted into a pseudoanonymised file 3. Here we can see NHS numbers becoming ALF numbers, Addresses becoming LSOAs and Date of births becoming week of births.

Linking

As mentioned, this file 3 is crucial for cross linking datasets within SAIL. It is also needed to supply demographic information for the datasets. The actual results or key information of a dataset are not contained within this file 3. This is another security layer added by the SAIL team to prevent the data from being misused. The key information of a dataset is sent directly to SAIL in a file referred to as 'File 2'. This file 2 may in fact be several tables, all linked by this unique linkage field for that dataset shown in the diagram above as the SYSTEM_ID. This file 2 should not contain any patient identifiable information. If there is the possibility that it does, that field will get suppressed by the SAIL team, so the researcher cannot see it. An example of this is a column which contains 'free text', as this may contain a patient's name.

An example of how the different datasets are linked is shown below in Figure 15 - Linking between datasets;

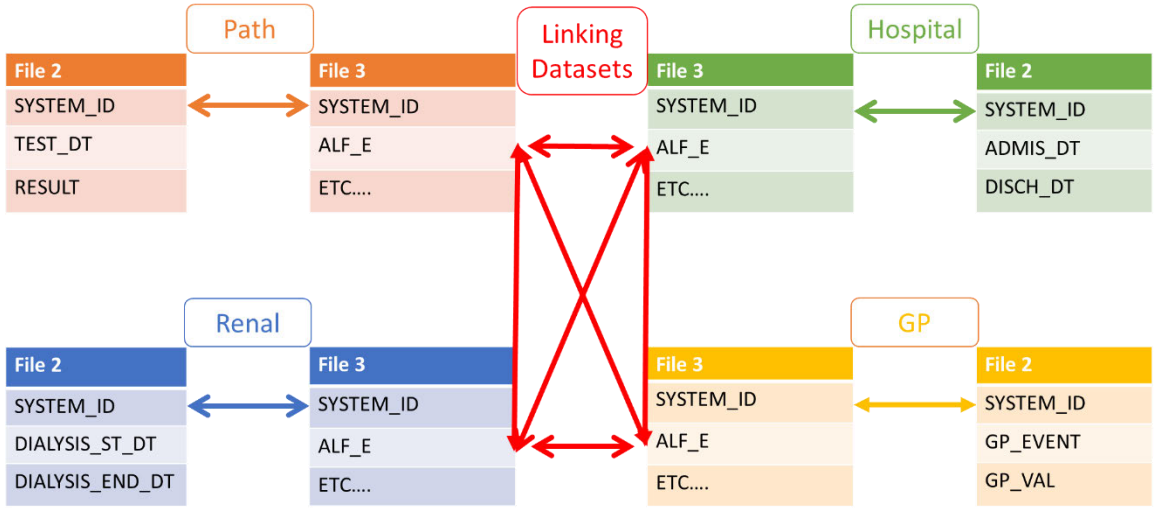


Figure 15 - Linking between datasets in SAIL

Within SAIL there are large datasets, some containing billions of rows of information. In order to analyse and link the different data within it, a database management system (DBMS) is needed. The DBMS used within SAIL is International Business Machines' database 2 (IBM DB2). The syntax language used in this is Structured Query Language (SQL). For me to gain confidence in the datasets used, and to understand the structure of the data, I (TMS) have learned how to use this SQL code. I have explored each of the datasets that I have access to. Some of these datasets are well used and have publications(235-243), others have not been extensively used such as the Swansea and Bridgend pathology data. We have also imported the data from the renal electronic patient record in the All Wales Renal Dataset (AWRD).

Exploring the Data

As mentioned, SAIL data are housed in an IBM DB2 database management system. In order to explore the data, I developed a knowledge of structured query language (SQL). This was developed using books, online practice resources and observing the analyst (Gareth Davies) and adapting his code. As a result of this I can confidently join datasets and run a number of queries. All the analysis in this methodology section was performed by myself, examples of the code appear in the appendix (Example of my SQL coding).

Ethics

Ethical approval has been granted through the independent governance review panel (IGRP) of SAIL project 505. This panel contains members of the British Medical Association (BMA), National Research Ethics Service (NRES), public health Wales, NHS Wales informatics service (NWIS) and consumer panel.

Statistics

All statistics are carried out by myself (TMS) using IBM SPSS Statistics for Windows, version 26 (IBM Corp., Armonk, N.Y., USA) or Microsoft Excel.

The Datasets

The SAIL gateway houses hundreds of tables from different datasets. Each project within SAIL has its own schema and within this there are the datasets agreed as per the IGRP. Over the time of the study, there are several updates of these datasets. Each time the dataset was updated I carried out several checks to validate the datasets. The datasets used with in the project include;

Datasets	Table name
Bridgend Pathology	PABR
Swansea Pathology	PAMO
All Wales Pathology from Welsh Results report service (WRRS)	PATH
Annual District Death Extract	ADDE_DEATH
Patient Episode Database for Wales	PEDW
Primary Care GP dataset	WLGP
Welsh Demographic Service	WDSD
Critical care dataset	CCDS
Outpatient dataset	OPD
All Wales Renal Dataset	AWRD

Table 13 - SAIL tables used

These datasets are used to create a cohort for the subsequent study investigating those with Acute Kidney Injury (AKI), those who have a serum creatinine test (at risk of AKI) and those without AKI (chronic dialysis) dataset. These datasets are linked by the patients ALF and are described in more detail in this chapter. The key information they contain is visualised in this figure;

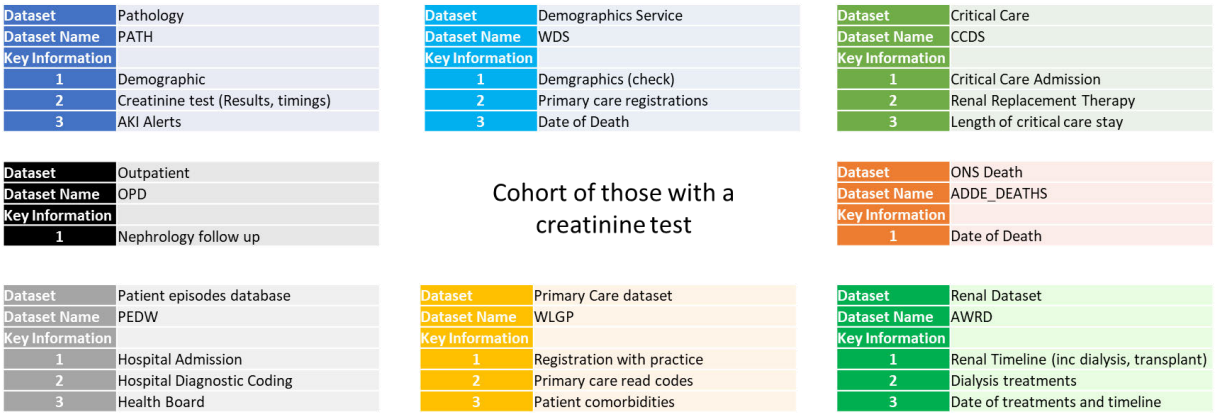


Figure 16 - Dataset Diagram of Key components

ONS = Office of national statistics

Pathology – WRRS, PAMO & PABR

To create a cohort of patients at risk of Acute Kidney Injury (AKI) we need to access the pathology data. These pathology data are housed in SAIL in three datasets and each of these have a different format. These three datasets come from the laboratory data, and cover primary and secondary NHS care. To reproduce and run a serum creatinine-based AKI algorithm on patients within these datasets, the format must be standardised. The patients

may also cross datasets, so the unique ALF is critical in identifying these patients and avoid duplications. The main dataset used for this study was the Welsh pathology dataset (PATH) which is taken from the Welsh Result Reports System (WRRS) and it covers the whole of Wales for varying time periods. In SAIL this table has been called "PATH". The smaller datasets from Bridgend (PABR) and Swansea (PAMO) have been available within SAIL for longer, therefore I have been able to explore these, to validate the PATH dataset and test the project plans prior to the arrival of WRRS within SAIL. These datasets have had minimal or no use by other researchers, therefore I have explored them in greater detail. For the basis of this study, these two datasets (PABR and PAMO) allow me to validate the PATH dataset and test the AKI algorithm, as there was an overlap period of the two datasets. The table (Table 14 - Pathology datasets by availability) below shows the final versions (after corrections described later in this section);

Pathology Data – Health Board Abertawe Bro Morgannwg University Health Board (ABMUHB)	**First reliable creatinine data**	**Last reliable creatinine data**	**Year of upload**
PABR 1st Upload	Jan-05	Jun-08	2008
PABR 2nd Upload	Jun-08	Apr-10	2017
PAMO 1st Upload	Jul-02	Sep-09	2009
PAMO 2nd Upload	Sep-09	Mar-15	2016
PATH (from WRRS)	**Varies by health board**		2019
***PATH - For Swansea and Bridgend**	Jul-11	Nov-19	2019

Table 14 - Pathology datasets by availability for Abertawe Bro Morgannwg University Health Board

PABR is Pathology from Bridgend and PAMO is Pathology from Morriston (in Swansea), together this makes up the region of Abertawe Bro Morgannwg University Health Board (ABMUHB). The 2nd PAMO upload includes Bridgend data from April 2010 to March 2015. PATH dataset is All Wales, and was implemented at different stages, for comparison, the Swansea data in PATH is shown here.

Bridgend pathology - PABR

Background

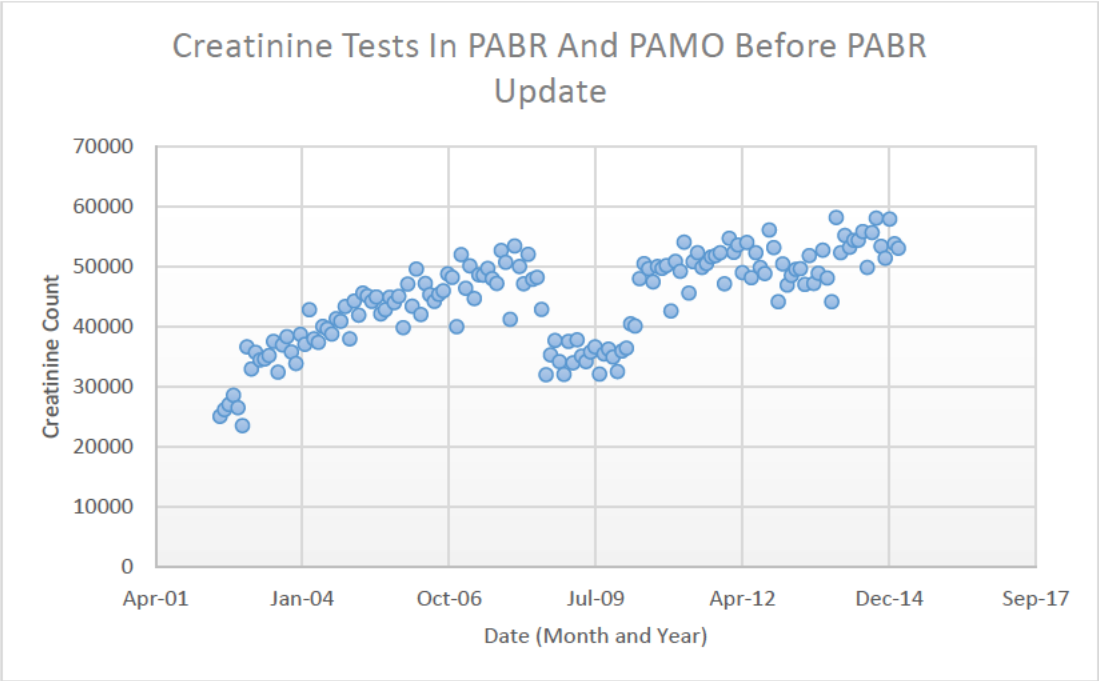
The Bridgend dataset is called 'PABR' which was originally uploaded to SAIL in 2008. The acronym stands for Pathology Bridgend. This contains data from the Bridgend pathology laboratory Information management system (LIMS) called TelePath© system. Prior to this

project, there was no evidence of this dataset being successfully used within SAIL. In 2010 the TelePath© system in Bridgend pathology was merged with the Swansea region's Masterlab© system. Therefore, the Bridgend data was only separate up until this point in 2010. A second update of the TelePath© data in SAIL was performed in 2017 following the identification of missing data. This data contains all creatinine tests, both from primary and secondary care, for the Bridgend region. It was used to test the AKI algorithm described in chapter 3 (Chapter 3 – The Creation of AKI Cohort) prior to the introduction of the all Wales pathology dataset and to validate the PATH (All Wales – PATH from WRRS) dataset.

Validation

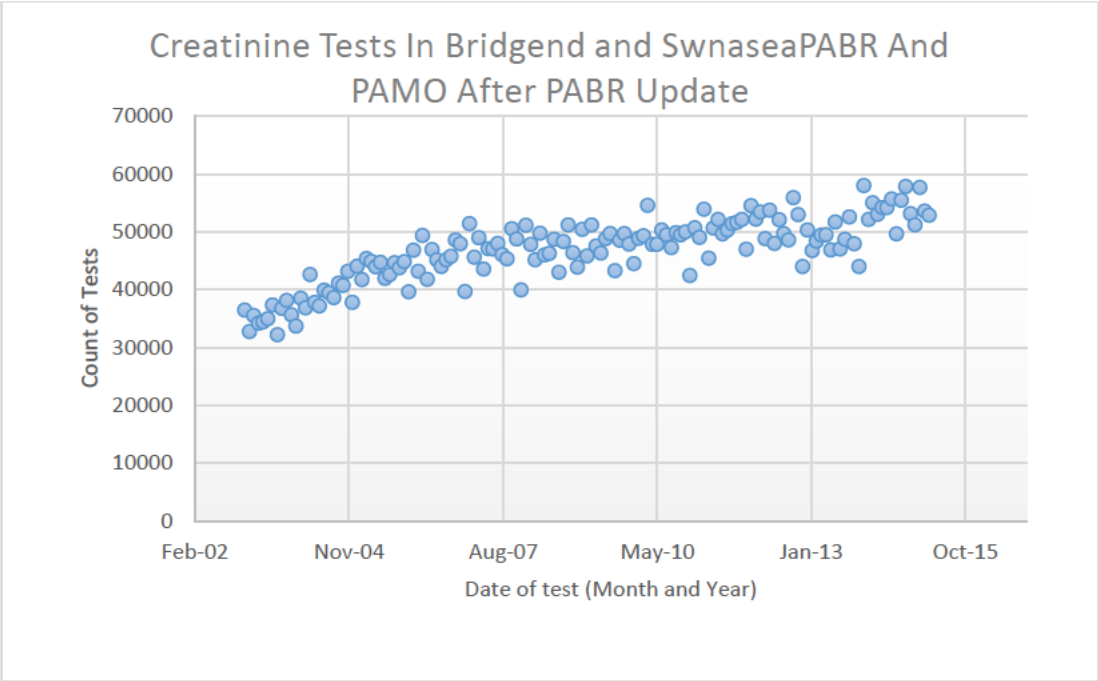
As mentioned, the original Bridgend pathology data was imported into SAIL in 2008 and it contains all primary and secondary care creatinine tests in the region reliably from January 2005 and June 2008. There are creatinine values from January 2003 to June 2008, but the tests prior to January 2005 appear significantly fewer in number and therefore that period cannot be deemed to be reliable. In this dataset there are 649,895 individual creatinine values. There are 11 different tables within the schema, although not all of them are required for this analysis and some simply describe tests sets.

Since the TelePath© system was changed to the Swansea Masterlab© system, an upload of this system in 2017 covers both Swansea and Bridgend under the PAMO view. It was hoped that this data would be complete for Swansea as well as Bridgend, however it was quickly evident that there was missing data as portrayed in the graph below where there was an obvious drop between 2008 and 2010;



Graph 1 - Combination of PABR (Bridgend pathology) and PAMO (Swansea pathology) before correction updated uploads

As mention, the test numbers before 2005 are lower, likely the result of missing data, and therefore not reliable. There was a gradual increase in the number of creatinine tests over time, this was something that has been observed elsewhere (244) and is likely to have multiple reasons for this increase, including ageing and growing population, increasing comorbidity burden, introduction of quality and outcome framework in primary care and also may reflect concern regarding the medicolegal consequences of undertesting (244). The large gap seen between 2008 and 2010 was explained by missing Bridgend blood tests between the initial upload from TelePath© in July 2008 and the merger with Masterlab© in April 2010. As a result of this, a further upload of the TelePath© data for this period was arranged. This update had 402,220 creatinine values in it and the combination of these two datasets resulted in a fix of this drop off.



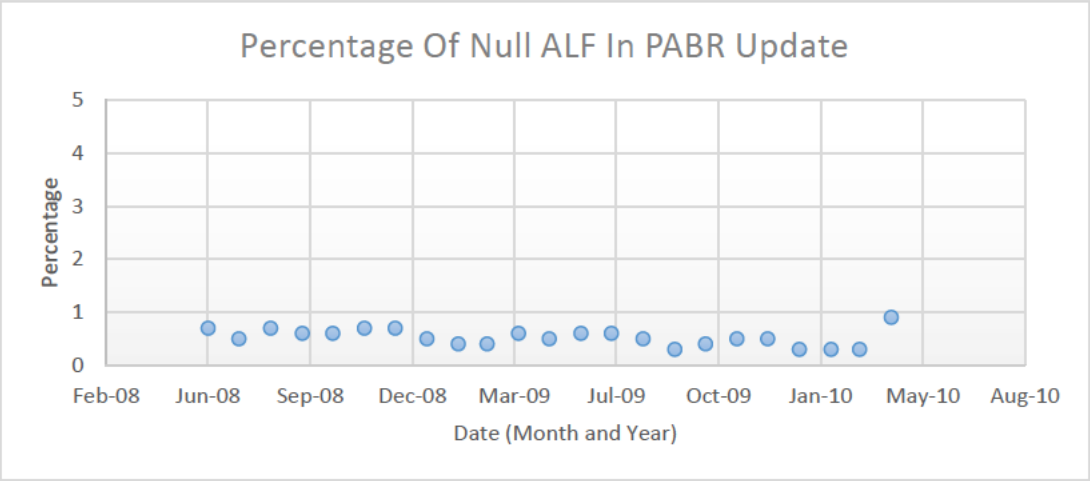
Graph 2 - Combination of PABR and PAMO after update

In total there are 32,033,283 test results in the two Bridgend datasets and just under a million of these are serum creatinine tests. Most of these creatinine tests have a corresponding ALF and so they are linkable with other datasets. There are some overlaps and therefore duplication in the two sources which required correction. The table below shows a breakdown of the uploads;

PABR - Creatinine Tests	**Number**	**%**
Total creatinine Tests	1,090,136	-
Original PABR creatinine tests	687,916	63.1
Updated PABR creatinine total tests	402,220	36.9
Distinct Creatinine Tests	**946,369**	**100**
Individuals with Creatinine Tests	**119,720**	
Distinct Rows – Missing ALF	10,002	1.1
Original Missing ALF	8,444	1.2
Update Missing ALF	2,024	0.5
Missing 'Medical specialty'	37,978	3.5
Creatinine unusable	10,287	1.1
Missing LSOA	18,676	1.9
Welsh LSOA	926,493	97.9
English LSOA	2,329	0.2
Scottish LSOA	38	0.0
Week of Birth (WOB) missing	0	0
Gender unknown	3972	0.4

Table 15 - Bridgend pathology validation

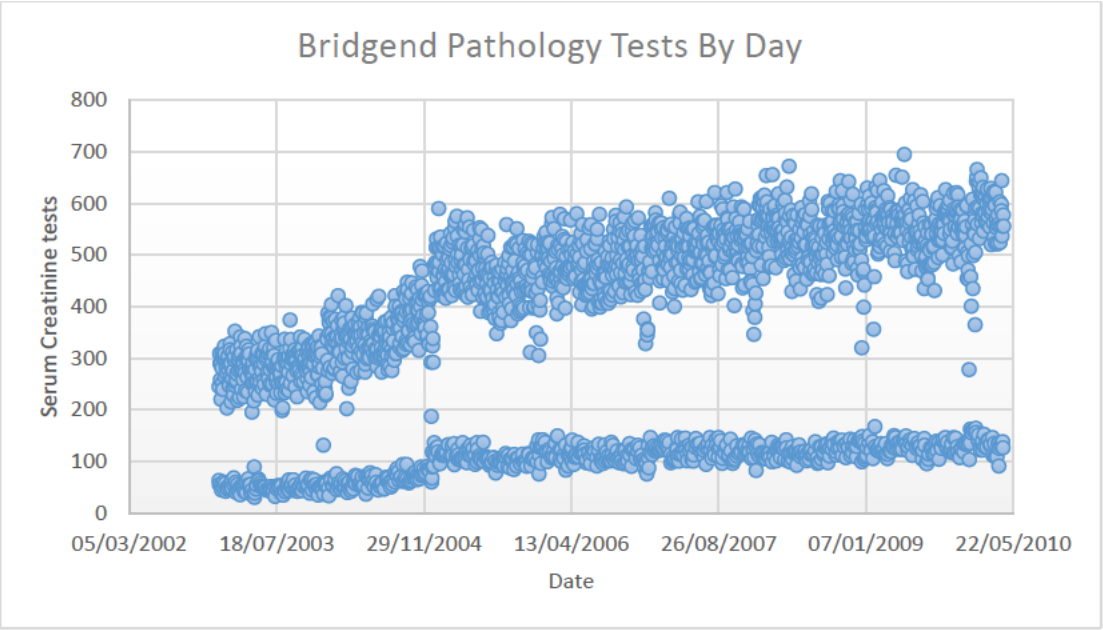
When we look at the percentage of missing ALF (null ALF) by month and year, it was clear that the quality of the demographic data are very good, meaning that over 99% of the results can be potentially linked with other datasets, as shown in the graph below;



Graph 3 - Bridgend Pathology missing linkage ALF

There are many reasons that a test may be missing an ALF, but given that these tests will be missing an NHS number, the likely reason is that the patient was unable to give an NHS number or demographic details at the time of the test, such as an unconscious, unaccompanied patients or patients not registered in the UK.

The mean serum creatinine in this dataset was 93.8µmol/L with a median of 80µmol/L.
To be extra vigilant with the datasets because of this, I looked at the number of creatinine tests by day as shown in the graph below;



Graph 4 - Bridgend pathology tests by day

From this graph we can see a gradual increase in the number of tests over time which was also observed in the Swansea data. There are two level of tests seen in this graph, this was weekday (upper tier) and weekend (lower tier) tests, with the ones in between the result of bank holidays. This was explained by only urgent tests being performed on the weekends and bank holidays, whereas routine tests are also performed during weekdays.

The original Bridgend data lacked test location coding, however it did contain a code for the speciality requesting the test. This allows for distinction between the requesting of tests by primary and secondary care but does not tell us if a test was taken as an inpatient or outpatient. In working with the pathology information technology team in Bridgend, the most recent Bridgend upload was able to contain test location information.

Columns of interest

The information from this dataset was joined as shown in the diagram below, the ALF_PE allows linkage across other datasets;

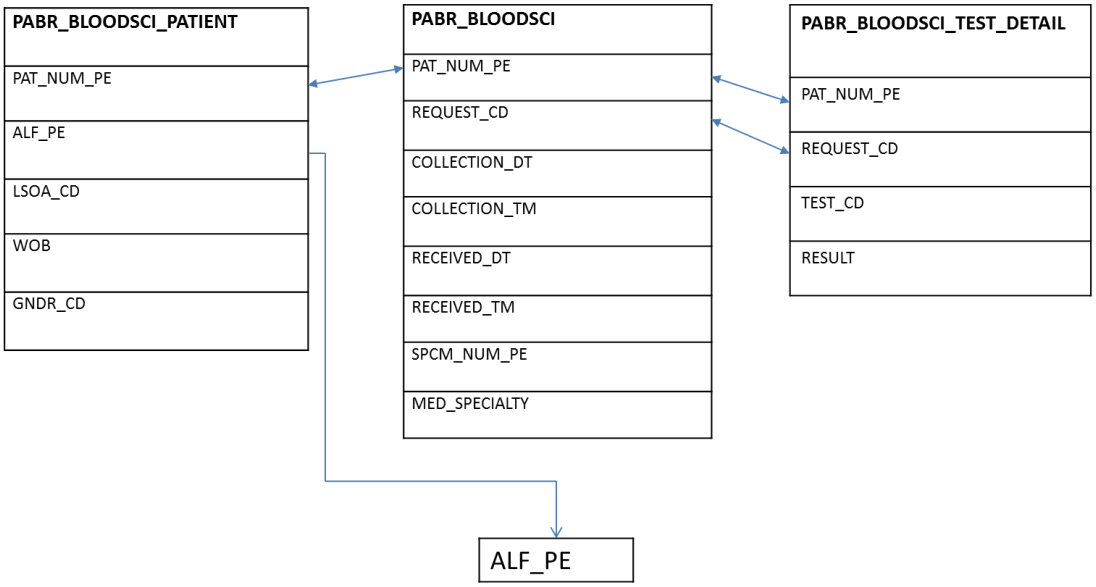


Figure 17 - Bridgend pathology linkage

The individual columns and their explanations for both PABR uploads are included in the Appendix - PABR – Bridgend Pathology on page 303.

Swansea pathology - PAMO

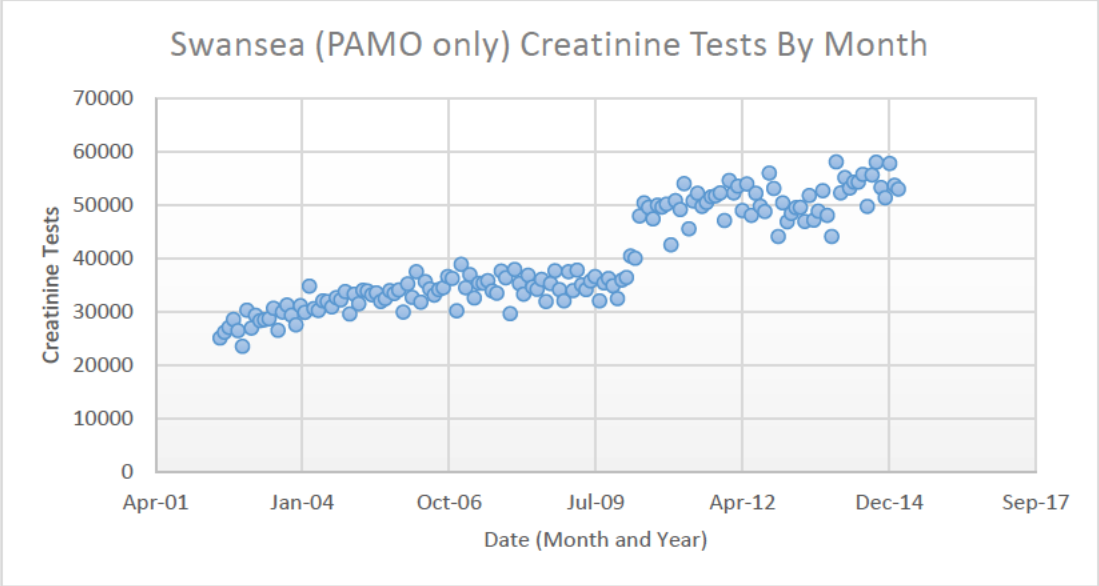
Background

The second dataset for blood tests from primary and secondary care is the Swansea based system from Masterlab© records. The PAMO abbreviation stands for Pathology Morriston with Morriston Hospital being the large hospital in Swansea. This originally provided complete data from July 2002 originally until September 2009, but following an update this has been extended to March 2015. This was the point when the system changed to an all Wales laboratory management system and becomes WRRS (in the PATH dataset).

Validation

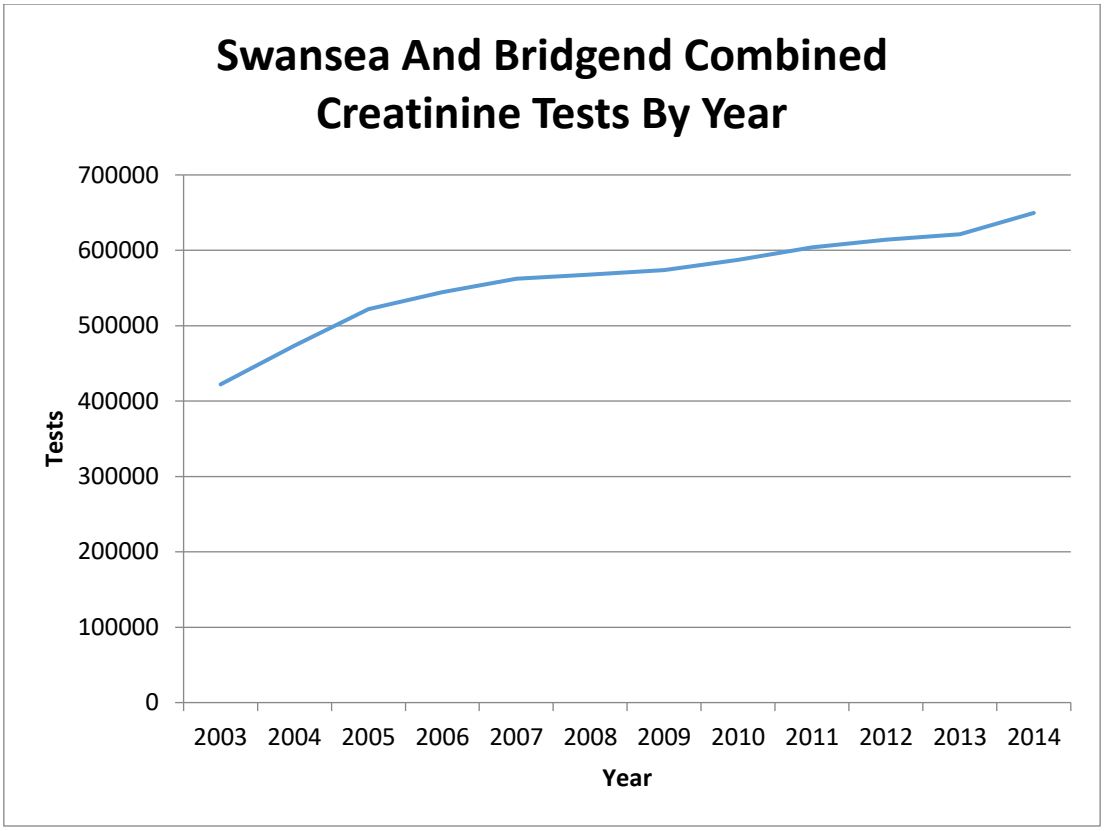
This dataset has also not been widely used so it requires the same vigilance given to the Bridgend pathology data. A previous SAIL project attempted to use this Swansea (PAMO) pathology data, which was the initial 2009 upload, but the researchers were unable to find the results. We discovered that this was a consequence of results containing free text which were then suppressed by the SAIL senior analyst team for fear of the risk of containing patient identifiable information (such as patient names). This was reviewed and the results were unsuppressed (no patients names are viewable). Once the results were released, initial testing of this first PAMO dataset by examining the number of tests by month suggested that the quality of the data was good. To complete the data however we needed an update of the pathology data to cover until the introduction of the all Wales LIMS in March 2015 which was used for the WRRS (PATH) dataset. This proved to be more difficult than expected as some of the expertise from the source (Swansea IT pathology team) no longer worked within the department. The result was an upload which when it was analysed had some puzzling findings. Even though the number of tests by month and year seemed to be gradually increasing (as expected) it was clear that there were many orphan rows and when there was an attempt at joining tables in PAMO, there seem to be duplicate system numbers (i.e. an encrypted blood test number) for patients. I also found that when we joined this table with other datasets such as the Welsh Demographic Service (WDS) dataset we got different week of births and demographic details in comparison to the pathology data. There was a key problem in the creation of the ALFs and the reason for this was shown by the fact that there were no over 85 year olds in the dataset. It became apparent that the date of births for the

patients were supplied in a two digit year format ('YY') not the standard four digit format ('YYYY'). As a result of this incorrect assumptions of century of birth were made. This resulted in the incorrect assignment of ALFs to patients without NHS numbers. This was a critical flaw in this upload and as a result we requested a re-upload in the correct format. Initially this re-send appeared to be successful, as shown in this graph;



Graph 5 - Swansea dataset (second update)

There was a clear jump in this table, but this was explained by the merge of the Swansea and Bridgend system in 2010 as explained previously. When Bridgend and Swansea blood tests results were combined we get this picture;

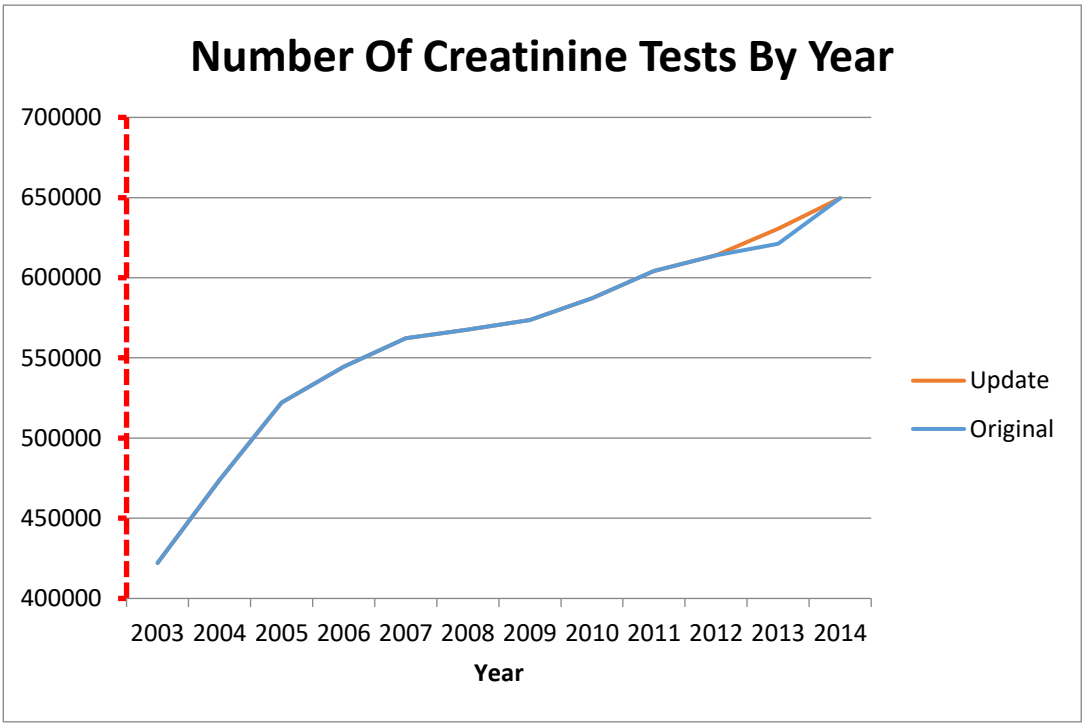


Graph 6 - Swansea and Bridgend creatinine tests following second update

Initially this appeared to be reassuring, however on closer inspection, there appeared to be a drop off in the number of tests in 2013. This change was subtle, particularly as there was no clear large drop for a single month and the drop in data was spread across the entire year. To check this, I contacted the information technology manager in the pathology department in Abertawe Bro Morgannwg University Health Board (Phil Morris). He was able to run the same queries in Masterlab (the source of the data) so we could compare with SAIL. He found 631809 creatinine tests in Masterlab and we had 584,373 for 2013 in SAIL, therefore Phil Morris and myself re-uploaded the data. This corrected the deficit, although after I checked the data

there was a further problem with linking initially (due to a data handling problem) which was promptly corrected.

After thorough testing the data for 2013 looks in keeping with the increasing numbers of creatinine tests per year, as shown in the graph below; note the Y axis does not start at zero.



Graph 7 - Swansea and Bridgend comparison of 2nd (original) and 3rd update.

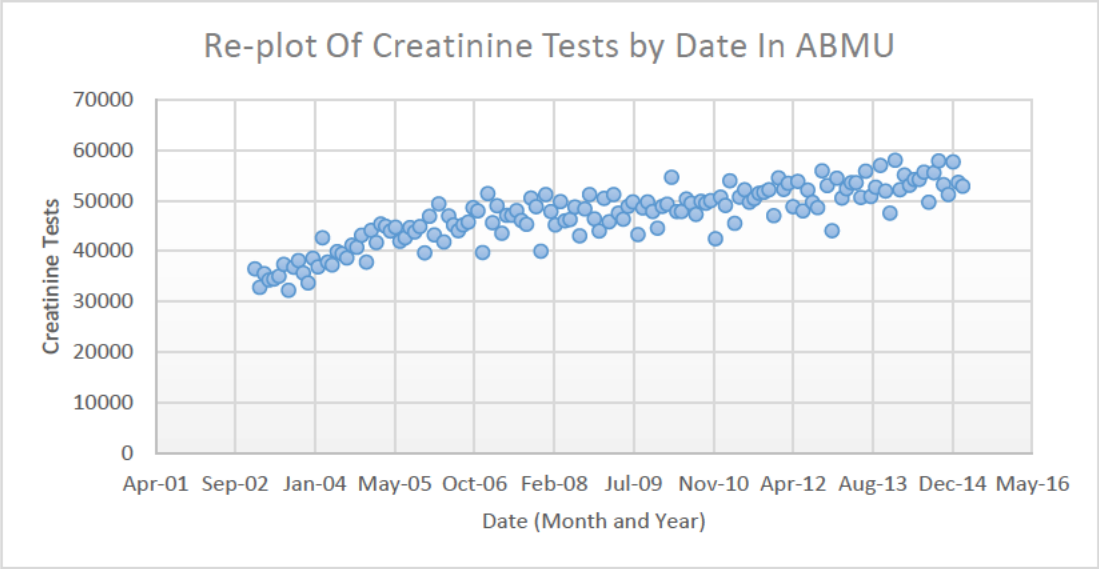
Using the combined Swansea PAMO pathology results, there were 434,353,031 blood tests results. A breakdown of the rows containing SCr values are displayed below;

PAMO - Creatinine Tests	Number	%
Total creatinine Tests	6,002,775	-
Distinct Creatinine Tests	5,994,914	100
Individuals with Creatinine Tests	556,596	
Null ALF	46,742	0.77
Date missing	0	0
Creatinine unusable (Text)	51,844	0.86
Missing LSOA	82,655	1.4
Welsh LSOA	5,886,718	98.2
English LSOA	25,009	0.4
Scottish LSOA	532	0
WOB missing	0	0
Gender unknown	4341	0.1

Table 16 - Swansea pathology validation

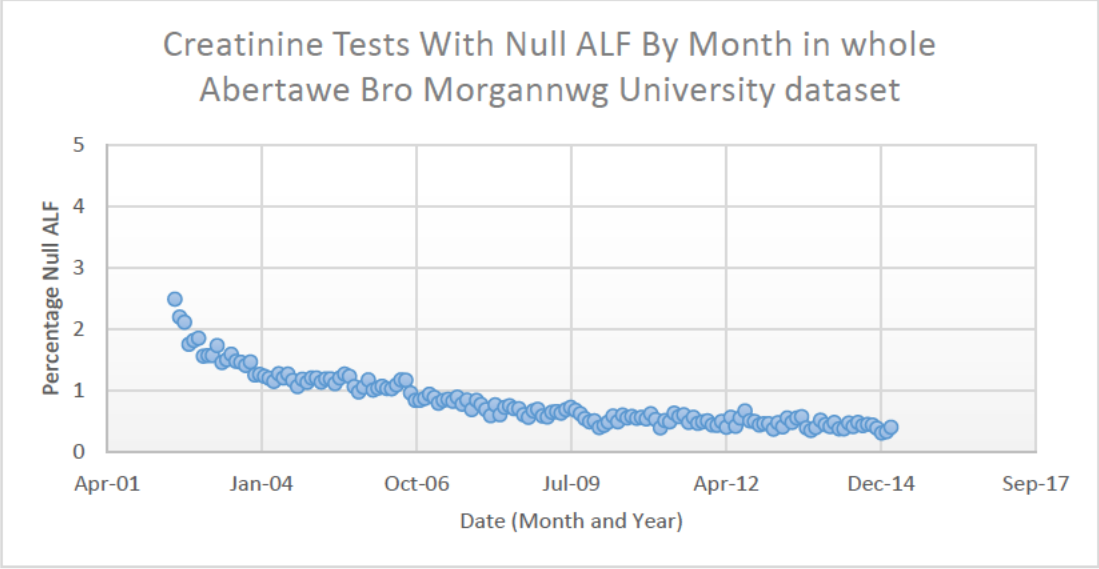
The Swansea PAMO results dependably span July 2002 to March 2015. There are some results before this period, but the numbers are very small and therefore cannot be deemed to be reliable. Another problem encountered with PAMO update was that all genders where "8" meaning unknown, as such we gathered gender data from the Welsh Demographics Service (WDS) dataset.

Overall, the completeness of the combined pathology data for the region was very good.



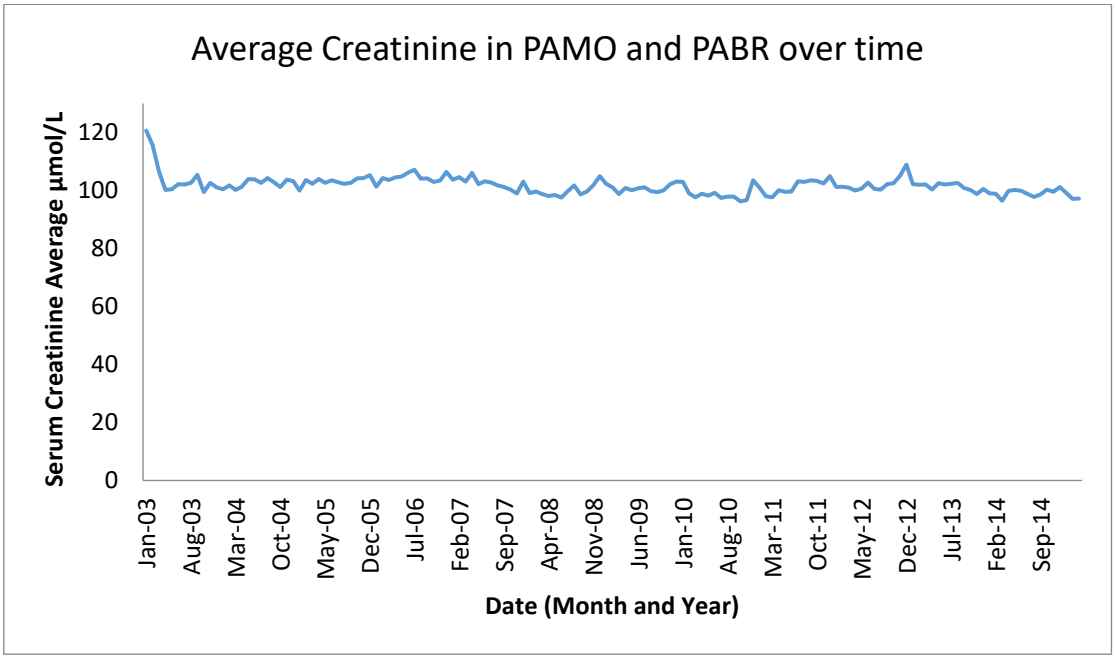
Graph 8 - Creatinine tests by month in Swansea and Bridgend (3rd update)

In a similar finding to that of the PABR dataset, the percentage of creatinine tests without an ALF decreases with time, as shown below;



Graph 9 - Swansea and Bridgend Pathology missing linkage ALF

Using a combination of PAMO and PABR dataset we can see that the average (mean) creatinine value has been stable over time;



Graph 10 - Average creatinine value in PABR and PAMO over time

Columns of interest

The diagram below shows the column headings and different tables within this dataset, as well as the how they can be linked;

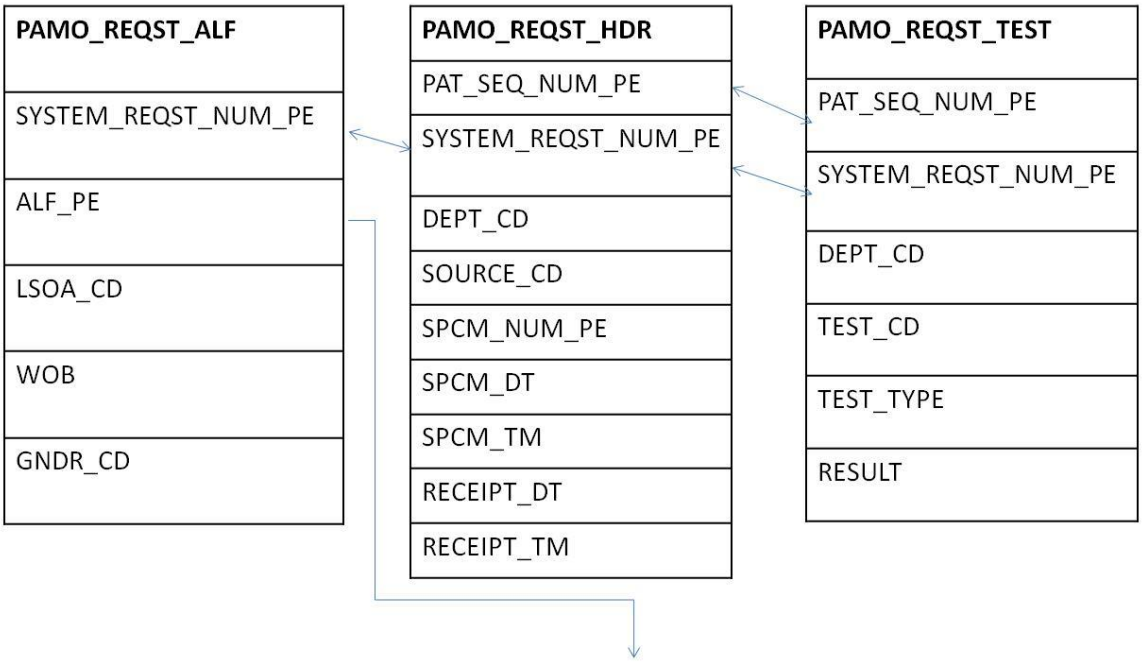


Figure 18 - Swansea (PAMO) linkage

The individual columns and their explanations are included in the Appendix - PAMO – Morriston Pathology on page 305.

All Wales – PATH from WRRS

Background

An all Wales laboratory information management system (LIMS) was introduced in a staggered approach across the Welsh health boards. At the same time as the introduction of this LIMS the electronic AKI alerts were introduced. The timing of the introduction across all the Welsh health boards is outlined below;

Welsh Health boards	Date of LIMS adoption
Abertawe Bro Morgannwg UHB	Mar-15
Aneurin Bevan UHB	Mar-14
Betsi Cadwaladr UHB	Sep-14
Cardiff and Vale UHB	Nov-14
Cwm Taf UHB	Mar-14
Hywel Dda UHB	Mar-14
Powys Teaching HB	Oct-14
Velindre NHS Trust	Nov-14

Table 17 - Introduction of the all Wales LIMS timeline

*UHB = University Health Boards

This LIMS provides data to a Welsh Results Reports Service (WRRS) and it was this database that was introduced into SAIL in September 2018 as PATH. The data covers varying periods in different health boards and covers all primary and secondary care tests processed in Wales in these periods. The table below shows the time periods that should be covered according to the Welsh Clinical Portal (WCP), a system used by clinicians across Wales to review results and documents which also uses WRRS.

Welsh Health boards	Biochemistry available from
Aneurin Bevan University (ABUHB)	Oct-16
Abertawe Bro Morgannwg University (ABMUHB)	Jul-11
Betsi Cadwaladr University (Central) (BCUHB)	Feb-08
Betsi Cadwaladr University (East) (BCUHB)	Dec-11
Betsi Cadwaladr University (West) (BCUHB)	Apr-08
Cardiff and the Vale University (CVUHB)	Jan-14
Cwm Taf (North) (CTUHB)	Nov-05
Cwm Taf (South) (CTUHB)	Nov-05
Hywel Dda (HDUHB)	Oct-02
Velindre (VEL)	Dec-14

Table 18 - Timeline of first LIMS data by health board (old names and sub-regions)

*UHB = University Health Boards

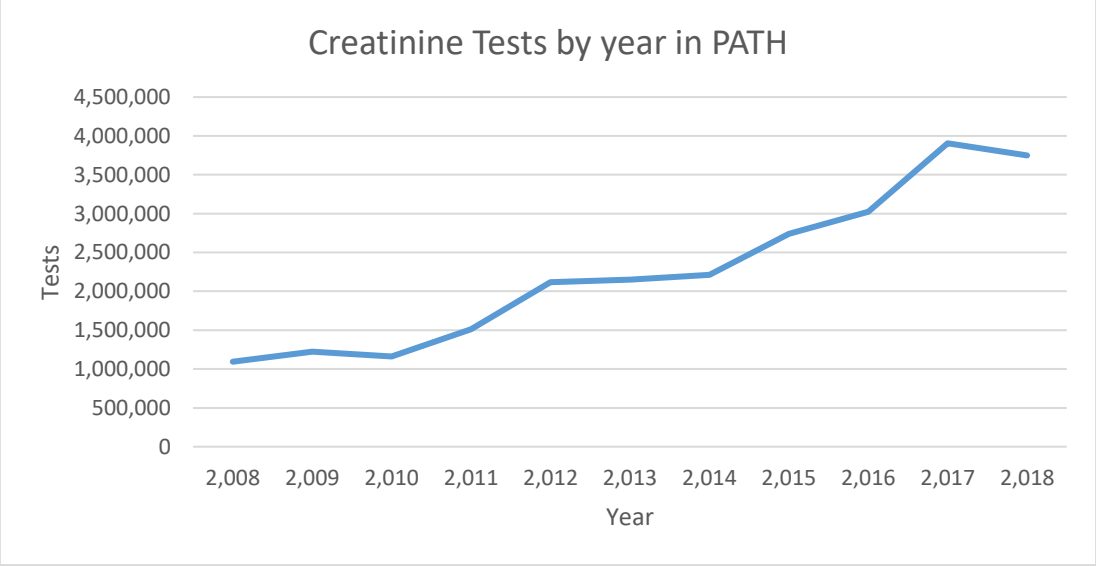
Validation

There are 788,974,310 rows of data in the PATH dataset. Careful handling of the data are required to avoid over burdening the computer processing and to avoid duplications of the results as there are some duplicate records in the dataset. This was particularly the case in ABMUHB where there are 1,063,208 creatinine results recorded in the dataset for 2017 but this number drops to 697,420 when distinct rows are used.

PATH - Creatinine Tests	**Number**	**%**
Total creatinine Tests	27,978,861	-
Distinct Creatinine Tests	**23,539,458**	**100**
Individuals with Creatinine Tests	**2,375,181**	
Null ALF	216,330	0.9
Date missing	0	0
Creatinine unusable (Text)	319,679	1.4
Missing LSOA	648,533	2.8
Welsh LSOA	22,692,271	96.4
English LSOA	21,257	0.1
Scottish LSOA	972	0
WOB missing	0	0
Gender unknown	49,125	0.2

Table 19 - All Wales pathology validation (WRRS)

The graph below shows the increasing number of creatinine tests available as the number of health boards providing data to the WRRS increases;



Graph 11 - All Wales pathology test by year

Columns of interest

The PATH table is presented in SAIL in one view which means that all the data are stored in one, albeit very large, table. The individual columns and what they mean are shown in the Appendix on page 306.

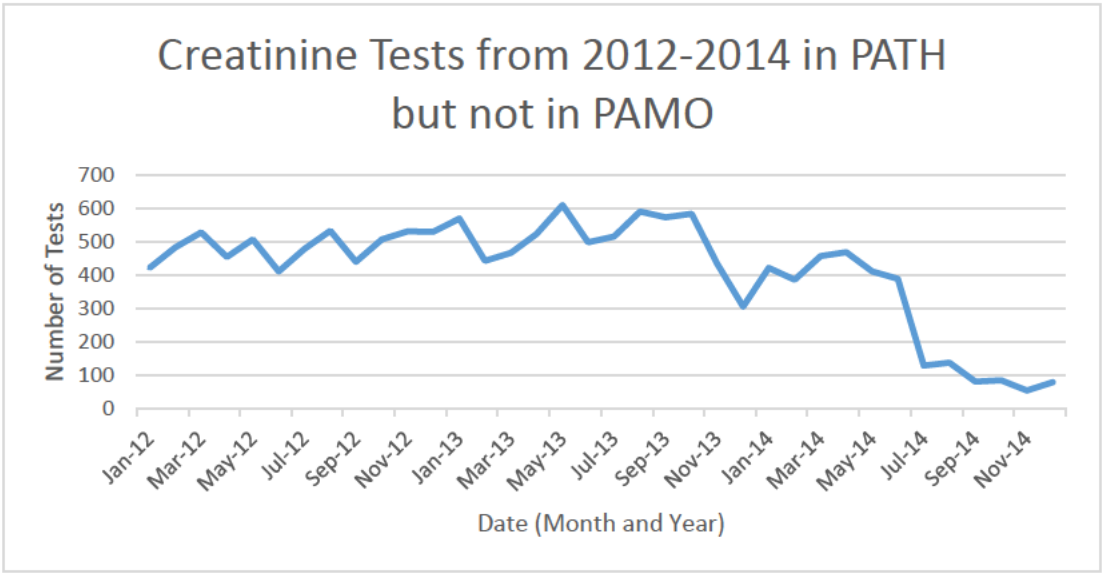
Cross check with PAMO/PABR

To validate the PATH pathology results I joined the PATH creatinine results with the PAMO dataset in SAIL using tests from between 2012 and 2014. By doing a full join I was able to see where gaps appear. Whether they are on the PATH side or the PAMO side. Over the 3 years there were 15,013 creatinine results in the PAMO dataset that were not in the PATH dataset and 5,918 results in the PATH dataset that were not in the PAMO data. These gaps were over three years are shown in the table below;

	Both by Year	Not in PATH	Not In PAMO
2012	601,158	5,814	2,267
2013	617,598	6,105	1,661
2014	640,172	3,094	1,990

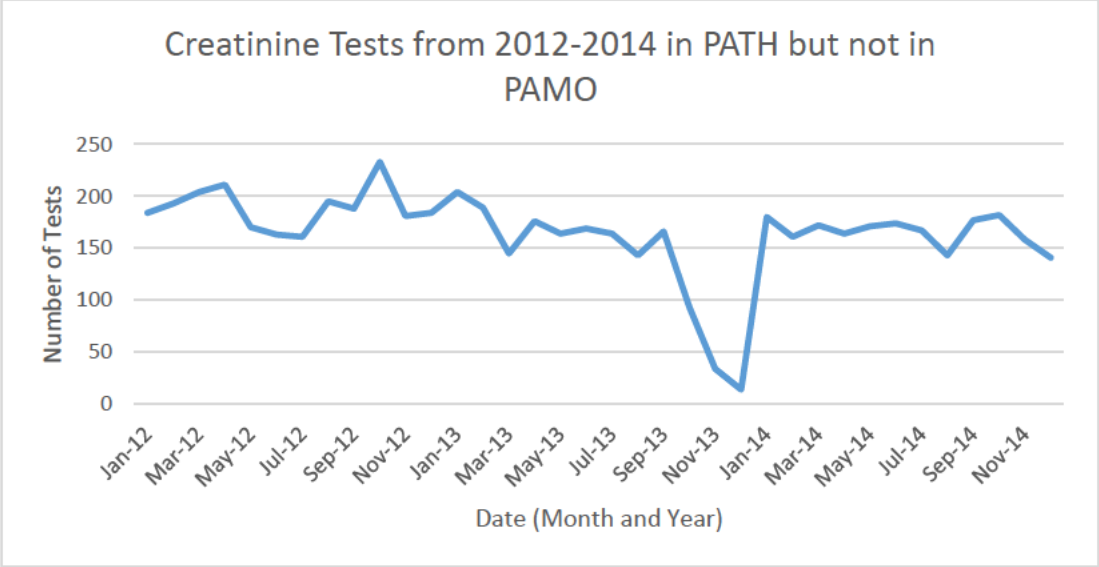
Table 20 - Comparison of all Wales(PATH) pathology data with Swansea(PAMO) data (Creatinine tests)

In an attempt to identify the reason for the problem, I plotted the missing tests over time, the graph below show the chronology of tests in PAMO (the original Swansea and Bridgend dataset for2012 to 2014) but not in PATH (the all Wales pathology dataset, but reviewing Swansea and Bridgend tests only);



Graph 12 - Creatinine tests in Swansea (PAMO) data and not all Wales (PATH)

This table shows the missing data from the PATH table. The number of missing tests appears to fall over the period studied.



Graph 13 - Creatinine tests in all Wales (PATH) data and not all Swansea(PAMO)

This table shows the data missing from the PAMO table (i.e. in PATH not PAMO). For both these gaps, I could find no obvious source for the gaps. I mapped out the locations of the missing tests, as shown in the table below;

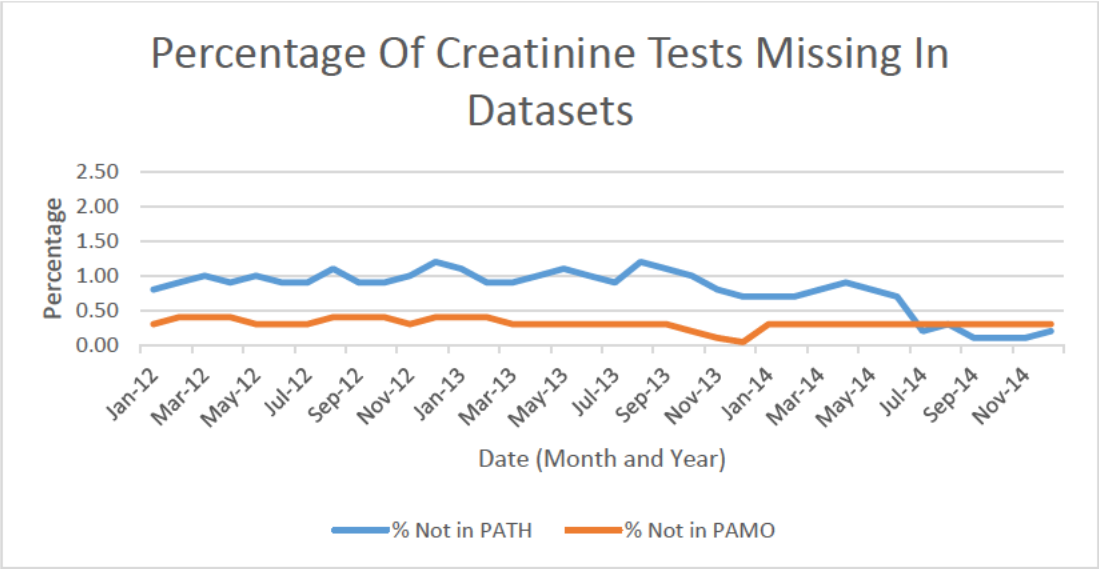
Top 10	Not In PAMO		Not In PATH	
1	Singleton Chemotherapy Unit	1,242	Bridgend A&E	4,154
2	Singleton Oncology Unit	499	Morriston A&E	2,209
3	Singleton Hospital	443	Singleton Assessment Unit	951
4	Morriston Hospital Outpatients	290	Bridgend Assessment Unit	902
5	Morriston Hospital	334	Morriston Assessment Unit	517
6	Singleton Outpatients	183	Morriston Burns Critical Care	478
7	Morriston A&E	145	Special Care Baby Unit Singleton	343
8	Rheumatology Outpatients	107	Morriston Coronary Care Unit	196
9	Special Care Baby Unit Singleton	91	Morriston Assessment Unit	156
10	Bridgend A&E	84	Morriston Renal Ward	154

Table 21 - Location of tests not in all Wales (PATH) or Swansea (PAMO) dataset

As can be seen, the missing PAMO data seems to be mainly for Singleton oncology/chemotherapy day unit, whereas the data missing in PATH appears to be spread between the different areas with the top 10 in places all amongst the highest overall users of creatinine tests. Location of the tests missing therefore do not provide an obvious explanation of the missing results. However, it could be hypothesised that the patients with missing data in A&E may have been related to non-linkable information. Some patients present to A&E in an unconscious state and therefore are unable to provide their names. Tests in these patients would initially be recorded as 'unknown' but once the clinical details are later known, the tests are recorded to the correct patient, it is possible this process led to a mismatch with the historical data (i.e. in PATH before March 2015 when the WRRS data for ABMUHB becomes prospective). The two tables were joined on ALF, results (creatinine value) and test received date. The missing data are spread across the years of the available data as shown in Graph 12 - Creatinine tests in Swansea (PAMO) data and not all Wales (PATH)).

On reviewing a selection of individuals, the problem appeared to be that there were no records of a creatinine test at all on the day that the result was missing in PATH. Yet on these examples I did find other tests such as full blood counts and liver function tests. These tests are often paired with creatinine tests. Although no obvious cause for the missing data was found, it is possible that the missing data was linked to authorisation of the results, as PATH receives authorised results only, but PAMO data (from Masterlab© laboratory information management system) contains all results authorised and not.

Overall, the missing creatinine tests account for a very small proportion (<1.5%) of the creatinine test, this was shown in the graph below;



Graph 14 - Creatinine tests missing by month Wales (Path) and Swansea (PAMO)

Creating look up tables – WRRS_PROV_SITE_HB20181209

To assess the WRRS table accurately, I needed to categorise request locations into health boards. The health board boundaries used were the 2009 definitions, so Bridgend remains part of Abertawe Bro Morgannwg University Health Board for this study and not part of Cwm Taf health board (which it changed to in April 2019). The categorisation required a manual review of the PROV_DEPT_SITE_DESC (Test provider site) of which there were 209 locations. In some regions, particularly in North Wales and West Wales, tests performed from general practices had a generic PROV_DEPT_SITE_DESC. As such, it required the SUBJECT_LOC_DESC to define the Health Board. In these cases where the health boards were not clear, I reviewed them and used my knowledge of Welsh NHS sites to place the locations into health boards, but where there was doubt, I looked the locations up on WWW.WALES.NHS.UK website.

I also reviewed the 7,076 different SUBJECT_LOC_DESC codes to categorise them into test location categorise – 'A&E', 'GP', 'Inpatient', 'Maternity', 'Outpatient', 'Research' and 'Unknown'. The tables below, shows the application of these two look up tables in categorising the health board and subject location;

PT	CODE	VALUE	PROV_DEPT_SITE	SUBJECT_LOC_DESC
1	CREA	80	Withybush Hospital	Ward 4
1	CREA	81	Gen Practi	Narberth HC (Allen)
2	CREA	82	Royal Glam	RGL AE
2	CREA	83	Princess of Wales	Ward 4
3	CREA	88	Gen Practi	St.Thomas' Surgery
4	CREA	79	Ysbyty Glan Clwyd	Outpatients MCHOPD

Look up tables

PT	CODE	VALUE	PROV_DEPT_SITE	SUBJECT_LOC_DESC	HEALTHBOARD	SUBJECT_LOCATION
1	CREA	80	Withybush Hospital	Ward 4	HDUHB	INPATIENT
1	CREA	81	Gen Practi	Narberth HC (Allen)	HDUHB	GP
2	CREA	82	Royal Glam	RGL AE	CTUHB	A&E
2	CREA	83	Princess of Wales	Ward 4	ABMUHB	INPATIENT
3	CREA	88	Gen Practi	St.Thomas' Surgery	HDUHB	GP
4	CREA	79	Ysbyty Glan Clwyd	Outpatients MCHOPD	BCUHB	OPD

Figure 19 - Creation of a test location look up table

Missing suppressed alert and eAlerts

When plotting out the electronic AKI alerts following a second WRRS upload in March 2019, it was clear that the eAlerts were not included. We also need to see suppressed alerts which have a standardised message 'No AKI alert generated as Patient Type is Dialysis' in practice, but these were not in the SAIL extract. As a result, I met with a data manager (Gareth John) in the NHS Wales Informatics Service headquarters in November 2019, at which time we were able to find the suppressed alerts and arrange for an upload. This allows us to gain a better understanding of any mismatches between our AKI code and the eAlerts in SAIL.

Creating an ABMU pathology table

A union of these tables was needed to create a cohort to assess for AKI. In order to do that we need to present the data in the same way. As mentioned, there are differences in names and coding which we need to correct. A simple example is the difference in sample date names – i.e. COLLECTION_DT (in the original PABR) versus SPCM_DT (in PAMO) and DATE_COLLECTED (In the most recent PABR update).

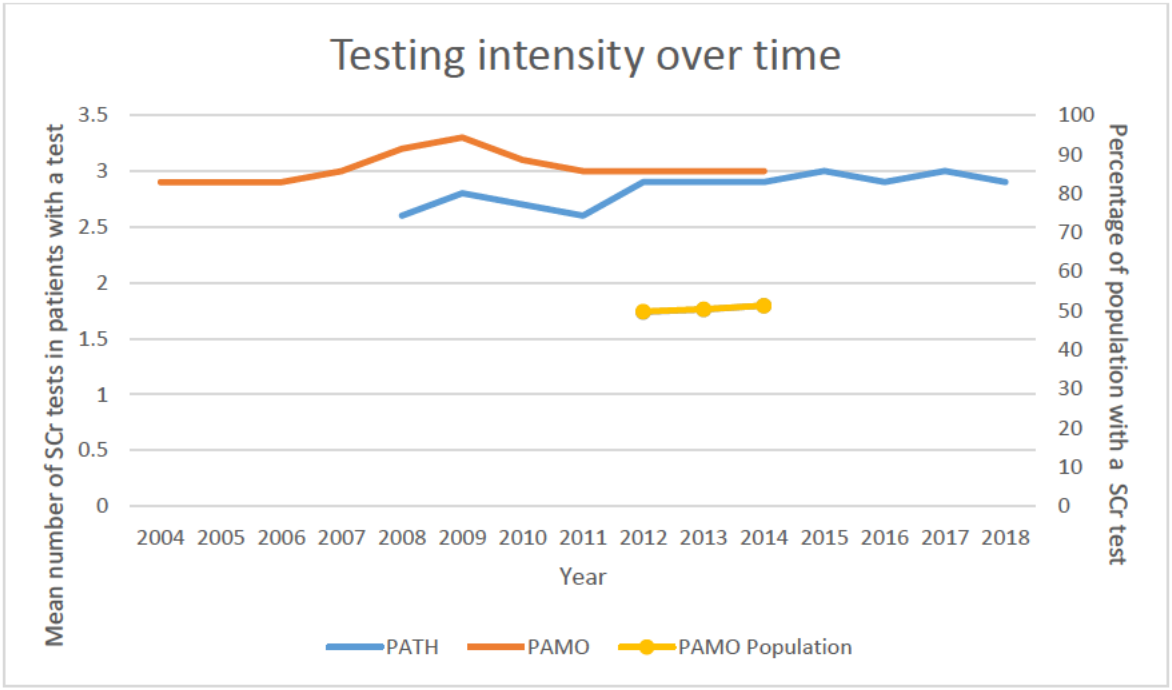
Along with standardisation, we also must clean the data. To analyse the data, we need to convert it into decimal (initially it was in text format), as well as making sure that the tests reviewed are only serum creatinine (SCr) test and not from other fluids. In PABR, this was simply done by the 'TEST' which was 'CREAT' as urine creatinine was called 'UCREAT'. In PAMO it was more difficult as the 'TEST_CD' of 'CREA' was not specific. The SPCM_TYPE_CD was the column with this specification with 'S' for serum or 'B' for blood corresponding to the desired results.

Creating an all Wales creatinine table

The all Wales pathology table was created using this SCr WRRS data. The AKI eAlert were joined with the SCr tests that caused the AKI trigger. This also includes where there was evidence that the alert had been suppressed. The tests were also joined with hospital admissions dataset (PEDW), the All Wales renal dataset, the death data and the critical care dataset.

Testing Intensity

In the Welsh population the average (mean) number of creatinine tests per year in those that are tested was around 3 tests per person. Of the adult population in Abertawe Bro Morgannwg University Health Board, covered by the PAMO data, 50% have a SCr test each year;



Graph 15 - Testing intensive per person in dataset - Wales (PATH) and Swansea (PAMO)

Office of national statistics death records – ADDE_DEATHS

Background

Within SAIL there is a dataset from the Office of National Statistics (ONS) which contains all deaths registered in Wales. This is called Annual district death extract (ADDE) in SAIL. The period with complete data that this extends from was January 1996 through to January 2019. There are 757,479 deaths recorded in this dataset. In the year before the dataset upload there are usually a few hundred deaths not accounted for in the data which I am able to deduce by comparing the previous uploads. These deaths may be related to delays in the death certificate being entered into the datasets or due to delayed death certification, for example in the cases of coroner's inquests. With each iteration the coverage of the deaths data improves. This dataset was important for the understanding of mortality from AKI. It enables the comparison of AKI deaths before and after the introduction of the all Wales eAlerts.

Validation

Of the 757,479 deaths, 35,370 of them are not linkable due to the absence of ALF_PE (unique identifier), however 35,117 of these are before February 1997, so before the time frame required for my research. After February 1997 the percentage of missing ALF_PE by month falls to less than 0.3% with many months having no missing ALF_PE.

Within the death data, was ICD-10 coding for the cause of death. This allowed us to identify deaths where the doctor completing the death certification feels acute kidney injury or acute renal failure has played a role. For example, over this period, 11,028 patients had AKI ('N17' or one of its derivatives) as part of their cause of death.

Originally there were diagnosis fields with free text within this dataset, whilst validating this dataset, it was apparent that some of the free text contained coroner's reports (narrative information). As a result, I fed this back to the SAIL team and the information was suppressed. Prior to me finding the narrative information, I was able to check that the N17 code did correlate to 'acute renal failure'. Most of this was coded N17.9 ('N179') which correlates to acute renal failure unspecified. There were 11,028 patients coded for acute renal failure in the cause of death in diagnosis fields.

Columns of interest

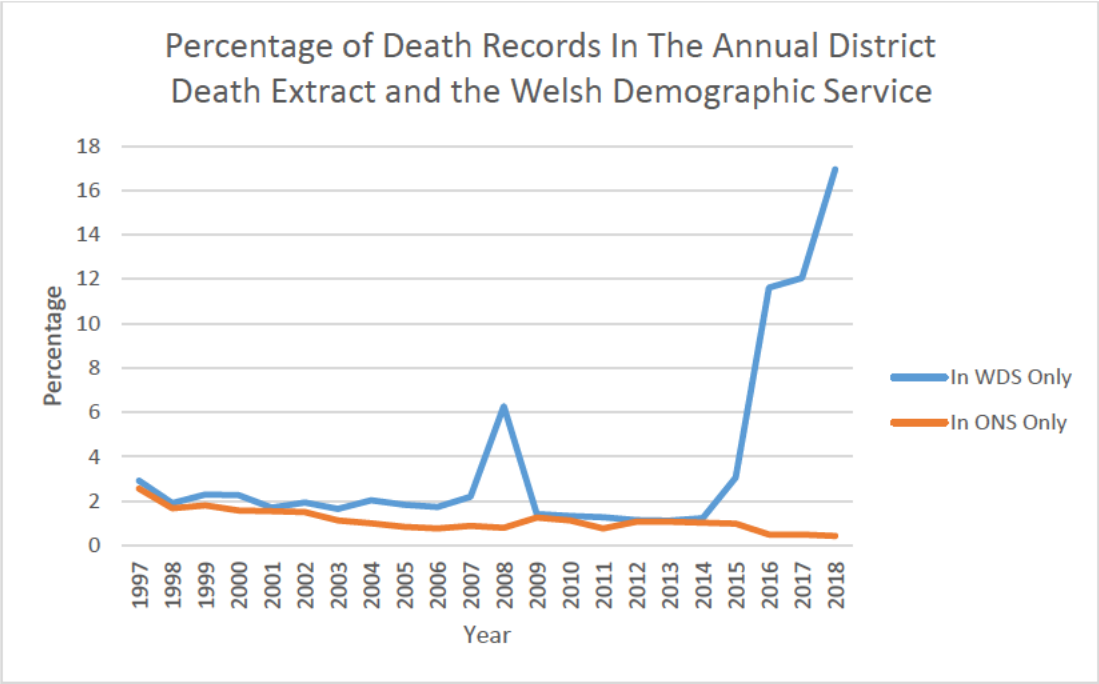
SAIL0505V.ADDE_DEATHS_20190328	
Column Name	**Description**
ALF_PE	Link
DEATH_DT	Date of Death
DEATHCAUSE_DIAG_1_CD	ICD-10 coding for cause of death (1)
DEATHCAUSE_DIAG_2_CD	ICD-10 coding for cause of death (2)
DEATHCAUSE_DIAG_3_CD	ICD-10 coding for cause of death (3)
DEATHCAUSE_DIAG_4_CD	ICD-10 coding for cause of death (4)
DEATHCAUSE_DIAG_5_CD	ICD-10 coding for cause of death (5)
DEATHCAUSE_DIAG_6_CD	ICD-10 coding for cause of death (6)
DEATHCAUSE_DIAG_7_CD	ICD-10 coding for cause of death (7)
DEATHCAUSE_DIAG_8_CD	ICD-10 coding for cause of death (8)
DEC_LSOA_CD	LSOA at time of death
DEATHCAUSE_DIAG_UNDERLYING_CD	ICD-10 coding for the underlying cause of death

Table 22 - Office of national statistics death table columns

The columns starting with DEATHCAUSE_…… correlates with the '1a','1b','1c' etc and '2' on the death certification. The 'DEATHCAUSE_DIAG_UNDERLYING _CD' column correlates to the underlying cause of death on the death certificate (i.e. the last filed in row of the '1' section on a death certificate). If for example there was the same ICD-10 code in DEATHCAUSE_DIAG_3_CD as DEATHCAUSE_DIAG_UNDERLYING _CD but there was also a DEATHCAUSE_DIAG_4_CD or more, then these are for the '2' section of the death certificate (i.e. those conditions that contribute to ill health but not directly to death).

Comparison to Welsh Demographic Service

Along with death records in the ONS's there are also the Welsh Demographic Service (WDS) death records. For the most part there was a match between the WDS records for deaths and the ADDE data, however there are occasions where the deaths are recorded in one dataset and not the other. As can be seen below, the WDS data appears to be the most complete data;



Graph 16 - Death comparison between ONS and Welsh demographics service

In this graph there was a large increase in the number of deaths that are in the WDS but not in the in ONS (ADDE) dataset towards from 2016 onwards. There are also some that are in ONS but not WDS. It was clear, that when reviewing mortality, both the ADDE and WDS datasets should be used to prevent missing deaths. There are also times where the dates don't match, but these are small with 71 being later in WDS compared to ONS and 437 being later in ONS compared to WDS.

Patient episode database for Wales – PEDW

Background

The patient episode database for Wales (PEDW) contains the admitted patient care (APC) episodes data which is the hospital admission records for Wales. The period that was currently accurately covered was between April 1999 to Dec 2019. There was data going back to January 1995 but there was a step in the records in April 1999, following this the numbers seem consistent. PEDW has data for all Welsh hospital admissions as well as admissions of Welsh patients into English hospitals. The PEDW dataset allowed us to look at hospital admission spells, therefore identifying whether a person was an inpatient or outpatient at a point in time.

The dataset can also be used to identify the reason for the admission through the diagnostic coding within it. Every time a patient was admitted to hospital a record was created, then hospital coders (non-clinical) interpret the hospital notes and discharge summary and use ICD-10 coding to code it. This was used for the validation of coding chapter (Chapter 5 on page 189). The hospital admissions are recorded as consultant episodes, for periods when the patient was under individual hospital consultants and then also as hospital spells which can be a combination of more than one consultant episodes during a single continuous hospital admission. The tables are joined by spell number (SPELL_NUM_PE) and the provider unit (PROV_UNIT). The diagnostic codes used are from the 10th revision of the International Classification of Disease (ICD-10). The operation codes are Office of Population Censuses and Surveys 4 codes (OPCS-4). The PEDW dataset includes day attender and regular attenders. The regular attenders' admissions are not assessed in the analysis of completeness and depth. The information regarding whether a spell was as a 'regular attender' admission is stored in a column called 'PAT_CLASS_CD'. In some Welsh units, haemodialysis treatments are entered as regular attender admissions.

Although PEDW is the Welsh equivalent of the English Hospital Episode Statistics (HES) there are some differences. These have been highlighted in a document by the NHS Wales Informatics Service (245). An example is that HES admissions to not have admission codes 25 or 27 (meaning 'Domiciliary visit by consultant' and via 'NHS direct Services' respectively). The

differences do not affect our study as we have selected patient intended management code 1 and 2, excluding day case.

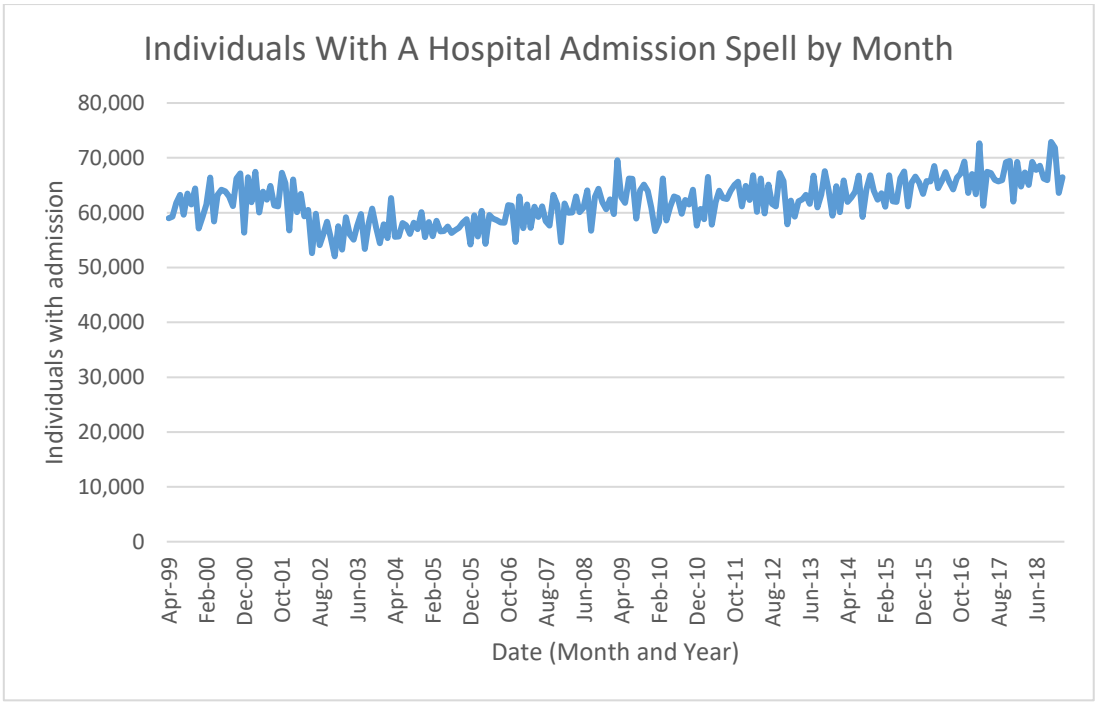
Validation

The PEDW dataset was split into 5 tables. The total counts in and table descriptions are shown in the table below;

Table Name	Total count (Distinct)	Description
PEDW_DIAG_20190515	87,234,721 (Admissions 20,162,273)	This contains the diagnosis ICD-10 code. Each row corresponds to a diagnosis, so for each admission there may be more than one.
PEDW_EPISODE_20191213	25,120,724 (Admissions 21,353,338)	This contains the patient admission information as well as the end consultant information.
PEDW_OPER_20190515	37,012,144 (Admissions 13,317,959)	This contains the information on any operations performed during the hospital episode.
PEDW_SPELL_20190515	22,174,611 (Admissions 21,353,338) (Distinct ALF: 3,456,094)	This contains the hospital spell information including admission, discharge source as well as demographics.
PEDW_SUPERSPELL_20190515	25,120,724 (Admissions 21,353,338)	Joins individual spells as a hospital superspell.

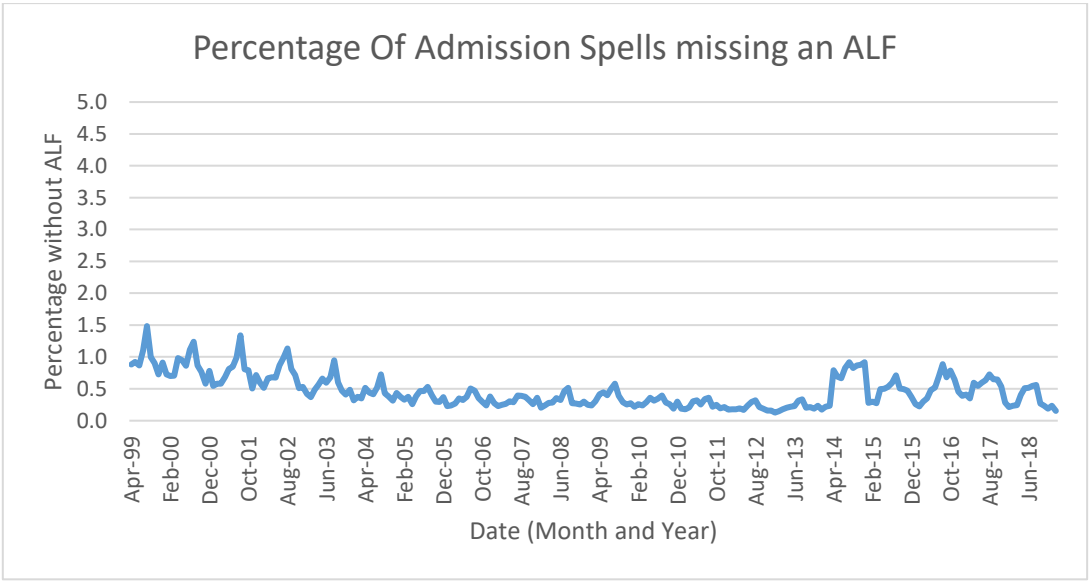
Table 23 - PEDW tables (Distinct based on SPELL_NUM_PE unless otherwise specified)

The majority of the data are in the SPELL table, however the other tables are still important. There are 1,040,240 spells with missing ALF_PE and therefore, not linkable.



Graph 17 - PEDW admissions by year

This graph shows the number of people with hospital admissions by year with the percentage of null ALF code (i.e. not linkable) shown below;



Graph 18 - PEDW missing linkage ALF

Diagnosis

The diagnosis codes can appear in several different positions. The way these are recorded are highlighted in the table below;

Value	Meaning
1	Primary Diagnosis
2	Subsidiary of the primary diagnosis
3	Secondary diagnosis (1st)
4	Secondary diagnosis (2nd)
5	Secondary diagnosis (3rd)
6	Secondary diagnosis (4th)
7	Secondary diagnosis (5th)
8	Secondary diagnosis (6th)
9	Secondary diagnosis (7th)
10	Secondary diagnosis (8th)
11	Secondary diagnosis (9th)
12	Secondary diagnosis (10th)
13	Secondary diagnosis (11th)
14	Secondary diagnosis (12th)

Table 24 - Diagnostic ICD-10 coding positions

Provider Look Up Table

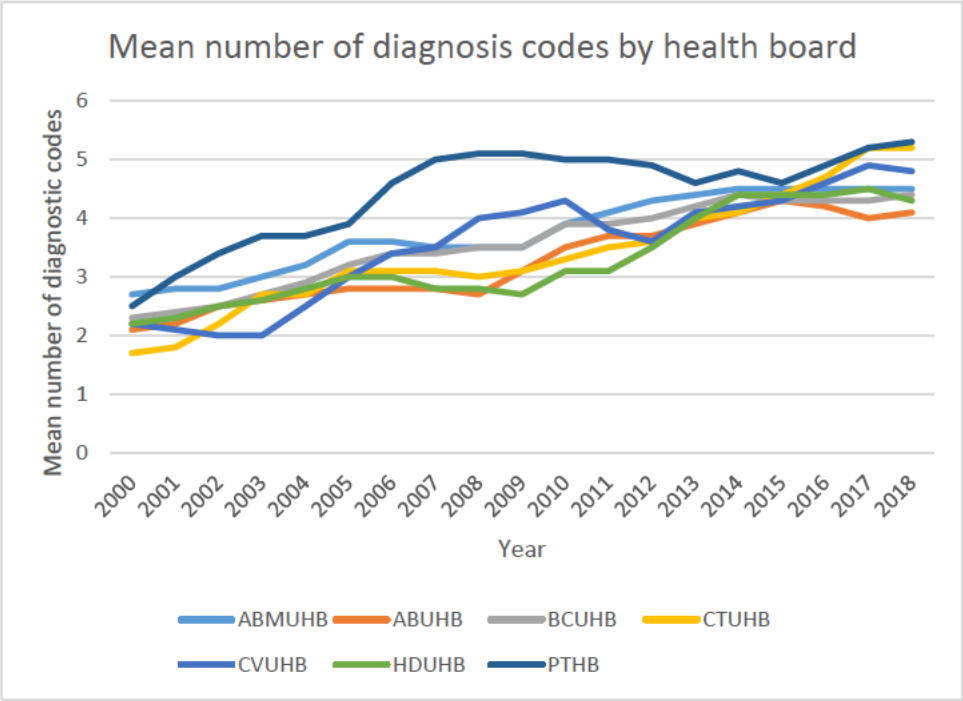
A look up table was created (by TMS) for all the health boards, using the PROV_UNIT_CD code. This table bins some provider units into their current name (at time of study); for example 'Gwent' becomes 'Aneurin Bevan', 'UHW' becomes 'Cardiff and Vale'. This was because Trusts have changed names over time, and they have been now merged into health boards. This allowed the provider units to be categorised into the different health boards for analysis.

Data Quality

Hospital episode data are monitored for the depth and the completeness of the coding by the NHS. The depth was based on the average number of codes in those patients who have a primary diagnostic code (i.e. denominator does not include those episodes that have no diagnosis code). The completeness is the number of finished consultant episodes (FCE) with a primary diagnosis, the target of this was 95% of all FCEs at 3months and 98% at 12months (246). In this section, I have assessed these two measures within the SAIL data.

Depth

The depth of coding appears to improve over the last 2 decades across all the health boards. By 2018 all the health boards had a mean depth of coding above 4 diagnostic codes per episode.



Graph 19 – Depth of coding - Mean number of diagnosis codes by health boards

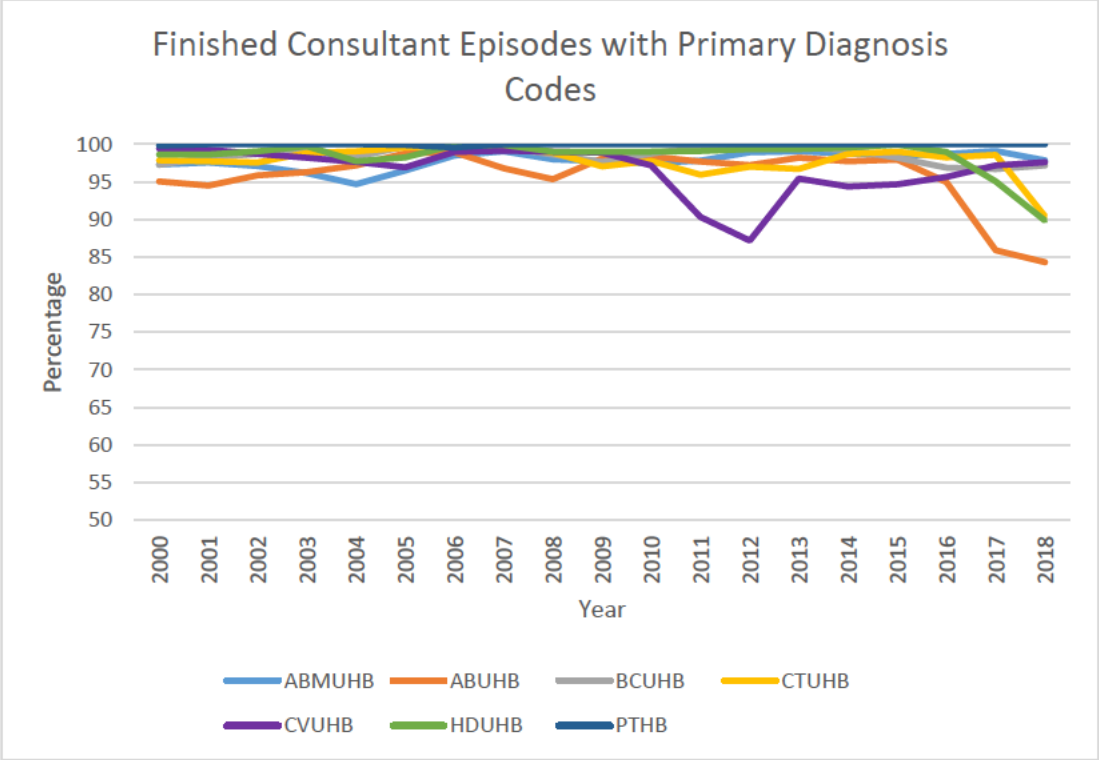
Key –ABUHB - Aneurin Bevan University Health Board, ABMUHB - Abertawe Bro Morgannwg University Health Board, BCUHB - Betsi Cadwaladr University Health Board, CVUHB - Cardiff and the Vale University Health Board , CTUHB – Cwm Taf University Health Board, HDUHB - Hywel Dda University Health Board, PTHB - Powys Teaching Health board

Depth of coding is very important in a condition such as Acute Renal Failure (equivalent to AKI). This is because, most AKI occurs as the result of another illness such as pneumonia, heart failure etc.... If there is poor depth in coding, it means that AKI may be potentially under coded. The standard deviation from the mean is displayed in a table in the appendix on page 312.

Completeness

The completeness of coding has been relatively consistent over time, however there are occasions where there are drops in the quality. In 2018 there was a reduction in the completeness of coding. This is because coding is done after the admission, in some cases months after the admission therefore the coding has not been done at the time of the extract. The official data quality checks look at financial, not calendar years (i.e. 1st April to the 31st

March) so are not directly comparable to the graph below. Of note, to highlight the fluctuations, the Y axis starts at 50%.



Graph 20 – Completeness of coding – y axis starts at 50%

Key –ABUHB – Aneurin Bevan University Health Board, ABMUHB – Abertawe Bro Morgannwg University Health Board, BCUHB – Betsi Cadwaladr University Health Board, CVUHB - Cardiff and the Vale University Health Board , CTUHB – Cwm Taf University Health Board, HDUHB – Hywel Dda University Health Board, PTUHB – Powys Teaching Health board

Selection

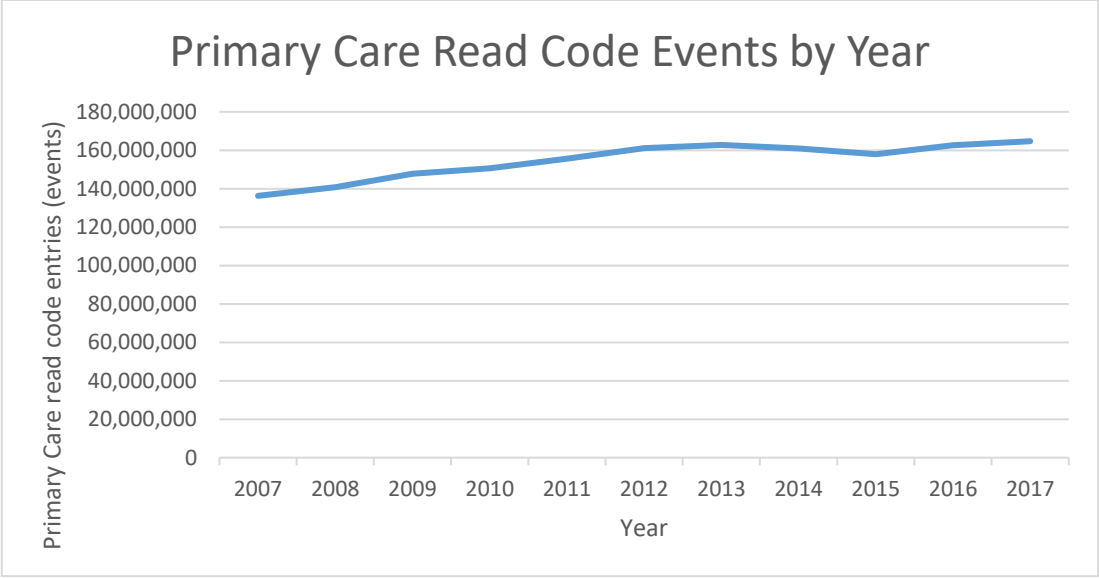
To select the admission types a few rules must be applied;

A join based on SPELL_NUM_PE and PROV_UNIT_CD (+/- EPI_NUM if episodes data are needed) must be used. This was because around 300,000 of the spells share a SPELL_NUM with another person/admission in a different health board.

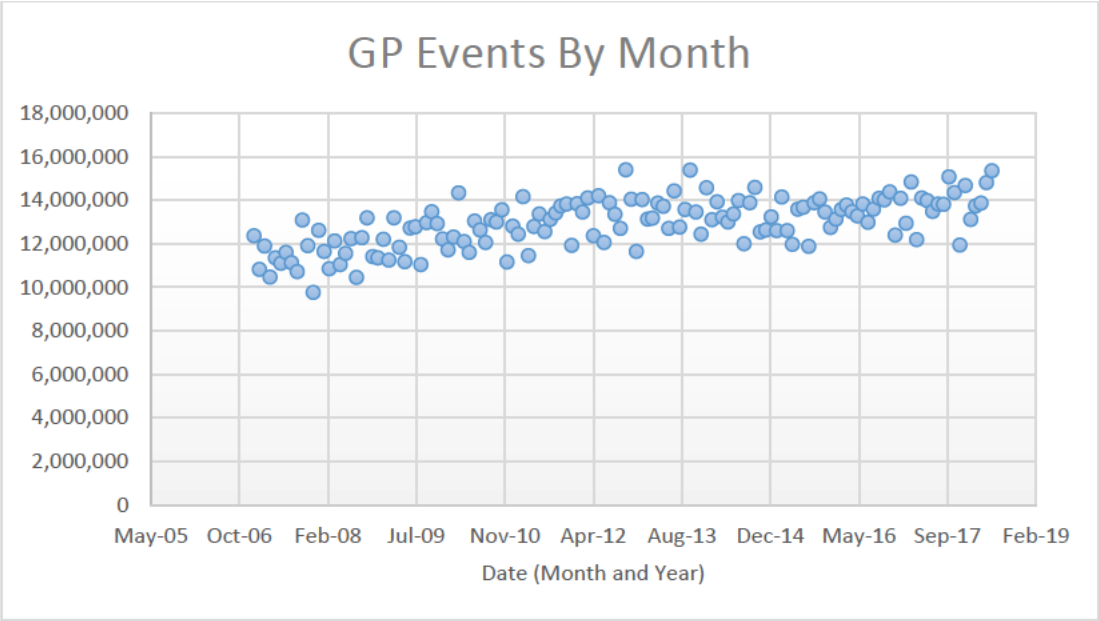
Primary Care GP dataset – WLGP

Background

This dataset contains patient's information from the general practice (GP) records of 341 practices in Wales. Some general practices in Wales have not agreed to permit their data to be sent into SAIL. There were 454 primary care practices in Wales in 2015 (247) and there were 663 practice numbers in SAIL. Of these practices, 52% have regular data within SAIL. This was because some of these practices are based outside Wales, and some of the practices are closed practices. When we include only Welsh practices, SAIL data covers 75% of Welsh practices. The GP events table holds information on 2,706,777,153 interactions (events) with primary care, recorded using Read codes. The vast majority of these events are recorded in Read Code version 2. There are 7,590,380 rows of GP registration data for 4,083,520 people.



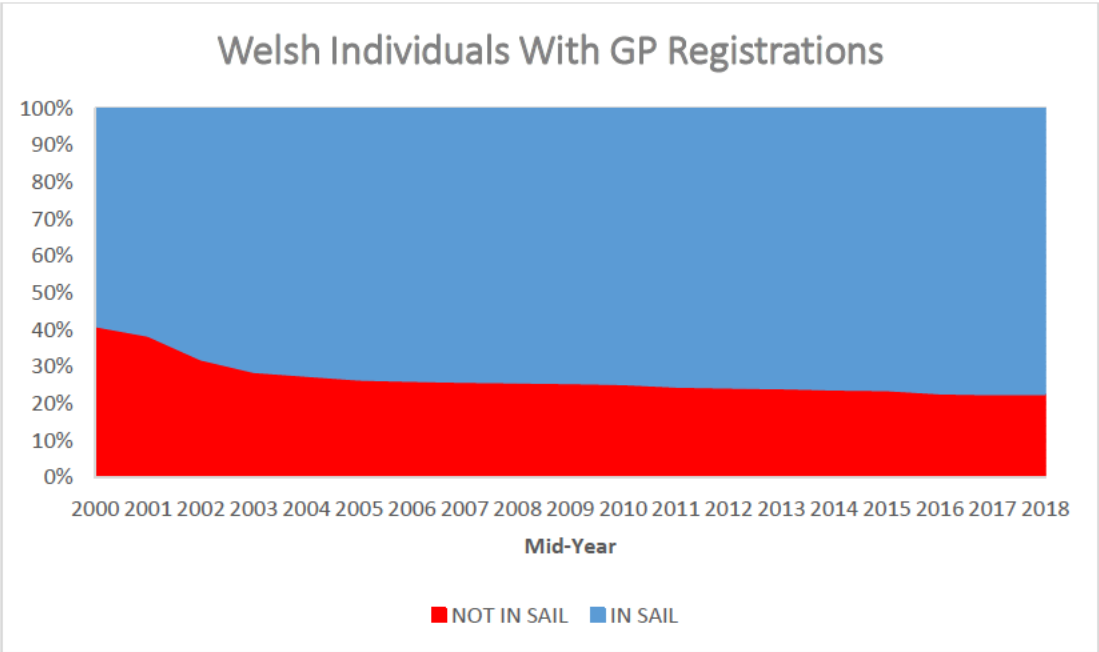
Graph 21 – Primary care events in SAIL by year



Graph 22- Primary care events in SAIL by month

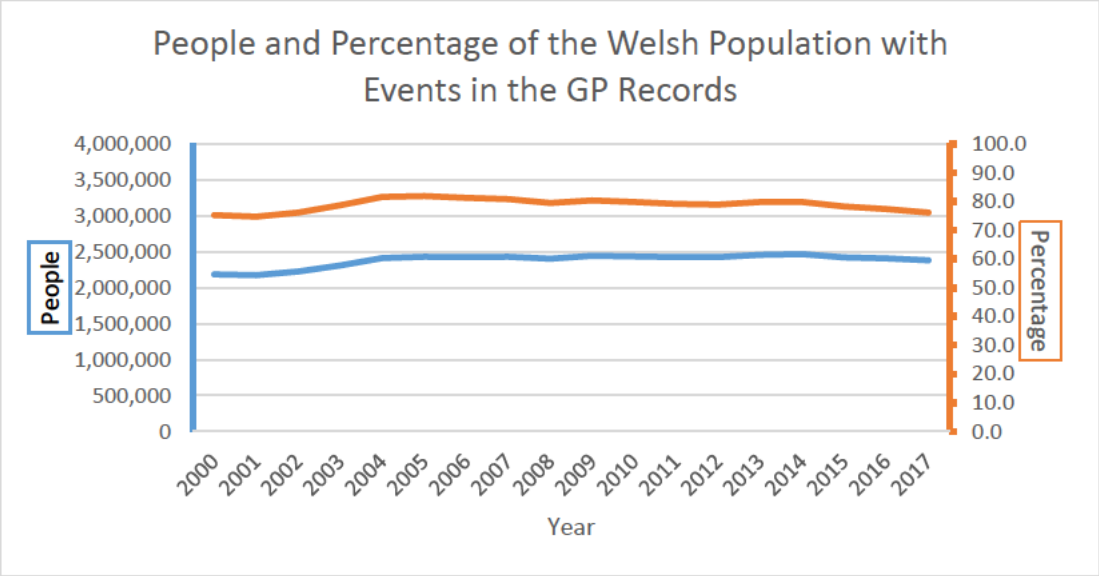
Validation

As mentioned, the GP dataset does not cover the entire Welsh population. To feel confident in using the GP dataset we need to get an impression of the coverage of the dataset across the period being studied. This can be done in a number of different ways, one is to use the GP registration table (WLGP_CLEAN_GP_REG_BY_PRAC_INCLNONSAIL_MEDIAN_20180820). This table has a flag for GP data (1 it is present, 0 it isn't present in sufficient quantity), so I have looked at this coverage at the mid-point of the year (30th June), as shown below;



Graph 23 – Percentage of all Welsh patients with primary care SAIL records

This graph shows that there was a gradual improvement in the percentage of the Welsh population registered with a practice with SAIL data from 71.4% in 2003 to 77.4% in 2018. When the people with a primary care event (Read code entries) are plotted out (Graph 24 – People and population with primary care event records), we can see that the percentage of the Welsh population with a GP event was higher than expected (over 80%). The reason this is the case is because some people have a GP event but are registered with practices which are felt not to have sufficient data as a whole (so their GP Flag is 0). This is because the senior analyst team within SAIL developed a data handling procedure based on the number of events by each practice to determine if the coverage is good enough quality. The graph below shows the number of events and the percentage of the Welsh population with a Read code entry by year.



Graph 24 – People and population with primary care event records

These graphs give us a picture of the Welsh population, but it does not aid our understanding of the regional variations in coverage across Wales. The graph below shows the percentage of the Welsh Population by local area description with GP records highlighting that coverage was not uniform across different regions;

IN SAIL	Blaenau Gwent	Bridgend	Caerphilly	Cardiff	Carmarthenshire	Ceredigion	Conwy	Denbighshire	Flintshire	Gwynedd	Isle of Anglesey	Merthyr Tydfil	Monmouthshire	Neath Port Talbot	Newport	Pembrokeshire	Powys	Rhondda Cynon Taff	Swansea	The Vale of Glamorgan	Torfaen	Wrexham
2000	40	60	57	76	65	81	56	32	50	58	46	62	24	77	57	37	37	68	83	61	30	57
2001	41	79	60	76	66	81	57	36	59	59	65	61	24	78	58	44	37	68	83	62	30	58
2002	49	92	60	78	69	81	60	53	60	64	80	61	46	81	58	45	37	77	95	72	36	76
2003	46	93	68	81	69	81	60	51	61	79	81	69	48	89	59	45	38	82	97	71	62	76
2004	50	93	69	83	70	81	61	54	63	81	82	73	47	89	60	45	38	83	98	74	62	76
2005	63	98	70	83	70	81	61	54	63	81	96	73	47	89	60	45	38	83	98	74	63	77
2006	63	98	71	85	70	82	61	54	63	81	96	73	47	89	60	46	38	84	98	74	66	77
2007	67	98	71	85	70	82	60	54	62	81	96	73	47	89	60	46	38	85	98	75	66	76
2008	67	98	72	85	70	82	61	54	63	81	96	74	47	89	60	46	39	85	99	75	66	76
2009	68	98	72	85	70	82	61	54	63	81	96	80	47	89	60	46	39	86	99	75	66	77
2010	73	98	72	84	70	82	61	54	63	81	96	80	47	89	60	46	39	87	99	75	66	77
2011	73	98	75	87	70	82	61	54	63	81	96	80	47	89	61	46	39	88	99	76	66	79
2012	72	98	76	87	70	83	61	54	63	81	96	81	47	89	61	46	39	89	99	76	66	80
2013	72	98	76	87	76	82	61	55	64	83	96	81	47	87	61	39	39	89	99	76	66	80
2014	72	98	76	86	77	84	61	55	64	84	96	82	47	87	63	39	39	90	99	77	66	81
2015	72	98	76	86	77	86	62	52	64	84	96	83	46	88	63	39	39	91	100	77	66	81
2016	74	96	81	86	77	86	62	52	66	90	97	92	48	89	63	38	39	91	100	77	66	81
2017	74	95	81	86	78	86	62	56	66	89	97	91	48	87	63	40	41	92	100	77	66	81
2018	74	95	82	86	78	86	62	56	67	91	97	91	49	89	63	40	42	93	92	82	66	81

Graph 25 -Percentage of population coverage with primary care SAIL data by Local Area

Key	
	≥75
	51-75
	0-50

Some regions, particularly those with some of the highest population density such as Swansea, Cardiff and Bridgend have excellent coverage within SAIL however Powys, Pembrokeshire and Monmouthshire in particular have poor coverage. To create this table, I created a table which grouped a practice with the most common LSOA code in that individual practice, this was then used to work out the local area. This table was then joined with the registration table to find the number of patients with the GP_DATA_FLAG 0 (not in SAIL) or (in SAIL).

One concern regarding the completeness of the dataset is the potential problem of GPs removing their permission. To assess this, I have plotted the GP events across the year with the individual practices and the local area descriptions;

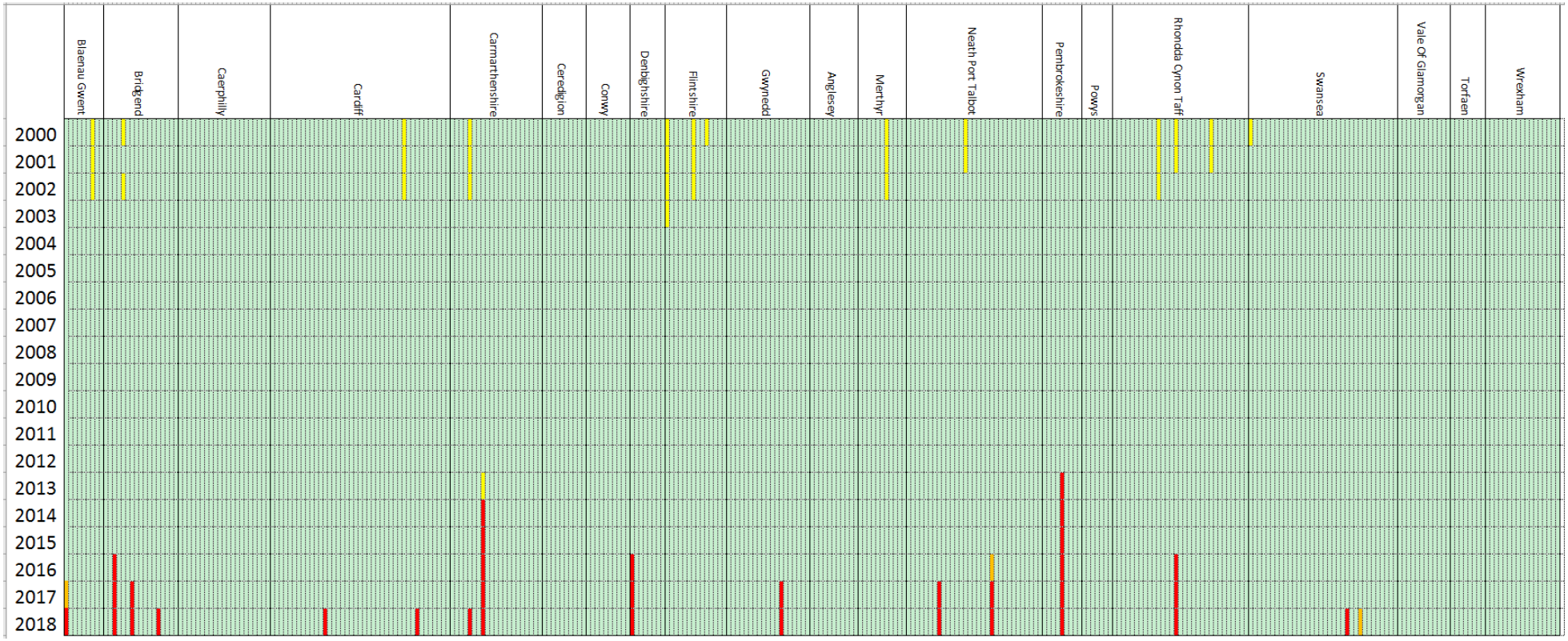


Figure 20 – Average number of Primary care events by practice between 2000 and 2018

Each column represents an individual general practice and they are grouped by local area descriptions.
Number of primary care Read code events; Red < 100 |Orange – 100-999 |Yellow 1000- 5000 events |Green ≥5000

This shows that the number of GP events in the different practices remain stable but there are several practices where the number of events fall, this may be the result of practice closures or removal of consent (red colour).

The primary care dataset covers the whole region of Wales with around 70% of the population in the SAIL dataset and 75% of the GP practices. There was some variation in the primary care practices with SAIL data over time. The figure below (Figure 21 -Percentage coverage of primary care practice with SAIL coverage by local area) shows these changes in availability of primary care data in SAIL over time.

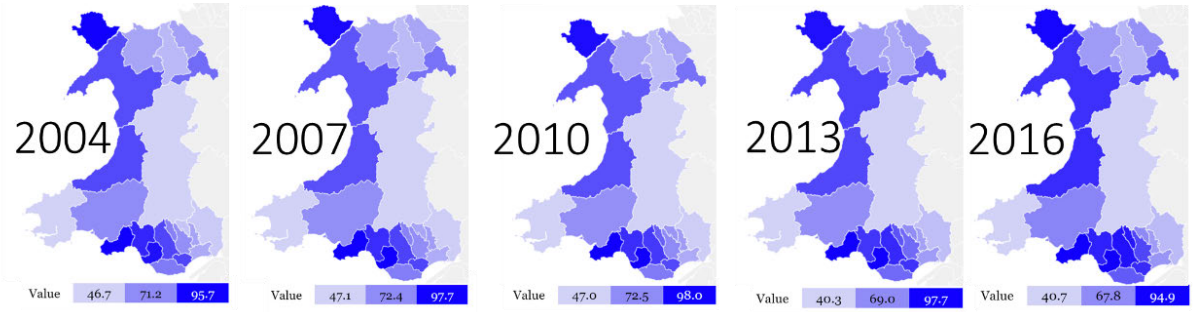


Figure 21 -Percentage coverage of primary care practice with SAIL coverage by local area

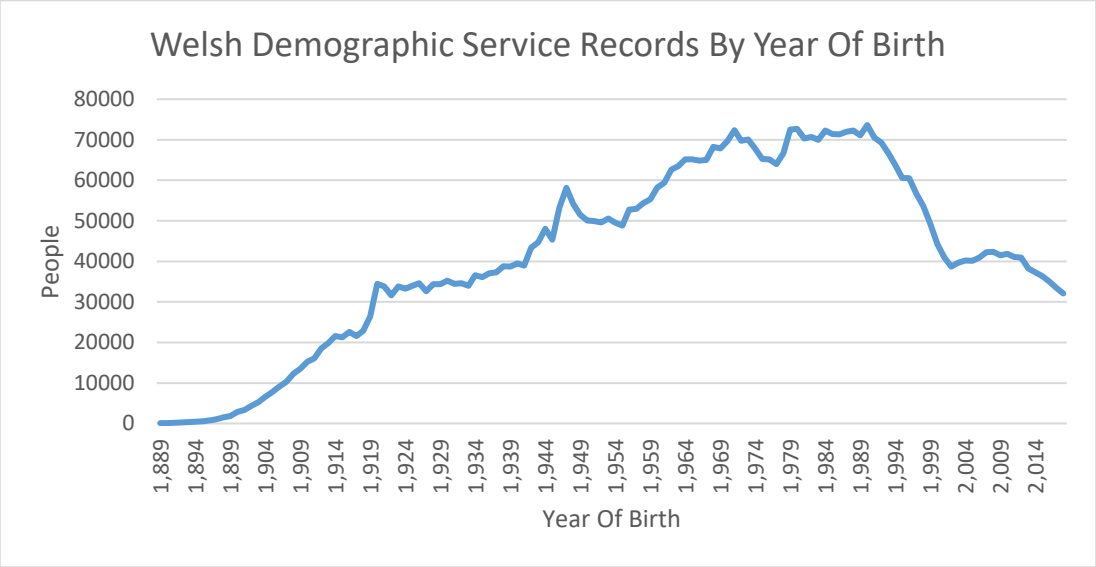
Welsh Demographic service Dataset – WDSD

Background

The Welsh Demographic Service dataset contains the administrative information for all patients in the Welsh national health service (NHS). It contains information on most of the Welsh population, including addresses (in the form of LSOA in SAIL), the start and end of an address registration, week of birth (WOB), gender, date of death (DOD), as wells as information on general practice registrations.

Validation

Within the WDS person table there are 5,389,616 patients, of which 894,264 have died. There are 2,669,416 males, 2,720,180 females and with 20 people of unknown gender. In the WDS addresses are stored as LSOAs, of which there are 14,858,424 in 5,411,419 people. 1,198,623 rows were missing LSOA. The week of birth spread was shown below;



Graph 26 – People in Welsh Demographics service by year of birth

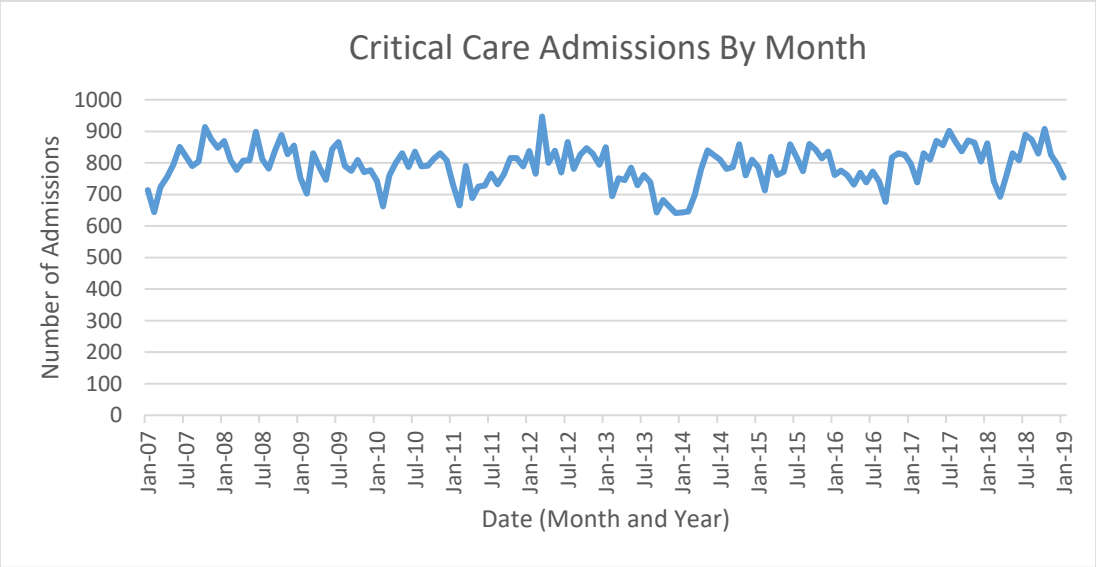
In the WDS general practice registration table there are 15,290,972 registration records in 5,411,417 people. In this dataset there are 665 different general practices.

Critical care dataset – CCDS

The critical care dataset contains comprehensive data on Welsh critical care admissions. The dataset contains information about the patients admitted to intensive care, where they came from (location, speciality, trust) as well as organ support, discharge location and demographic information (ALF, Age, GP location etc…).

Validation

It contains data from April 2006 to January 2019. There were 117,699 admissions in 94,927 patients. Of those patients 51,449 are male, 42,676 are female and 1,148 are unknown.



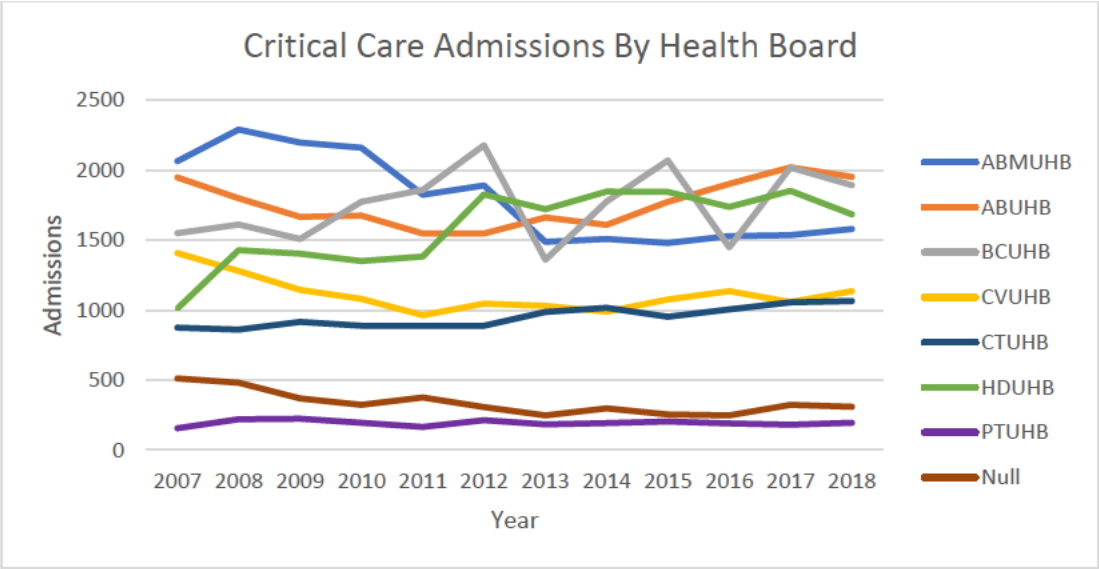
Graph 27 – Critical care admissions by month

These admissions are from across the Welsh Health Boards;

Health Board Name	Admissions
Abertawe Bro Morgannwg University (ABMUHB)	22,290
Betsi Cadwaladr University (BCUHB)	21,702
Aneurin Bevan (ABUHB)	21,550
Hywel Dda (HDUHB)	19,541
Cardiff and Vale University (CVUHB)	14,118
Cwm Taf (CTUHB)	11,679
Powys Teaching (PTUHB)	2,393
Blank information [NULL]	4,426

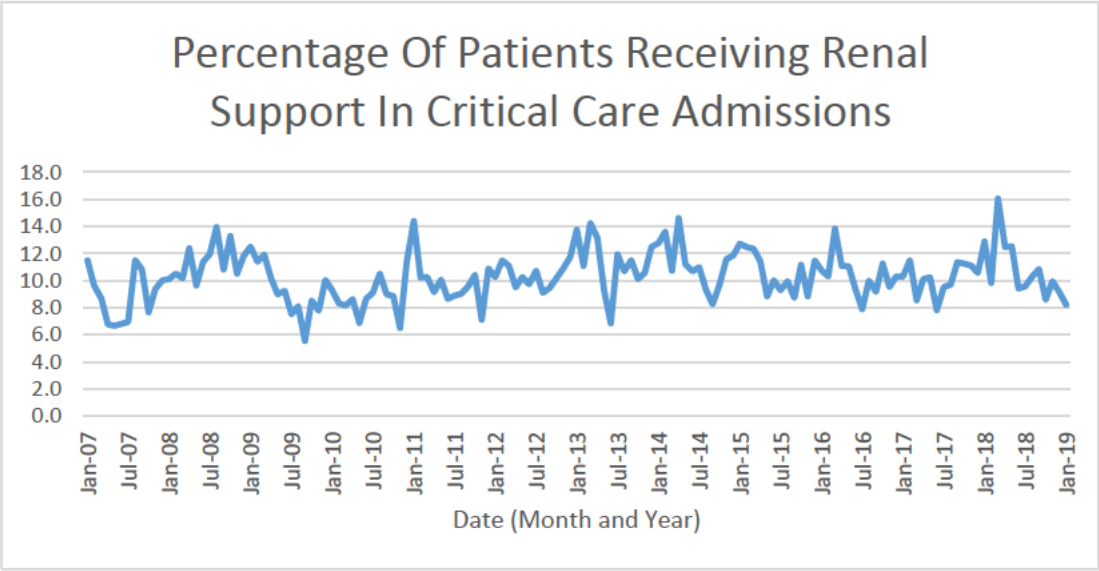
Table 25 – Critical care admissions by health board

These admissions can be further broken down by year;



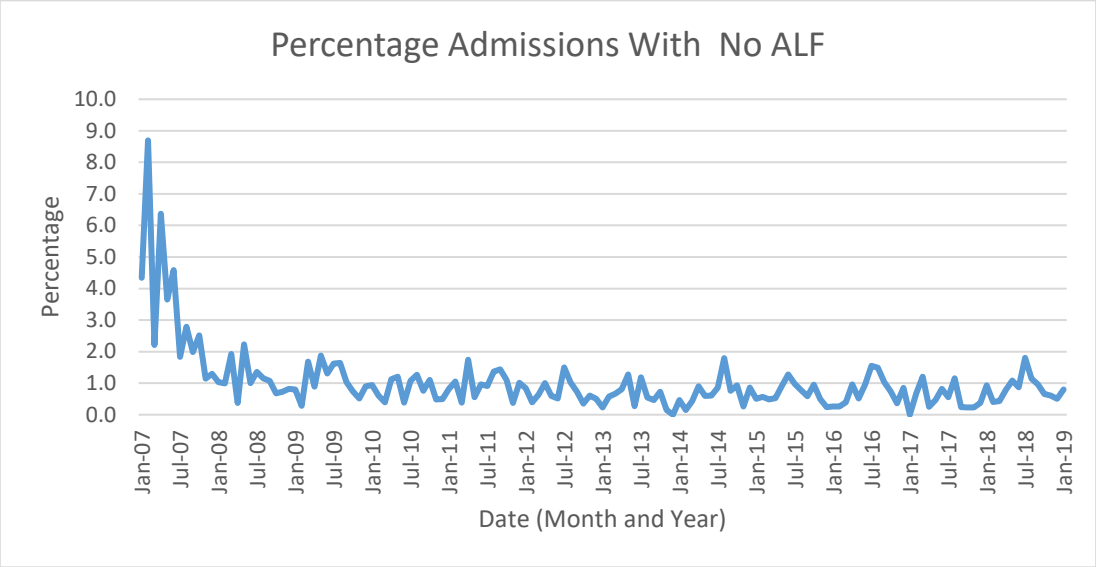
Graph 28 – Critical care admission by health board

The column DUR_RENAL_SUPPORT_DAYS can be used to identify patients who undergo renal replacement therapy in the intensive care department. The graph below shows the percentage of critical care admissions requiring renal support (renal replacement therapy – i.e. Haemodialysis, peritoneal dialysis, haemofiltration or haemodiafiltration);



Graph 29 – Percentage of critical care patients receiving renal replacement therapy

A small proportion of the admissions lacked an ALF_PE code, preventing cross linking of the data.



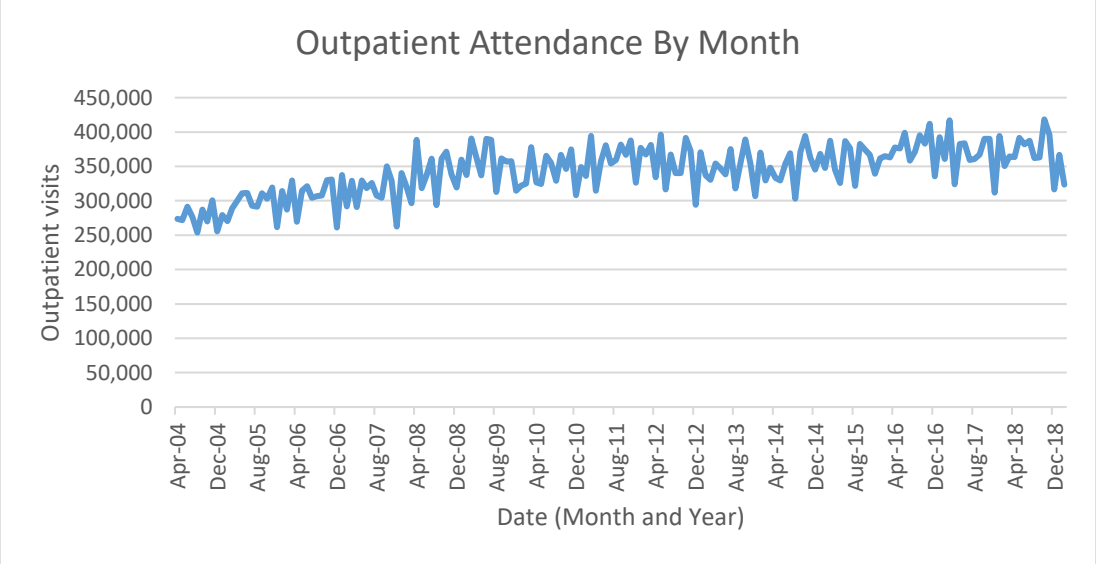
Graph 30 – Percentage of patients without link field (ALF)

Outpatient dataset – OPD

The outpatient dataset in SAIL, houses outpatient details for the whole of Wales, with the main table OPDW_OUTPATIENTS_20190502. In this table there are 61,596,518 rows in 3,407,856 people. There are no rows without the ability to link (i.e. no null ALF_PE). 44% of the outpatient reviews were with male patients and only 0.2% were in those with unknown genders. Most of the rows have LSOA information in the column LSOA2001_CD (missing in only 0.37%). The two supporting tables OPDW_OUTPATIENTS_OPER_20190502 and OPDW_OUTPATIENTS_DIAG_20190502 have 6,231,489 and 1,959,604 rows respectively.

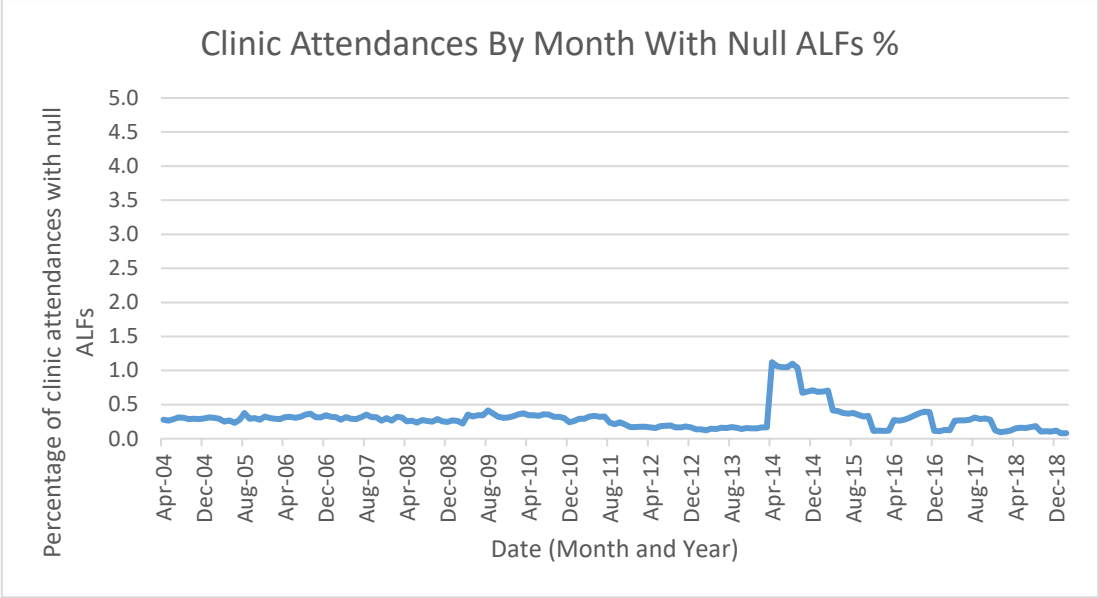
Validation

The OPDW_OUTPATIENTS_20190502 table covers the period of April 2004 to February 2019;



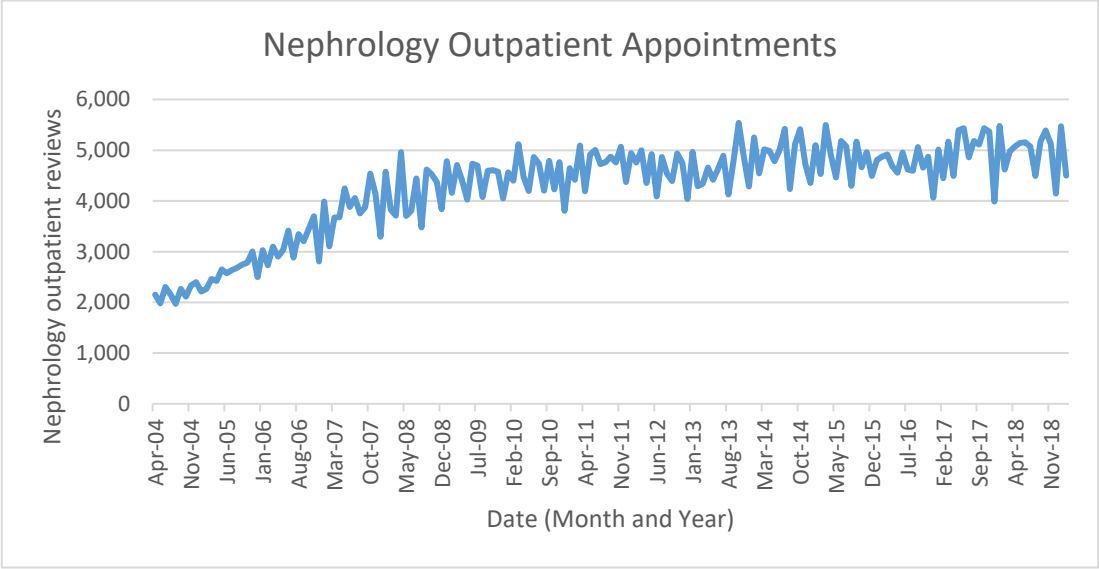
Graph 31 – Outpatient visits by year

The coverage was consistent over time with very low percentage of low ALFs;



Graph 32 – Clinic attendance without link field (ALF)

The graph below shows the nephrology outpatient reviews over the last 15 years, these reviews allow us to assess the nephrology follow up of patient following AKI;



Graph 33 – Nephrology outpatient visits over time

All Wales renal dataset – AWRD

Background

In Wales a single renal data system Vitaldata created by Vitalpulse ltd is used. It is housed at two sites (at the time of the research); Cardiff and Morriston (Swansea), as such the data are split into two table sets. Although the overall system was the same, there were some modifications and variations in its application between the different renal sites in Wales. The south west of Wales (i.e. Bridgend, Swansea, Pembrokeshire, Ceredigion, part of Powys and Carmarthenshire) use the Swansea based system, the rest of Wales uses the Cardiff system (including North Wales). The North Wales renal centres introduced Vitaldata much later than Swansea and Cardiff. This occurred in 2015, prior to this they used 3 separate systems. This dataset was important in ruling out AKI in patients who are on renal replacement for chronic renal failure, as well as helping to identify patients who have AKI requiring dialysis treatment. The initial upload of this data was in December 2016 with a second upload in August 2019. Additional data was also uploaded to SAIL from Bangor, Rhyl and Wrexham in August 2019 to improve the historical dialysis data.

Validation

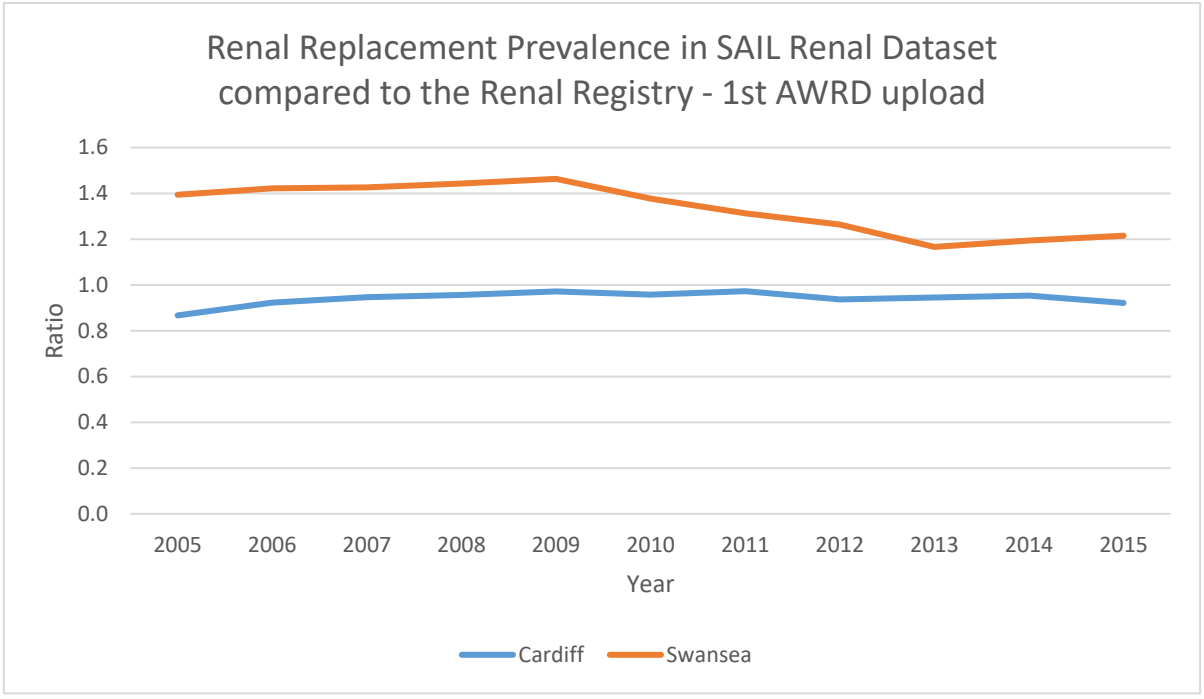
In the Swansea demographic table, there are 27,160 rows of patients (although 1,420 are without ALF_PE and 25,683 have a distinct ALF_PE). In the Cardiff demographic table, there are 47,805 rows (2,899 are without ALF_PE and 44,741 have distinct ALF_PE). There are some patient duplications between the databases. All the patients had week of birth (WOB) entries however, some appear to have a default WOB of 1900-01-01 (Cardiff = 125, Swansea = 164).

Following the initial upload of this data to SAIL, I ran some basic queries on the demographic (ALF table), I noticed some obvious errors in that we had fewer ALF_PE than expected, no gender details (all were GNDR_CD 8, which meant unspecified) and all the WOB were the default date 1900-01-01. We knew this was not the case, and after an investigation, it was apparent that the File 1 we imported had too few columns. This meant that when NWIS created the File 3, they used the wrong columns. This process was all computerised, so the mistakes were not spotted until I reviewed the data in SAIL. Without accurate WOB and

GNDR_CD the ALF could not be calculated. This was therefore fixed with a corrected repeat upload.

Comparison with the renal registry

The UK renal registry collects data on patients with kidney disease. Every year they publish the prevalence of renal replacement by asking renal units to tell them how many patients are on RRT in each unit on the 31st of December. This allows for the comparison with our renal dataset. It was unlikely that the datasets will equal a ratio of 1. This was because the registry does not collect data on acute dialysis patients (less than 90 days), however when they are chronic, they get reclassified to chronic on the timeline, hence they will be counted in the retrospective count as being on dialysis. The graph below shows the ratio of dialysis patient numbers that we have identified in Wales compared with the renal registry. The Cardiff data are for Cardiff region and north Wales, and Swansea was just the south West region;



Graph 34 – Comparison of number of patients on renal replacement therapy between SAIL dataset and renal registry

Cardiff falls below one, meaning our count was lower than that of the renal registry, this can be explained by incomplete data from the North Wales units. This is because when they transferred in 2015 to the Cardiff system, they only transferred patients who were alive at

the time of merger. Swansea's count was higher than 1, this is because acute dialysis patients are included in our numbers and not in the renal registries.

Tables

There are multiple tables within the renal dataset. There are tables for each source, i.e. a Cardiff demographic table and a Morriston (Swansea) table. The tables are shown below;

	AWRD_	
Site(s)	Initial upload	Second upload
C & M	ALF_20170127	-
C & M	BIOCHEMISTRY_20161231	BIOCHEMISTRY_20190829
M	CLINICVISIT_20161231	CLINICVISIT_20190829
C & M	CODES_20161231	CODES_20190829
C & M	COMORBIDITY_20161231	COMORBIDITY_20190829
C & M	-	COMORBIDITY_NEW_20190829
B & C & M & R & W	-	DEMOGRAPHICS_ALF_20190829
B		HDSESSIONS_20190708
C & M	HDTREATMENT_20161231	HDTREATMENT_20190829
C & M	MEDICATION_20161231	MEDICATION_20190829
R		PD_20190829
C & M	PERITONITIS_20161231	PERITONITIS_20190829
C & M	PREDIALYSISCHOICE_20161231	PREDIALYSISCHOICE_20190829
C & M	QUALITYOFLIFE_20161231	QUALITYOFLIFE_20190829
C & M	RENALDIAGNOSIS_20161231	RENALDIAGNOSIS_20190829
B		TIMELINE_20190708
C & M	TIMELINE_20161231	TIMELINE_20190829
W		TIMELINE_20190829
C & M	VALIDATION_20161231	VALIDATION_20190829
M	VASCULARACCESS_20161231	VASCULARACCESS_20190829
C	-	VASCULARACCESS_20190829
C	VITALPARAMETER_20161231	VITALPARAMETER_20190829

Table 26 – Difference table uploads, B = Bangor, C = Cardiff, M = Morriston, R = Rhyl and W = Wrexham

Improving the dataset

To accurately identify patients on dialysis, we need to have good data covering the whole period of the study. The renal dataset has good coverage in most regions for the period of the study except North Wales and the 3 renal centres there. This is because the North Wales systems (all held individual on different software) merged with the Cardiff system in 2015 and only included patients who were alive and under their care at that point. Therefore, more information from these regions was required.

Bangor AWRD_B

In Bangor they used a system called 'RenalLink©'. I was able to get hold of a copy of the database stored in a Microsoft Access© database from Bangor. I was able to improve the data (NHS numbers) in this dataset outside SAIL and then upload it to SAIL improving the data back to 2004 including all individual haemodialysis treatment sessions. This was imported into SAIL in 3 files;

Table	What it contains
AWRD_B_DEMOGRAPHICS_ALF_20190829	The File 3
AWRD_B_HDSESSIONS_20190829	Containing individual sessions
AWRD_B_TIMELINE_20190829	Containing dialysis timeline data

Table 27 – Bangor tables

The database contains data on 2044 individuals, 1840 of which have ALF_PE. 60.6% of the patients were male. 195 of the 2044 rows (9.5%) did not have the link field (ALF_PE).

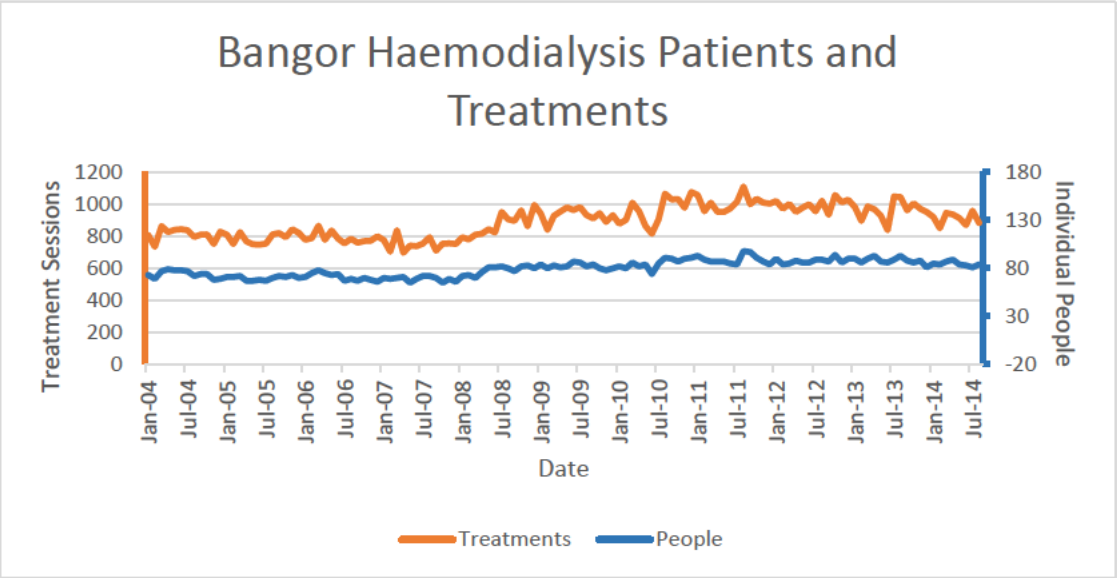
Bangor HD Sessions

The Bangor HD sessions table contains all the individual haemodialysis treatment sessions that were recorded in the RenalLink© database. This contains 113,838 treatments in 628 patients between the 2nd January 2004 and the 30th August 2014.

Column	Comment
SYSTEM_ID_PE	Unique ID for linking with File 3
BANGOR_TREATID_PE	Unique ID for treatment session
HD_DATE	Date of treatment
BANGORDEATHDATE	Date of Death in RenalLink©

Table 28 – Bangor sessions table

The haemodialysis treatments remain reasonably consistent over the 11 years (slight increase) of data as shown in the graph below;



Graph 35 – Bangor dialysis sessions

Bangor Timeline

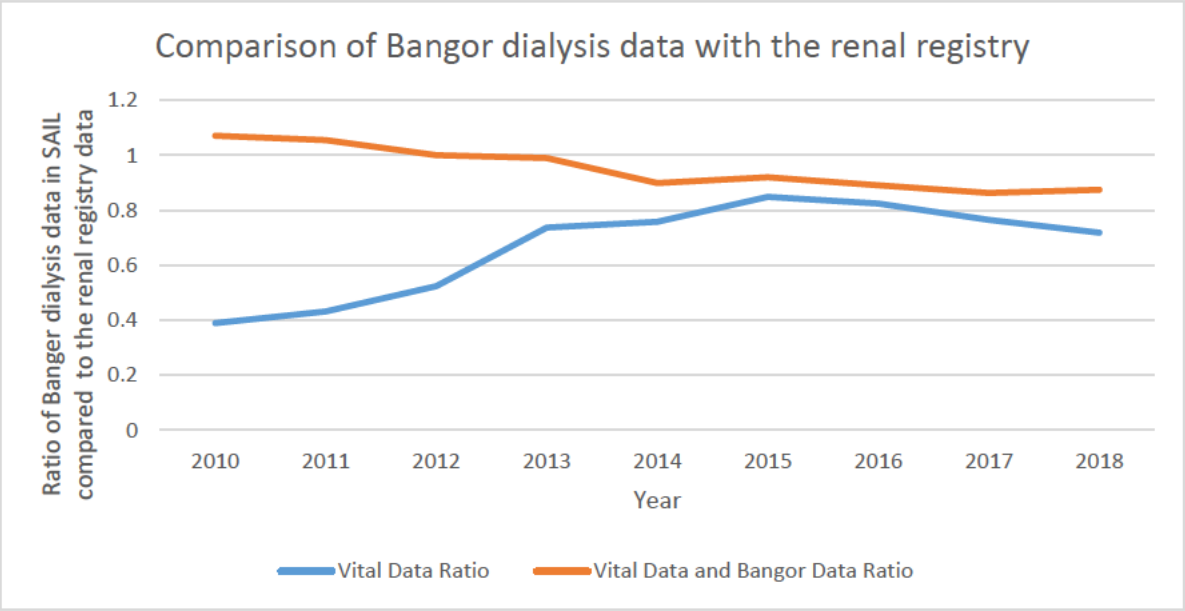
The Bangor timeline table contains 2880 rows of information in 1,688 patients.

Column	Comment
SYSTEM_ID_PE	Unique ID for linking with File 3
BANGORMODALITY	Timeline Code
BANGORCODE	Summary – i.e. HD, PD, Pre, etc…
SUBMODALITY	Extra detail – e.g. CAPD for PD code
STARTDATE	Date of Timeline start
ENDDATE	End of timeline spell date
STARTCODE	An extra code for the Modality
ENDCODE	End of timeline spell code
SYSTEM	Dialysis System used
REMARK	Comment
DEATHDATE	Death Date

Table 29 – Bangor timeline table

The BANGORCODE column was useful for the identification of renal replacement spells. These are categorised for the renal replacement cohort as shown in the appendix (Bangor Timeline codes).

The graph below shows the effect that this extra upload of dialysis data has had on the comparison with the renal registry data. We can see that the period covered by renal link (before 2015) has seen a significant increase in coverage;



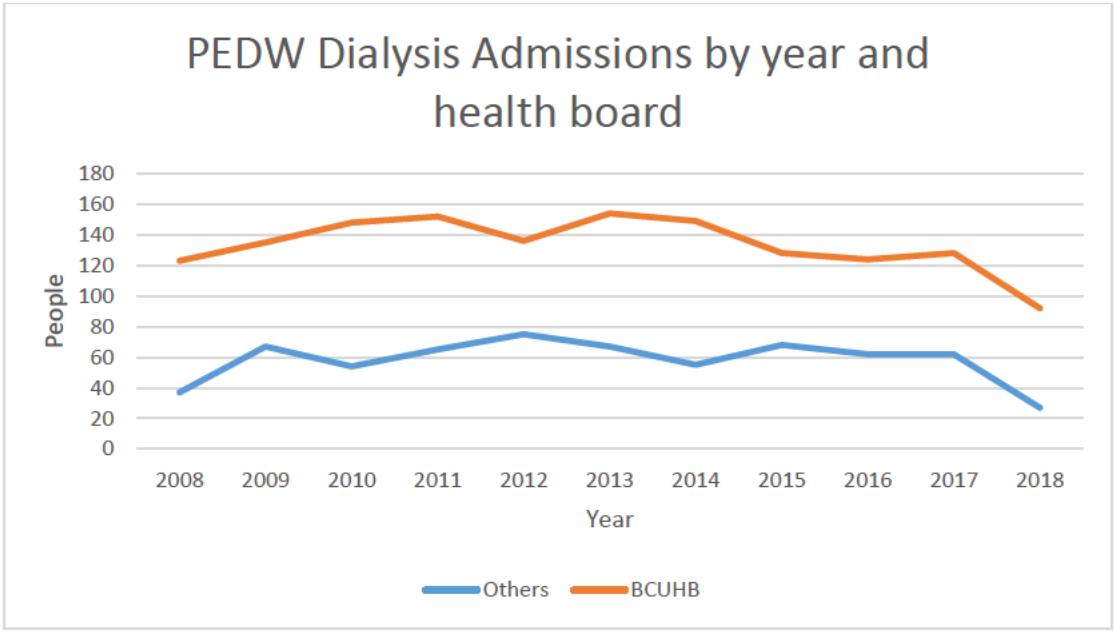
Graph 36 – Comparison with Renal Registry for Bangor dialysis (timeline and sessions)

Rhyl AWRD_R

In Rhyl they mostly used a paper-based system until 2015. I travelled to Rhyl to review the paper-based system and soon realised that it would not be possible to extract all the haemodialysis information from this system. This was because some of this was incomplete and relied on names without other demographics such as hospital or NHS numbers. However, discovered that each haemodialysis sessions was entered as a hospital admission on the patient administration system. Following this finding I was able to locate the admission in the PEDW dataset in SAIL using this SQL code;

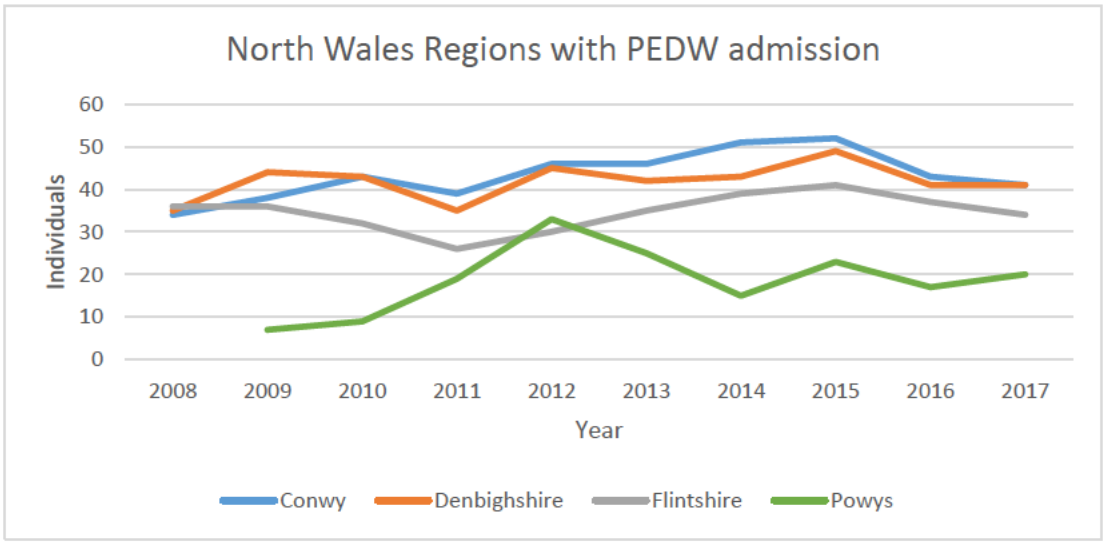
```
Select a.* from SAIL0505V.PEDW_SPELL_20190515 a
WHERE hrg_referencecost_desc  IN
        ( 'Chronic Kidney Disease with length of stay 1 day or
        less associated with Renal Dialysis',
        'Chronic Kidney Disease with length of stay 1 day or
        less, associated with Renal Dialysis')
        OR  hrg_referencecost_desc LIKE 'Same Day Dialysis
        Admission or Attendance%')
```

The dialysis treatments by year are shown below from PEDW are shown below;



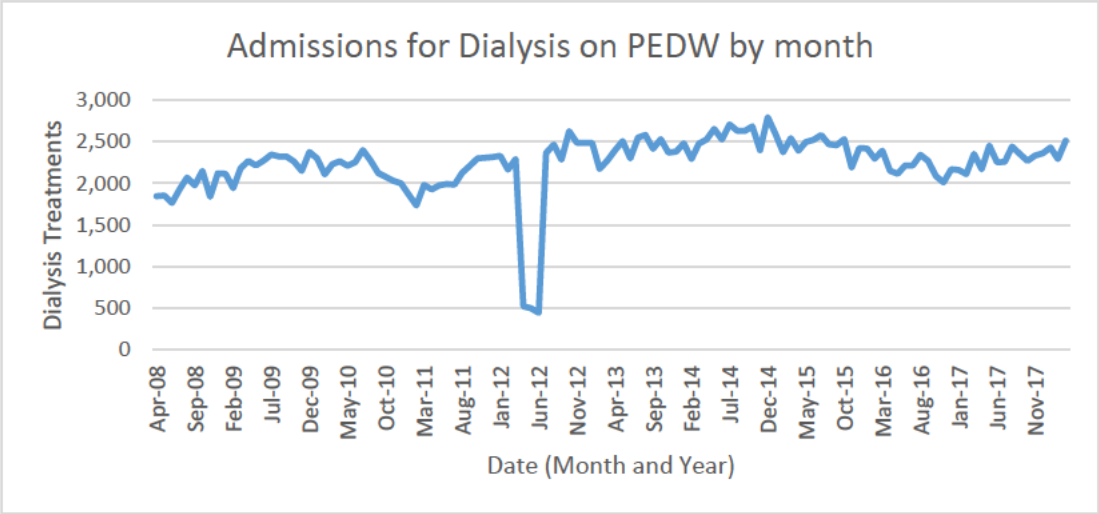
Graph 37 – Rhyl dialysis sessions in PEDW

These sessions are mostly in BCUHB and if we look at the local areas of these patients, we can see that most of these are in the area that was covered by Glan Clwyd dialysis unit (Rhyl);



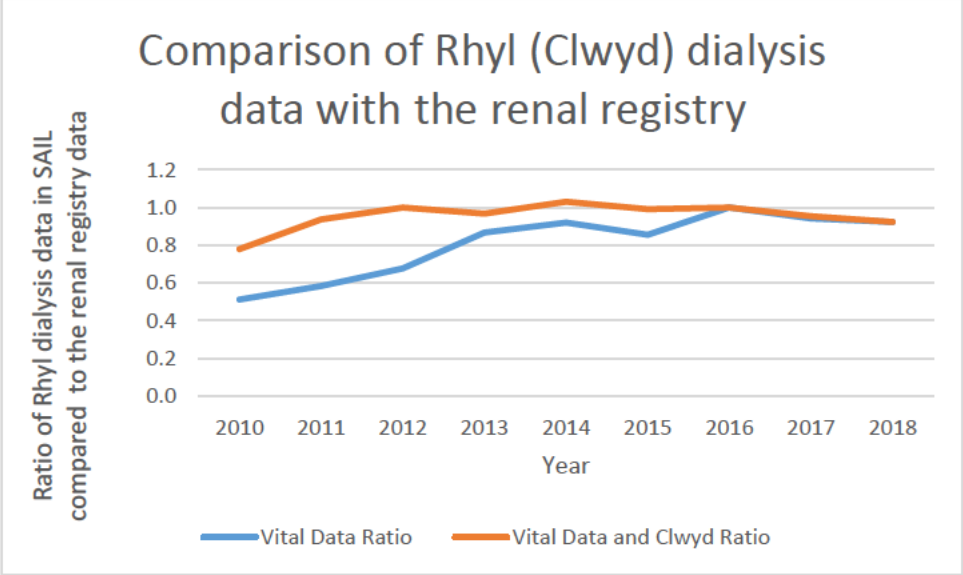
Graph 38 – Rhyl dialysis sessions in PEDW by local area

This data was put into a dialysis spell in the same way as the individual dialysis treatments from the AWRD (Vitaldata), discussed later (page 149). Interestingly, there was a drop in the dialysis treatment sessions in 2012 which represents Glan Clwyd when reviewed;



Graph 39 – Individual dialysis sessions by month

This drop in treatment sessions falls outside the study period and does not have an effect on the prevalence of dialysis compared to the renal registry as shown below;



Graph 40 – Comparison of Rhyl dialysis (timeline and sessions) data with renal registry

Rhyl Peritoneal Dialysis

The peritoneal dialysis patients are not included in PEDW, therefore I gathered the information on these patients from the paper records. Unfortunately, the paper records were of relatively poor quality in that some of them did not have the exact date of starting or ending

of the treatment and they did not have NHS numbers or date of births recorded. However, I was able to obtain these by asking an admin staff in Glan Clwyd (Rhyl Hospital) to find this information based on the hospital number and names. This record was then imported into SAIL and it contains 53 patients (67.9% male).

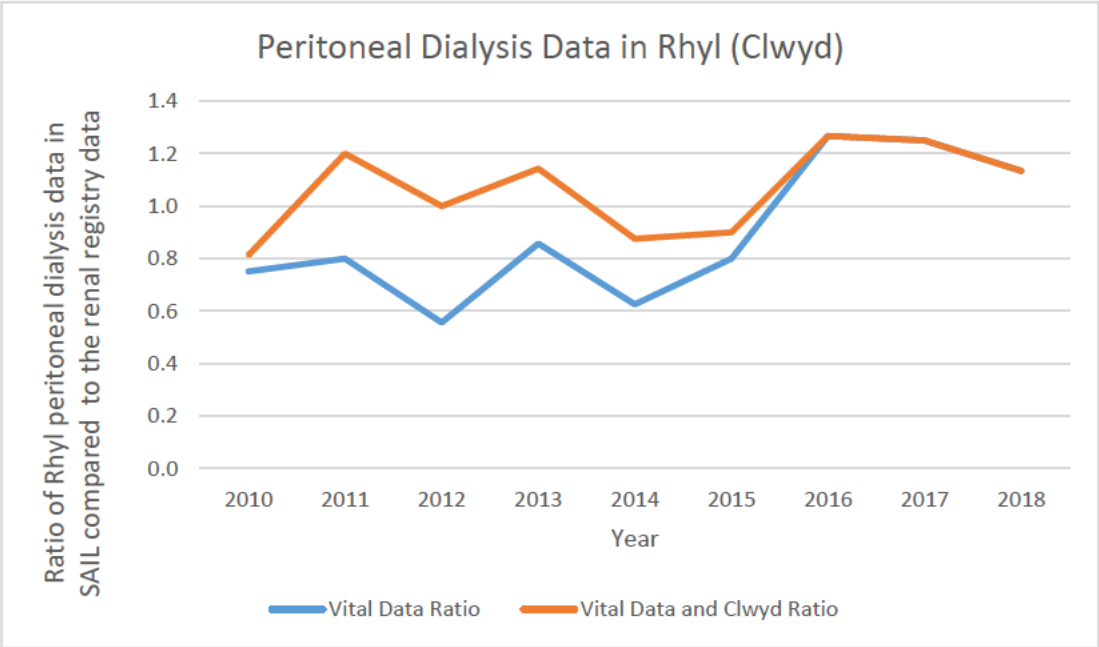
PD Table

The PD table (AWRD_R_PD_20190829) contains a peritoneal dialysis timeline for 53 patients.

Columns	Comment
SYSTEM_ID_PE	Unique ID for linking with File 3
START_DATE	Date of start of treatment
END_DATE	Date of end of treatment
COMMENT	Reason for end of treatment
2011	Name in 2011 PD record
2012	Name in 2012 PD record
2013	Name in 2013 PD record
2014	Name in 2014 PD record
2015	Name in 2015 PD record
DOD	Date of death
AVAIL_FROM_DT	Record in Vitaldata (column name is wrong in SAIL)

Table 30 – Peritoneal Dialysis Rhyl

Using this peritoneal dialysis data, I was able to improve the quality of the peritoneal dialysis data for Rhyl in SAIL;



Graph 41 – Comparison of Rhyl peritoneal dialysis data with renal registry

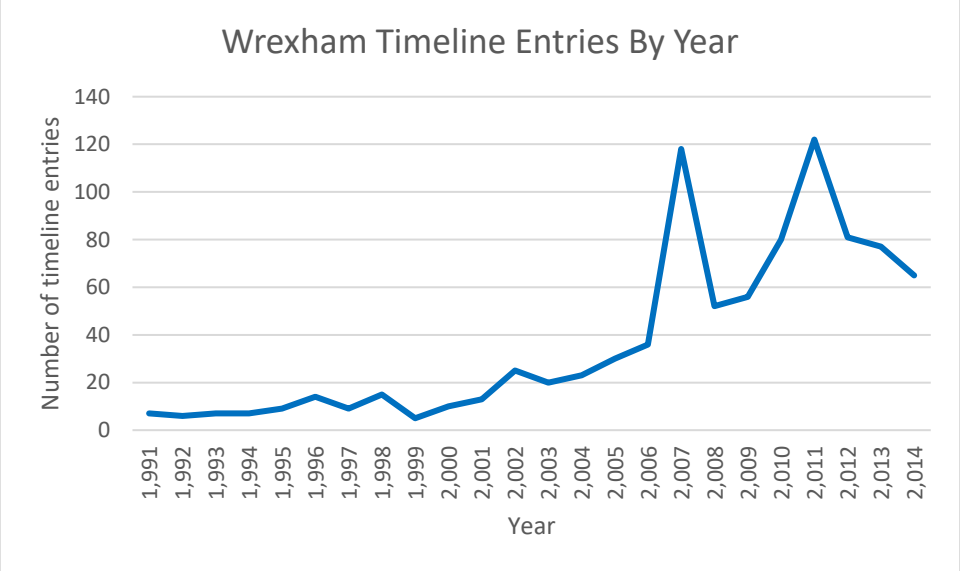
Wrexham AWRD_W

The historic data from Wrexham was stored in a system called 'RenalPlus©'. This system was archived following the transfer to Vitaldata. We were able to get access to the server for this system and therefore able to get the historical data to update the data for this region. This data was then cleaned and imported into SAIL in the AWRD_W tables. In this dataset there are 3,403 people, 56.2% of these were male. The timeline table was in a similar format to the Cardiff and Morriston (Swansea) timelines, the useful columns are below;

Columns	Comment
SYSTEM_ID_PE	Unique ID for linking with File 3
WREXHAM_TIMELINE_DATE	Date of Modality Start
WREXHAM_TIMELINE_MODALITY	Modality

Table 31 – Wrexham Timeline

There were 904 timeline entries between February 1976 and October 2014. The frequency of these entries increased in the later years of RenalPlus © use as shown below;



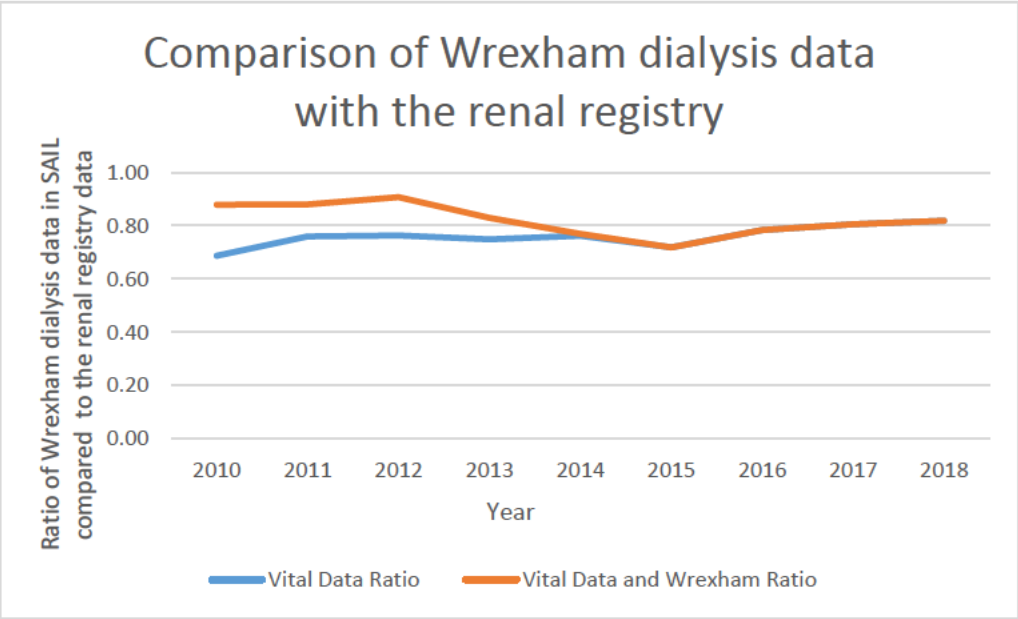
Graph 42 – Wrexham timeline entries from Renalplus ©

Unlike other timeline datasets, there are no entries of recovery of renal function or death. The different modalities are shown below;

WREXHAM_TIMELINE_MODALITY	Meaning
APD	Peritoneal dialysis (automated)
Acute	Acute haemodialysis
CAPD	Peritoneal dialysis (Continuous ambulatory)
Elsewr HD	Out of area haemodialysis
Elsewr PD	Out of area peritoneal dialysis
Elsewr TX	Out of area transplant
HD	Haemodialysis
HHD	Home haemodialysis
PlasmaX	Plasma exchange
T/P – cad	Transplant – cadaveric donor
T/P – live	Transplant – live donor
Trans Out	Transferred out

Table 32 – Wrexham timeline codes

With this data, there was an improvement in the comparison with the renal registry data, nevertheless, the Wrexham data are the least complete;



Graph 43 - Comparison of Wrexham dialysis data (timeline and sessions) with renal registry

The application of these renal datasets is discussed in the next section Chapter 3 – The Creation of AKI Cohort.

Summary

This chapter outlines the datasets that are to be used to create the cohort of patients with serum creatinine values and AKI. From this chapter we can see how the datasets perform over time. Some of these datasets have been used in previous research and publications (235, 236, 248, 249)(Primary care, hospital episodes, death dataset) whereas others have not (Pathology datasets and the renal dataset). In this chapter, we can see when these datasets develop a period of consistent results and how they perform against comparators, such as the all Wales pathology (PATH) when compared with the ABMUHB dataset (PAMO) or the all Wales renal dataset (AWRD) when compared to the renal registry data. Now that we have established confidence in these datasets, we can now set about creating an AKI cohort.

Chapter 3 – The Creation of AKI Cohort

Introduction

This chapter uses these aforementioned datasets to create a cohort of patients with AKI within SAIL. It demonstrates how this cohort can then be used to study the serum creatinine (SCr) testing frequency and incidence of AKI in Wales. The creation of this SCr identified AKI cohort requires complex SQL code, therefore the help of a SAIL analyst and coder, Gareth Davies (GD) was needed. We worked closely together to create the cohort with me scrutinising his output along the way, using the coding knowledge I had developed. This next section explains the difficulties encountered, problems with cleaning the data and mitigations we put in place. It clarifies how a renal replacement cohort was created allowing for the accurate identification of patients on dialysis and talks through the steps needed to develop a copy of the NHS England AKI algorithm within SAIL to produce a cohort of non-dialysis patients with AKI.

The AKI table was created using the following method;

Table 34

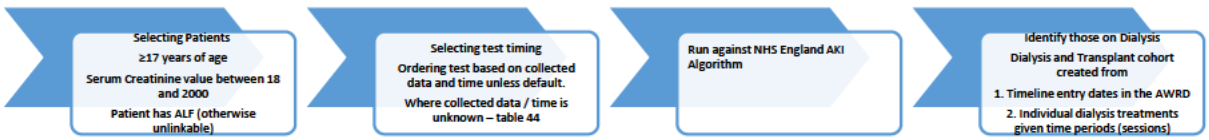


Figure 22- Creation of AKI table

Pathology data cleaning

To identify patients with AKI, we must first identify all patients at risk. At the beginning of this study the WRRS PATH dataset was not available in SAIL therefore we used the available biochemistry data to create and test this code. This was done by using the Abertawe Bro

Morgannwg University Health board (ABMUHB) tables in PAMO (Swansea) and PABR (Bridgend), forming a union as previously described (page 88).

To create an accurate cohort, we need this sample to include only patients with serum creatinine (i.e. Not urinary or other non-blood test creatinine values). This can be done by just using results where 'TEST_CD' is 'CREAT' in the Bridgend dataset. In the Swansea dataset it was not quite as simple, it involved selecting samples where 'TEST_CD' is 'CREA' or 'ECRE' (Enzymatic assay) but then also where 'SPCM_TYPE_CD' is B (blood) or S (Serum). Another way to help exclude those patients with erroneous creatinine was to remove patients with extremely high serum creatinine (SCr) values, i.e. >2000µmol/L. We also excluded tests below the reference range, which in ABMUHB was <18 µmol/L.

We included only adult patients i.e. ≥18 years of age, however in order to identify these patients, we need to make sure we include patients >17 at time of the sample. This was because we are using a one year look back for baseline creatinine value, so this allows inclusion of these patients. The columns of this table are displayed in the appendix on page 325.

Patients without ALF_PE cannot be linked, therefore they were excluded from the analysis. Likewise, those without 'WOB' (Week of Birth) also require exclusion as the person's age is unknown. When a WOB was missing the patients usually get allocated a default WOB of 1900-01-01. In view of this, any patients with a year of birth < 1901 were excluded. This means, when reviewing the earliest dataset, i.e. 2004 with the Swansea pathology data, those >103 years of age were be excluded (<0.1%).

The result of this cleaning, and the union of these tables created a SCr blood test cohort. This includes all those at risk of AKI by the SCr definition.

Following the introduction of the all Wales pathology data (PATH), this method was then reproduced to create the creatinine test cohort used in the subsequent research chapters.

Test Timing and rules used

One of the potential problems with the implementation of the AKI algorithm in clinical practice, was that tests on the same day may be wrongly ordered chronologically. This may occur if the time of sample was not recorded (n=1,303,547, 18.4% in ABMUHB data), therefore a default time was entered by the pathology staff. An example of where this would cause an alert error is; if a sample was taken in a general practice (GP) and arrives in the hospital after the patient has been admitted and had bloods in hospital. I have shown two patients below, as an example of how this may come about;

Pt	Sample lab. ordering	Date Collected	Time Collected	Date Received	Time Received	Result	Alert	Source
1	1	19/01/16	00:00	20/01/16	01:00	86	No	MAU
1	2	19/01/16	06:30	19/01/16	08:30	40	No	MAU
2	1	19/01/16	17:30	19/01/16	17:40	80	No	A&E
2	2	19/01/16	11:00	19/01/16	18:00	50	No	GP

Table 33 – Example of how timing of test can lead to misinterpretation of AKI alerts

(MAU is Medical Admissions Unit; A&E is Accident and Emergency; GP is General Practice)

In patient 1 it is likely that the first sample was sampled from the patient after the second. This is inferred by the time difference between the second sample being taken and received (i.e. 2 hours). Sample one was the same location, but the time is the default time (suggesting an unfilled in blood form). In this example, if we assumed that the time it took to get the sample to the laboratory was the same as the first, then in fact we are looking at 23:00 being the time of the sample, which is 23 hours after the default for 'time collected'. In this case this patient would have AKI stage 1. This is a problem for use using retrospective data. It is not documented in the available resources how the laboratory would have processed this in clinical practice with regards to the alerts. Patient 2 shows the problem with using time received as it orders tests differently to the collection time and date. Again, this patient has been erroneously labelled as not having AKI, however sample 2 taken at the GP practice was taken before 1 but received in the laboratory later. This means that sample 1 is processed first (and therefore the algorithm is run) resulting in the absence of the alert.

To get around this we have created some rules on test timing to try and maintain the actual order of testing, the highlighted cells are the ones we use to define the data and time;

Pt	Date Collected	Time Collected	Date Received	Time Received	Comments	Number
1	19/01/2016	23:00	20/01/2016	01:00	Both accurate	5,721,775
2	19/01/2016	Null	19/01/2016	08:30		1,276,337
3	19/01/2016	Null	20/01/2016	10:40		12,578
4	Null	Null	19/01/2016	18:00		12
5	19/01/2016	88:88	19/01/2016	20:00		2,010
6	19/01/2016	88:88	20/01/2016	10:00		49
7	19/01/2016	99:99	19/01/2016	21:00		128
8	19/01/2016	99:99	20/01/2016	10:10		
9	19/01/2016	00:00	19/01/2016	21:00	where DATA_SOURC‘ = ’SWA'	54,421
10	19/01/2016	00:00	20/01/2016	12:01	where DATA_SOURC‘ = ’SWA'	264

Order – Yellow is selected field

1. Where date collected and time collected
2. Date collected matches date received but time default – Use received time
3. Where time collected is ‘Null’, but date collected does not match date received – use date and time received
4. Only received details available – Use them
5. – 10. describe the same problems as 1.-4. But instead of ‘Null’ use a default number

Table 34 – Handling used for missing test timing

Where date and time collected are filled appropriately, we used that date and time (Pt 1), however if it was a default time, we used a few different methods. To enable compatibility in SAIL the times 88:88 and 99:99 needed to be given a 24-hour clock time. Fortunately, due to the second PABR dataset being smaller than the other two datasets, there were a couple of times without a test (02:57 and 03:49), so we changed these times to the default times. To negate this problem, where a default time was used (00:00 in PAMO, 88:88 or 99:99 in the second PABR dataset, or where the entry was null – mainly in the first PABR upload) we used the received time and date.

Identifying AKI patients

NHS England Algorithm

The NHS England AKI algorithm has been used across England, Scotland and Wales to create electronic AKI alerts. It uses SCr values and can classify AKI according to the KDIGO staging. The schema for this algorithm is displayed on this page (157) and there is text explanations in the appendix (322);

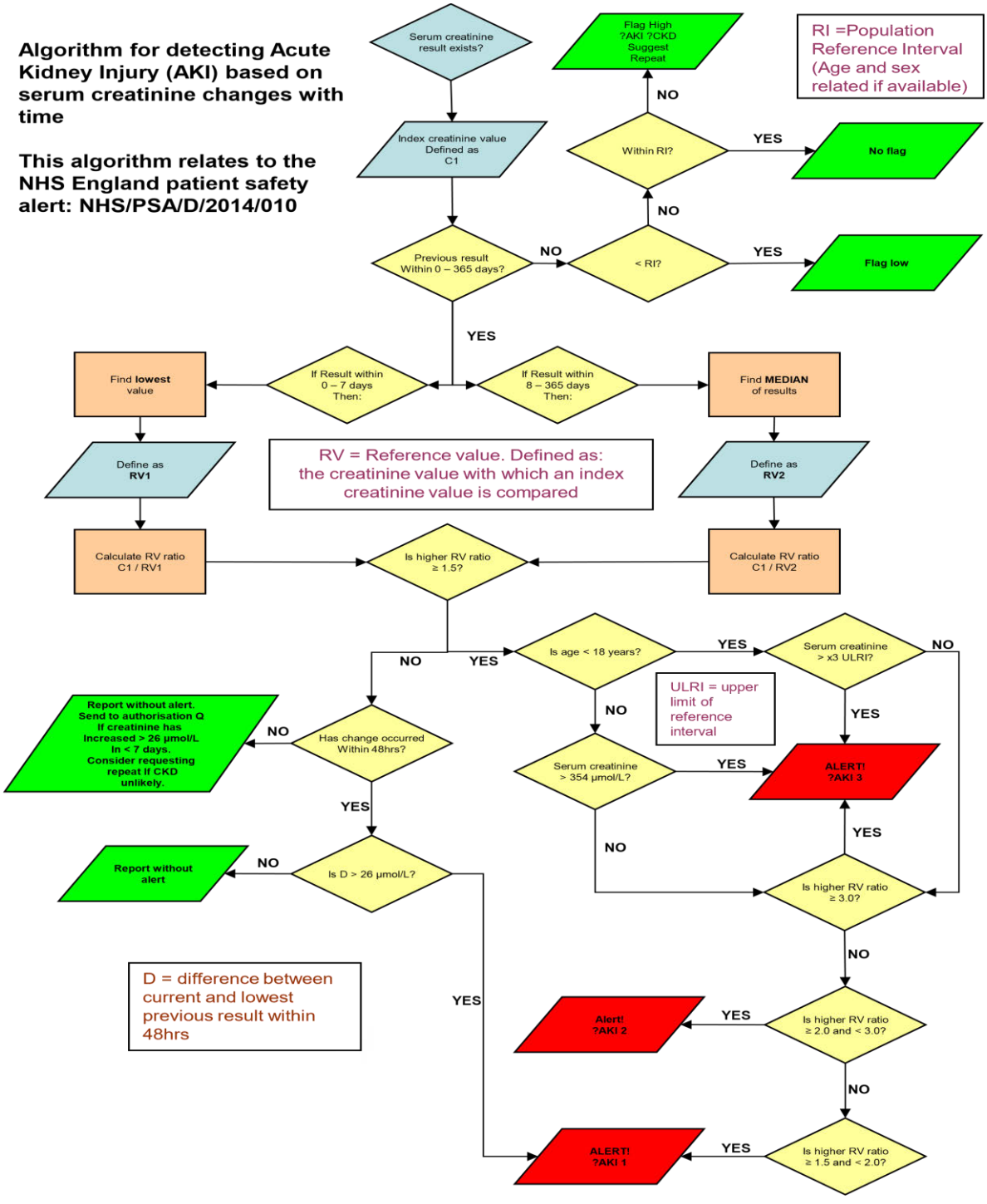


Figure 23 - NHS England AKI alert algoirthm schema

We have adapted our version of this algorithm to run within SAIL in SQL language. To validate this, I created a dummy dataset to test this algorithm. From this we identified some changes that were required and made adjustment to the algorithm. The dummy dataset was created with the idea of picking up any small problems, such as the use of less than, instead of less than or equals to, or problems with date and time analysis, for example a creatinine 366 days prior to the index sample should not be used as a baseline creatinine. An example of this test data are shown in the table below with the results of the trial;

NUMBER	PREV. CR	RV1	RV2	RV2	RV2	DAY 1	DAY 2	DAY 3	DAY 7	ALERT
	31/10/2015	31/10/2016	08/11/2015	09/11/2015	10/11/2015	01/11/2016	02/11/2016	03/11/2016	07/11/2016	
1	20					57				FLAG LOW
2	20					45				FLAG LOW
3	20					110				NO FLAG
4	20					58				NO FLAG
5	20					92				NO FLAG
6						46				NO FLAG
7							111			FLAG HIGH
8								111		FLAG HIGH
9									111	FLAG HIGH
10						93				FLAG HIGH
11			81	82	83	122	122			REPORT WITH NO ALERT
12		80				106				NO ALERT
13		80				107				AKI1
14			73	74	75	355				AKI3
15			117	118	119	354				AKI3
16			151	152	153	354				AKI2
17			100	101	102	300				AKI2
18			149	150	151	300				AKI2
19			75	76	77	150				AK1
20			100	101	102	199				AK1
21			149	150	151	200				No ALERT
22		100				354				AKI3
23						100	200	300	355	AKI3
24		100				101	300			AKI3
25		20					90			AKI3
26		50						149		AKI2
27		50						100		AKI2
28		50						99		AKI1
29		50						75		AKI1
30		100				126				NO ALERT
31		100				127				AKI1
32		100						127		NO ALERT

Table 35 - Testing of the algorithm

Aberdeen algorithm

As part of a collaboration across the Farr institute, we used an algorithm created by the Grampian group using STATA© created by Simon Sawhney which has be published and validated (118). This code was not exactly the same as the NHS England eAlert algorithm, it contains a few adjustments such as fixing the baseline creatinine when the first AKI was identified, using a median SCr for a period of the last 8-90 days, then the same for 91-365 days if no previous samples are available before that (the NHS England algorithm just uses a median of 8-365). We have used this to help validate and check our code, as it creates a similar number of AKI alerts (250).

Creating the Renal Replacement cohort

To get an accurate picture of AKI, we needed to exclude patients who are undergoing dialysis treatment. We are able to do this with precision using the All Wales Renal Dataset (AWRD). This is mainly comprised from the Vitaldata system which is currently used across Wales. Wales is divided into 5 regional renal teams (most have one or more satellite dialysis units). The two largest are in South Wales in Swansea and Cardiff. These two centres have used a system called Vital Data developed by VitalPulse© for the past 15 years. There have been separate developments in these systems at the two sites, so there are differences, hence they had their data uploaded to SAIL separately. In 2015 the 3 smaller sites, based in North Wales (Bangor, Rhyl and Wrexham) transferred their data into the Cardiff Vital Data database including all active patients at that point. The detail and the thoroughness of the timeline and dialysis sessions data varies between sites. To maximise the sensitivity in identifying patients on dialysis we have used two methods of recognising them. One was based on the timeline information, which was information used by the UK renal registry to identify patients on dialysis and was recorded as a date and coded modality. The other method was based on individual dialysis treatment sessions.

The North Wales region lacks some historical dialysis data. This was because only data on active patients was imported into Vital Data excluding those who had moved from the area or who had died. As a result, I sort to improve the data from the 3 North Wales sites and included this in the renal replacement cohort table.

Of note, acute dialysis (people treated with dialysis for < 3 months) was unreliable in Vitaldata as historically it has not been collected by the United Kingdom Renal Registry (RR). This was particularly the case in intensive care unit based dialysis, however this was recorded in the Critical Care Dataset (CCDS).

Timeline Table – RRT1

The first method used to find dialysis patients was based on their timeline information in the same way as that used by the renal registry (251). The timeline entries are done using codes which cover a variety of different renal replacement (RRT) techniques, as well as transplant work up, recovery, transfer of care and death, amongst others. We used SQL code to identify the start codes and end codes of renal replacement (see page 313 in the appendix). After ordering the dates chronological we utilised these codes to create a row in the timeline table. In this table, a patient with a timeline modality of RRT starts a new row with any subsequent change of modality starting a different row. Some patients transfer between the Cardiff and Morriston dataset, particularly if they had a kidney transplant, as such, a more accurate picture was created by reviewing each dataset individually and then combining them (called union). This table was called RRT1 and the steps are outlined in the next image, and explained in greater detail below;

Figure 24 - Creation of dialysis timelines

Step 1

To facilitate this table creation, I created a combined timeline, demographic and dialysis sessions table from the two sources (Cardiff and Morriston) with a column called FIELD_1 identifying these two sites (see page 313 of the appendix).

Step 2

After we combined these tables, we pooled timeline codes into different categories. Any timeline entry that are the start of a RRT treatment were termed start triggers. These triggers are sub-categorised into; 'HD' for haemodialysis, 'PD' for peritoneal dialysis, 'Acute' for acute dialysis and 'Transplant' for kidney transplantation. Breakdown of these definitions are included in the appendix (page 313).

We also categorised entries that end a therapy (End triggers), these fell into 4 definitions; 'Death', 'Recovered', 'Transferred Out' and 'Stopped'. Again, the breakdown of these are included in the appendix (page 313).

We gave these categories a hierarchy. This was to allow a true ordering of the timeline events based on date and entry. This was particularly important with transplant patients, because they potentially also get 'Transferred out' for the transplant. This will often happen on the same day in the timeline, so if the transplant was ordered first then it will be immediately closed as a session by the transfer out. A similar thing can happen with death. The hierarchical order is shown below;

Trigger	Order
Acute	1
HD	2
PD	3
Stopped	4
Recovered	5
Transferred out	6
Transplant	7
Death	8

Table 36 - Timeline trigger hierarchy

This allowed for the correct ordering of a timeline, an example of how this looked is shown below in a fictional patient;

Patient Number	Timeline Date	Timeline code	Timeline Meaning	Category
1	12/11/1999	19402	Registration	Null
1	20/02/2002	140264	Opted For HD	Null
1	13/06/2002	19301	Haemodialysis	HD
1	13/09/2002	19304	Haemodialysis > 4 days per week / daily	HD
1	14/09/2002	5151	Activated on Transplant list	Null
1	18/06/2003	19338	Patient transferred out (RRT)	Transferred Out
1	18/06/2003	19321	Transplant; Live related - sibling	Transplant
1	20/08/2005	5280	Acute Dialysis ITU	Acute
1	26/08/2005	-310	Transplant recovered function	Transplant
1	01/09/2009	19301	Haemodialysis	HD
1	05/12/2009	19310	CAPD standard	PD
1	30/01/2010	19312	Cycling PD >= 6 nights /wk dry	PD
1	12/05/2012	19301	Haemodialysis	HD
1	13/06/2013	19391	Patient choice- treatment stopped (without recovery of function)	Stopped
1	15/07/2013	19370	Died	Died

Table 37 - Timeline representation

In this example '-310' meaning Transplant recovered function was categorised as 'Transplant', this was for ease of coding (not 'Recovered'), because this needs to start a new transplant period since the graft is now functioning. The timeline codes with 'Null' in the category are not start or end triggers and are therefore excluded from analysis.

Step *3*

The categorisation of these codes allows for the creation of treatment episodes. An episode was started by a start trigger (HD/PD/Acute/Transplant) and then ended by a different start trigger or an end trigger (Recovered/Transferred Out/stopped/Death). Using these definitions we then created a table with rows where a 'Start Reason' trigger also filed it's 'End Reason' and a 'End Reason' trigger had 'null' for 'Start Reason. This is shown below;

Patient Number	Start Reason	Start Date	End Reason	End Date	True End
1	HD	13/06/2002	HD	13/06/2002	0
1	HD	13/09/2002	HD	13/09/2002	0
1	NULL	NULL	TRANSFERRED OUT	18/06/2003	1
1	TRANSPLANT	18/06/2003	TRANSPLANT	18/06/2003	0
1	ACUTE	20/08/2005	ACUTE	20/08/2005	0
1	TRANSPLANT	26/08/2005	TRANSPLANT	26/08/2005	0
1	HD	01/09/2009	HD	01/09/2009	0
1	PD	05/12/2009	PD	05/12/2009	0
1	PD	30/01/2010	PD	30/01/2010	0
1	HD	12/05/2012	HD	12/05/2012	0
1	NULL	NULL	STOPPED	13/06/2013	1
1	NULL	NULL	DIED	15/07/2013	1

Table 38 - Timeline start and end triggers only

In this table, there is an extra row called 'True End', this was used to flag those timeline codes where it was just an 'End Reason'. This was important for the next step.

Step 4

Using the table above, Gareth Davies used a 'Lead' code to take the 'End Reason' from the subsequent row where the patient's ALF number matched. This is shown in the tables below;

Patient Number	Start Reason	Start Date	End Reason	End Date	True End
1	HD	13/06/2002	HD	13/06/2002	0
			↑		
1	HD	13/09/2002	HD	13/09/2002	0
			↑		
1	NULL	NULL	TRANSFERRED OUT	18/06/2003	1
			↑		
1	TRANSPLANT	18/06/2003	TRANSPLANT	18/06/2003	0
			↑		
1	ACUTE	20/08/2005	ACUTE	20/08/2005	0
			↑		
1	TRANSPLANT	26/08/2005	TRANSPLANT	26/08/2005	0
			↑		
1	HD	01/09/2009	HD	01/09/2009	0
			↑		
1	PD	05/12/2009	PD	05/12/2009	0
			↑		
1	PD	30/01/2010	PD	30/01/2010	0
			↑		
1	HD	12/05/2012	HD	12/05/2012	0
			↑		
1	NULL	NULL	STOPPED	13/06/2013	1
			↑		
1	NULL	NULL	DIED	15/07/2013	1

Table 39 - Timeline handling 1

This results in the following table;

Patient Number	Start Reason	Start Date	End Reason	End Date	True End
1	HD	13/06/2002	HD	13/09/2002	0
1	HD	13/09/2002	TRANSFERRED OUT	18/06/2003	0
1	NULL	NULL	TRANSPLANT	18/06/2003	1
1	TRANSPLANT	18/06/2003	ACUTE	20/08/2005	0
1	ACUTE	20/08/2005	TRANSPLANT	26/08/2005	0
1	TRANSPLANT	26/08/2005	HD	01/09/2009	0
1	HD	01/09/2009	PD	05/12/2009	0
1	PD	05/12/2009	PD	30/01/2010	0
1	PD	30/01/2010	HD	12/05/2012	0
1	HD	12/05/2012	STOPPED	13/06/2013	0
1	NULL	NULL	DIED	15/07/2013	1
1	NULL	NULL	NULL	NULL	1

Table 40 - Timeline handling 2

Step 5

Using this table, we can then delete rows where the Start Reason was null and when the True end trigger was “1”. This gives an accurate timeline picture for these patients;

Patient Number	Start Reason	Start Date	End Reason	End Date
1	HD	13/06/2002	HD	13/09/2002
1	HD	13/09/2002	TRANSFERRED OUT	18/06/2003
1	TRANSPLANT	18/06/2003	ACUTE	20/08/2005
1	ACUTE	20/08/2005	TRANSPLANT	26/08/2005
1	TRANSPLANT	26/08/2005	HD	01/09/2009
1	HD	01/09/2009	PD	05/12/2009
1	PD	05/12/2009	PD	30/01/2010
1	PD	30/01/2010	HD	12/05/2012
1	HD	12/05/2012	STOPPED	13/06/2013

Table 41 – Example Table with triggers only after removing rows with null Start Reasons

Where there was a start reason but the end reason was null, we changed the End Reason to 'Ongoing' and the End Date to 2999-01-01, as this means the treatment was ongoing according to the dataset at the time of extraction.

Step 6

The timeline table was created using the Morriston (Swansea) and Cardiff data separately. This meant that a Swansea dialysis spell was not stopped by a Cardiff end trigger. I anticipated that there may be contradictions between the two data sources. To correct this, I wrote code to check patients who had entries from both sources. The diagram below shows the handling of the two data sources;

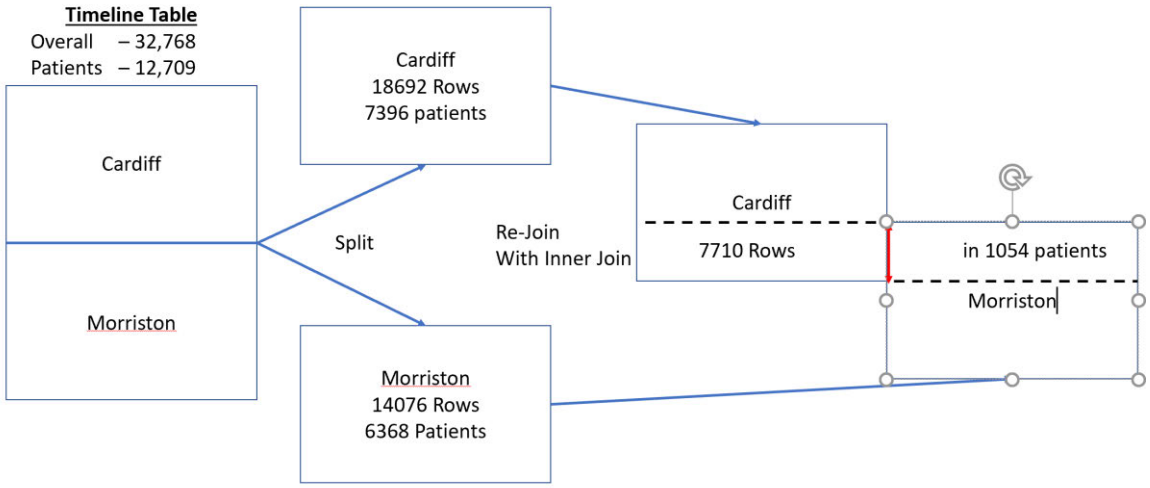


Figure 25 - Cardiff and Swansea dialysis combination

Using this output, I manually reviewed the treatment spells of these 1054 patients to check for contradictions that would affect our AKI research. For example, in one dataset dialysis was ongoing, whereas the other had a subsequent kidney transplant. We then manually changed these entries and there were less than 100 of these. These changes were recorded in SAIL and cannot be extracted from the data safe haven due to potential risk of de-anonymisation of records.

Step 7

The timeline table was joined with the dialysis treatment table to give dialysis session counts for the spell and in total. The total dialysis sessions count (DS_TOTAL_CT), counts all sessions including future sessions.

This allows for the creation of this table below;

Column Name	Description	Timeline Table
ALF_PE	Unique patient ID	ALF code
TST_CODE	Timeline Start Trigger	T9MOD code
START_DT	Start Date	Start Date
START_REASON	Timeline Description	Acute, HD, PD, Transplant
TET_CODE	Timeline End Trigger	T9MOD code
END_DT	End Date	End Date
END_REASON	Timeline Description	Start Reason, Death, Recovered, Stopped, Transferred out
DS_SPELL_CT	Dialysis Sessions Spell Count	Dialysis sessions between start and end date
DS_TOTAL_CT	Dialysis Sessions Total Count	Dialysis sessions in total (future and past)
RRT_TRIGGER	Row Source Code	1
ACUTE_TRIGGER	Acute trigger code	1 or 2 or 4
FIELD_1	Source of Data	C or M

Table 42 - Cardiff and Swansea combined columns

Difficulties encountered

The timeline table was not as easy to create as it seemed in theory. Initially we tried to create it using a loop code, before I realised that the above method would be more appropriate. One of the problems found was where acute patients had ongoing treatment (i.e. no later subsequent timeline start or stop triggers). This was picked up by examining the timeline table and filtering it to a start reason of acute and an ongoing end point. With these patients, we found some (mainly from the Cardiff renal system) that had acute triggers but no further timeline entries. For these patients I have applied a 90-day cut off. This is because acute

dialysis does not go beyond 90 days as it becomes chronic dialysis at that point. If someone has ongoing dialysis beyond 90 days then there should be dialysis session entries, which means the patient will be covered (and excluded from the AKI cohort) using that table. Another problem was that where the timelines from different sources (M or C) contradicted one another. I addressed this by manually reviewing all the patients who had entries in these two sources and correcting them. We also found some entries where there were clear errors such as the date of entry being 0211 instead of 2011, again we corrected the small number of cases like this, where the underlying data was entered incorrectly.

To help identify errors, I used the following method to spot problems, each time we tried to create the timeline cohort;

1. Apply filter, add column 'Date Difference' and apply this formula ("=END_DT-START_DT") using the grid codes to each row in the table.
2. Filter the following; START_REASON = 'ACUTE', COMMENT = 'ongoing'
    a. In these patients, particularly in the Morriston patients, there should not be long gaps between the START and END_DT.
    b. Where this was the case, I would look at that patient in the raw data in SAIL by joining the demographic and timeline data in eclipse© using SQL code. By doing this and choosing a few samples, I found many patients with 'Acute Haemodialysis' as their only timeline entries.
    c. This points to a problem in the way that data was recorded in that centre and not to a SQL syntax problem.
3. Applied filter, picked a modality (i.e. START_REASON = 'HD'), then sort by date difference.
    a. This original showed some with minus date differences pointing to Syntax code problems, which Gareth could correct.
    b. Those with long date differences I checked for any changes in treatment modalities between the Start and End_DT.
4. Filter the following; START_REASON = 'HD', END_REASON = 'TRANSPLANT'
    a. By reviewing those with long date differences here, there was the potential for spotting errors. You would not expect someone to be on dialysis for 10-15 years to then have a transplant (although it can happen). This would then

warrant further analysis, as outlined above and shown in the code in the appendix on page 318.

Adding Bangor timeline

Additional timeline data from Bangor was housed in the AWRD_B views outlined in the previous chapter (Bangor AWRD_B on page 123). The data are stored as an spell episode, not just an individual entry like the Morriston and Cardiff data. This means that it was in a similar layout to the RRT1 table. It does however need several corrections and adjustments. The first was to categorise the end codes in the dataset as shown in the appendix (page 319).

The next step was to remove the entries that are not relevant for the RRT table such as Bangor code – 'Pre' and 'Donor' and remove those where the end codes are 'NULL' and the Bangor codes are 'Death', 'Transferred Out', 'Withdrawn' and 'Recovered Function'. This was because these appear to be automatic entries / duplications, the previous row for these patients will have appropriate start codes (Bangor code) and End code. Therefore, they have no role, and this was confirmed by reviewing the 100 or so times this occurred.

There are some with 'NULL' end codes (n=170, 15.6%), of which 49 had a death date, which we used to replace the end date and change the end code to 'Death'. In those remaining, without an end code, it can be assumed that they are still on RRT, in which case they should be in the initial RRT1 table (from AWRD_C). In the cases where they are in the RRT1 table we ended their AWRD_B based session by the start of a spell in the RRT1 table if the start date of the Bangor data was before the start date in the other dataset. By carrying out these steps, the Bangor table could be added to the RRT1 table.

Adding Rhyl timeline

The peritoneal dialysis (PD) timeline for Rhyl was stored in the AWRD_R, this has been collected manually by myself as there were only paper copies of the record. The data was collected securely and entered into the NHS digital systems prior to uploading before adjusting to create a PD timeline (Rhyl Peritoneal Dialysis). Some patients did not have dates for the start (n=38, 71.7%) and some did not have dates for the end of their treatment (n=24, 45.3%). For these patients, their treatment was recorded by year between 2011 to 2015. To

create a timeline, I used evidence of PD in a year to count the whole of that year as PD treatment when there were no clear start or end dates i.e. 01/01/YEAR as the start date and 31/12/YEAR as the end date. 19 of the patients (35.8%) had records showing PD in 2011, some of these will have been started on PD before 2011. If the patient does not have an end date, but they have died in a year that they have a record, then I have used the date of death (DOD) as the end date. A theoretical example is shown below;

Pt	Start Date	End Date	2011	2012	2013	2014	2015	DOD
1	02/02/2009	04/05/2014	1	1	1	1	0	04/05/2014
2	[NULL]	[NULL]	1	1	1	1	1	[NULL]
3	28/04/2012	[NULL]	0	1	1	0	0	12/12/2013
4	[NULL]	06/06/2014	0	1	1	1	0	[NULL]
5	03/10/2011	[NULL]	1	1	1	0	0	[NULL]

Pt	Start Date	End Date
1	02/02/2009	04/05/2014
2	01/01/2011	31/12/2015
3	28/04/2012	12/12/2013
4	01/01/2012	06/06/2014
5	03/10/2011	31/12/2013

Table 43 - Rhyl peritoneal dialysis timeline

This PD table was then formatted into a table that allowed for the union with the RRT1 table. There were no haemodialysis timeline records for Rhyl, however there were printouts of dialysis treatments, after initially starting to collect this data, it was soon apparent that this data was available in the PEDW dataset, therefore it was collected as dialysis treatment sessions and is explained later on page 152.

Adding Wrexham timeline

The final timeline table requiring addition to the RRT1 table was the Wrexham timeline table. This was in a similar format to the timelines in the AWRD_C and AWRD_M, however there

were very few end codes. The initial step was to categorise the WREXHAM_TIMELINE_MODALITY as shown in the Appendix (page 319). Once this was done, then the individual timeline entries needed to be turned into a spell as per steps 3, 4 and 5 previously mentioned (pages 141 to 143). There are very few end codes in the Wrexham dataset, therefore many of the spells are left without end reasons and dates. To address this, we have created a few rules;

1. Where the WREXHAM_TIMELINE_MODALITY is 'Acute' and there is no end – an end date of 90 days from the start date is added and the end reason becomes – 'Presume Recovered'
2. Like with the Bangor dataset, where there is no end date and reason, but the person is already in the RRT1 table (from AWRD_C_), then use the start date after the Wrexham episode to end this spell.
3. If the person is not in the RRT1 table but they have died, then the death is used as the end date and reason.
4. Finally, if they are not in the RRT1 table and they are not deceased then the date 01/01/2015 is used as the end date and the end reason is adjusted to 'Presume Recovered'.

This was then added to the RRT1 table to create a completed timeline table (RRT 1) using union function. This completed RRT1 timeline table now contains data from the Cardiff and Morriston data (from Vital Data ©) as well as the additional Bangor, Rhyl and Wrexham data.

Dialysis Session Table – RRT2

Within the AWRD there are records of individual haemodialysis treatment sessions. Using these sessions, we can create spells of haemodialysis sessions. The data recorded in these records varies by site. In some patients, the timeline may not be complete, particularly in people dialysed for less than 90 days, i.e. less than the renal registry definition of incident chronic dialysis which requires timeline recording. Using the dialysis sessions, we looked to negate this problem. Each time a patient was dialysed there should be an entry for that session. The first dialysis treatment starts an episode, then the stop date is triggered by a gap of 14 days. The steps described, are the initial steps used for the Cardiff (AWRD_C) and Swansea (AWRD_M) data before the additional datasets were added;

Step 1

To create this cohort, Gareth used the combined HD treatment table ordering patients by ALF_PE and then dialysis date. We gave each session a row number for that patient using this order. We made a date difference column, which calculated the date difference between the date of the current row minus the previous row for that patient. This means that the first row was always null. Therefore, we also added a second date difference row which was the future row, minus the current row date;

	A	B	C	D
1	**PT**	**Date**	**Date Diff1**	**Date Diff2**
2	1	29/08/2001	Null (=B2-B1)	20 (=B3-B2)
3	1	18/09/2001	20 (=B3-B2)	Null (=B4-B3)

Table 44 - Dialysis sessions date difference

Using this, each session can then be numbered based on 14-day gaps. There were no definitions of the cessation of dialysis using retrospective data. This duration was chosen because I felt it was a reasonable period to identify a stop in dialysis. Many of our patients go on holiday, and dialyse elsewhere, this is rarely for more than 2 weeks. A longer period could have been used (such as any future dialysis) but this would exclude those who have dialysis, recover then have dialysis again, therefore this pragmatic approach was chosen;

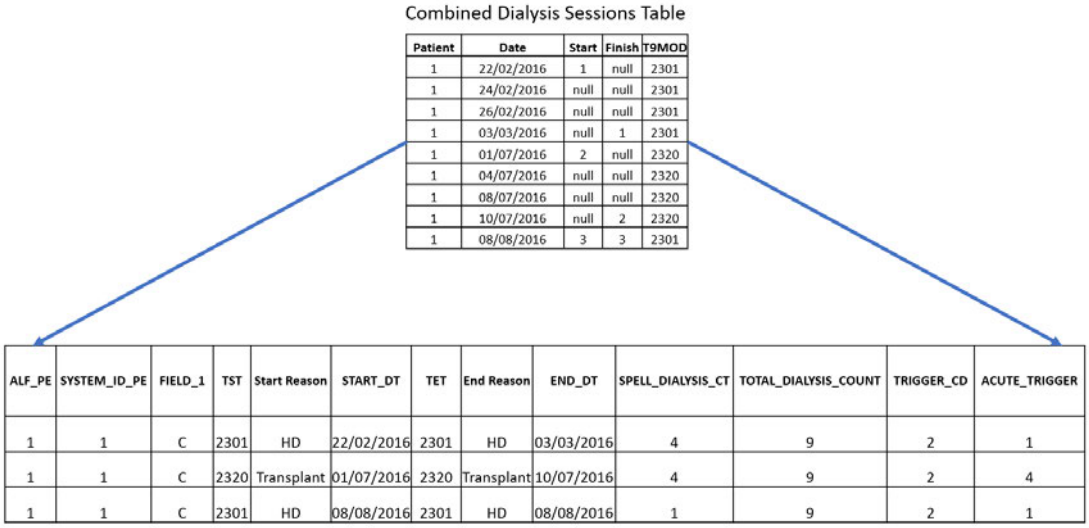
PT	Date	Date Difference	Row Number	Date Diff Flag	Dialysis session
1	02/02/2005	33	1	1	1
1	07/03/2005	28	2	1	2
1	04/04/2005	28	3	1	3
1	02/05/2005	28	4	1	4
1	04/05/2005	2	5	0	4
1	06/05/2005	2	6	0	4
1	08/05/2005	2	7	0	4
1	11/05/2005	3	8	0	4
1	13/05/2005	Null	9	0	4

Table 45 - Dialysis sessions - 14 day gap

Using the two date differences was a crucial step. This was because, if someone entered an erroneous date / or a default date was used, such as 01-01-1900, the table would count this one with the subsequent spell. Using the table above, we used the logic of where the date difference 1 or date difference 2 was more than 14, then 'Date Diff flag' was '1'. Then we used the 'Date diff flag' to increase session numbers.

Step 2

The tables below show how the dialysis sessions can be grouped into spells;



Combined Dialysis Sessions Table

Patient	Date	Start	Finish	T9MOD
1	22/02/2016	1	null	2301
1	24/02/2016	null	null	2301
1	26/02/2016	null	null	2301
1	03/03/2016	null	1	2301
1	01/07/2016	2	null	2320
1	04/07/2016	null	null	2320
1	08/07/2016	null	null	2320
1	10/07/2016	null	2	2320
1	08/08/2016	3	3	2301

ALF_PE	SYSTEM_ID_PE	FIELD_1	TST	Start Reason	START_DT	TET	End Reason	END_DT	SPELL_DIALYSIS_CT	TOTAL_DIALYSIS_COUNT	TRIGGER_CD	ACUTE_TRIGGER
1	1	C	2301	HD	22/02/2016	2301	HD	03/03/2016	4	9	2	1
1	1	C	2320	Transplant	01/07/2016	2320	Transplant	10/07/2016	4	9	2	4
1	1	C	2301	HD	08/08/2016	2301	HD	08/08/2016	1	9	2	1

Figure 26 - Dialysis sessions conversion into dialysis spell

In this figure, the timeline codes (T9MOD in the first table and TIMELINE_START or TIMELINE_END in the second table) correspond to the timeline entry present at that time (i.e. the timeline on or before that date). In this table, there was also a count of the dialysis sessions between the start and the end as well as a total count.

The ACUTE_TRIGGER are the same as the triggers in the timeline table with the addition of '3' for where the START_REASON are unspecified, i.e. they are not categorised codes like 'Registration' or it was null i.e. no timeline code before or on that date.

- Where START_REASON = HD/PD = 1
- Where START_REASON = Acute = 2
- Where START_REASON = Unspecified/Null = 3
- Where START_REASON = Transplant = 4

Bangor Sessions

The AWRD_B_HDSESSIONS_20190829 table also contains individual haemodialysis treatment sessions. These were added to improve the data in SAIL. This contains individual dialysis

session back to April 2004. The above described method for the session table was used to create spells in the same way as for AWRD_C and M.

Rhyl PEDW

As mentioned previously, following a trip to Rhyl and reviewing the dialysis books, I was able to find out that individual dialysis treatments in Glan Clwyd are entered as regular hospital admissions in the patient administration system, thus allowing us to access them through PEDW. There are some 269,282 dialysis admissions (1 day or less). The code used was shown in chapter 2 – "Rhyl AWRD_R". Most of the admission for this dataset come from Flintshire, Conwy and Denbighshire with very few from Gwynedd and Wrexham pointing towards Glan Clwyd (Rhyl) being the major source. The records for this begin in April 2008 and are consistent until January 2018 apart from a dip in the data in April, May and June of 2012, which I believe corresponded with the loss of admin support for that period in Glan Clwyd. These individual haemodialysis treatment sessions were handled like the other sources of dialysis sessions.

Renal Replacement Table

The timeline and session were joined by a 'Union' to create a complete renal replacement table, as shown below;

Column Name	Description	Timeline Table	Sessions Table
ALF_PE	Unique patient ID	ALF code	
TST_CODE	Timeline Start Trigger	T9MOD code	T9MOD before or on start date
START_DT	Start Date	Start Date	
START_REASON	Timeline Description	Acute, HD, PD, Transplant	
TET_CODE	Timeline End Trigger	T9MOD code	T9MOD before or on end date
END_DT	End Date	End Date	
END_REASON	Timeline Description	Start Reason, Death, Recovered, Stopped, Transferred out	
DS_SPELL_CT	Dialysis Sessions Spell Count	Dialysis sessions between start and end date	
DS_TOTAL_CT	Dialysis Sessions Total Count	Dialysis sessions in total (future and past)	
RRT_TRIGGER	Row Source Code	1	2
ACUTE_TRIGGER	Acute trigger code	1 or 2 or 4	1 or 2 or 3 or 4
FIELD_1	Source of Data	C or M	C or M

Table 46 - Union of Cardiff and Swansea renal replacement table

Implementation of RRT tables

Using the RRT table, we then highlight those patients that have alerts whilst receiving treatment including a renal transplant. The figure below (figure 23) shows how the patients triggering an AKI alert and then get screened for RRT.

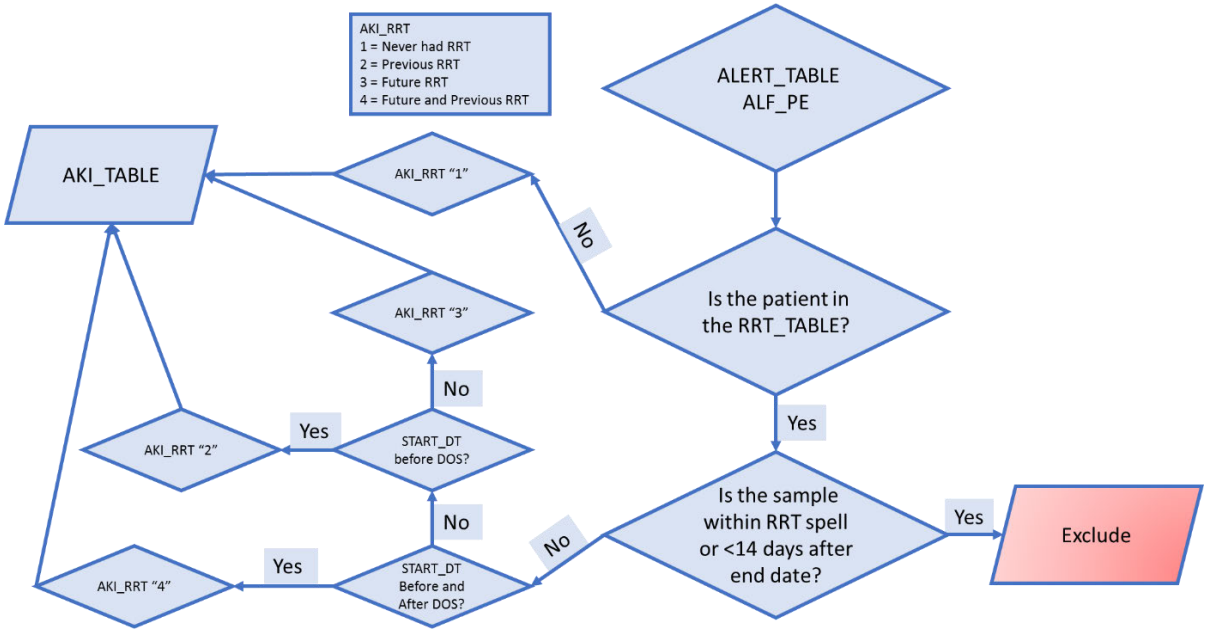


Figure 27 - Implementation of Renal replacement table (AKI_RRT)

DOS = Date of index sample/SCr

Using the AKI_RRT it was useful to look at those patients with AKI and RRT entries, particularly those with codes 2,3 and 4. Those patients with a code of '4' required closer investigation as potential haemodialysis patients. Those with a code of 3, i.e. future renal replacement (from date of sample) could potentially have AKI requiring dialysis (AKI-D), so the time to dialysis here is of interest.

To exclude patients, I have used the index test within the RRT spell or within 14 days after RRT spell ends. This is because, if someone has dialysis their creatinine will be artificially lowered, when they stop dialysis, it is likely that their creatinine rises. You would expect it to rise to the patient's baseline or potentially above it. This may trigger a new alert, but this would not be in keeping with AKI, so I have included an alert 'lockout' period.

Below are a couple of examples of this lockout period being applied;

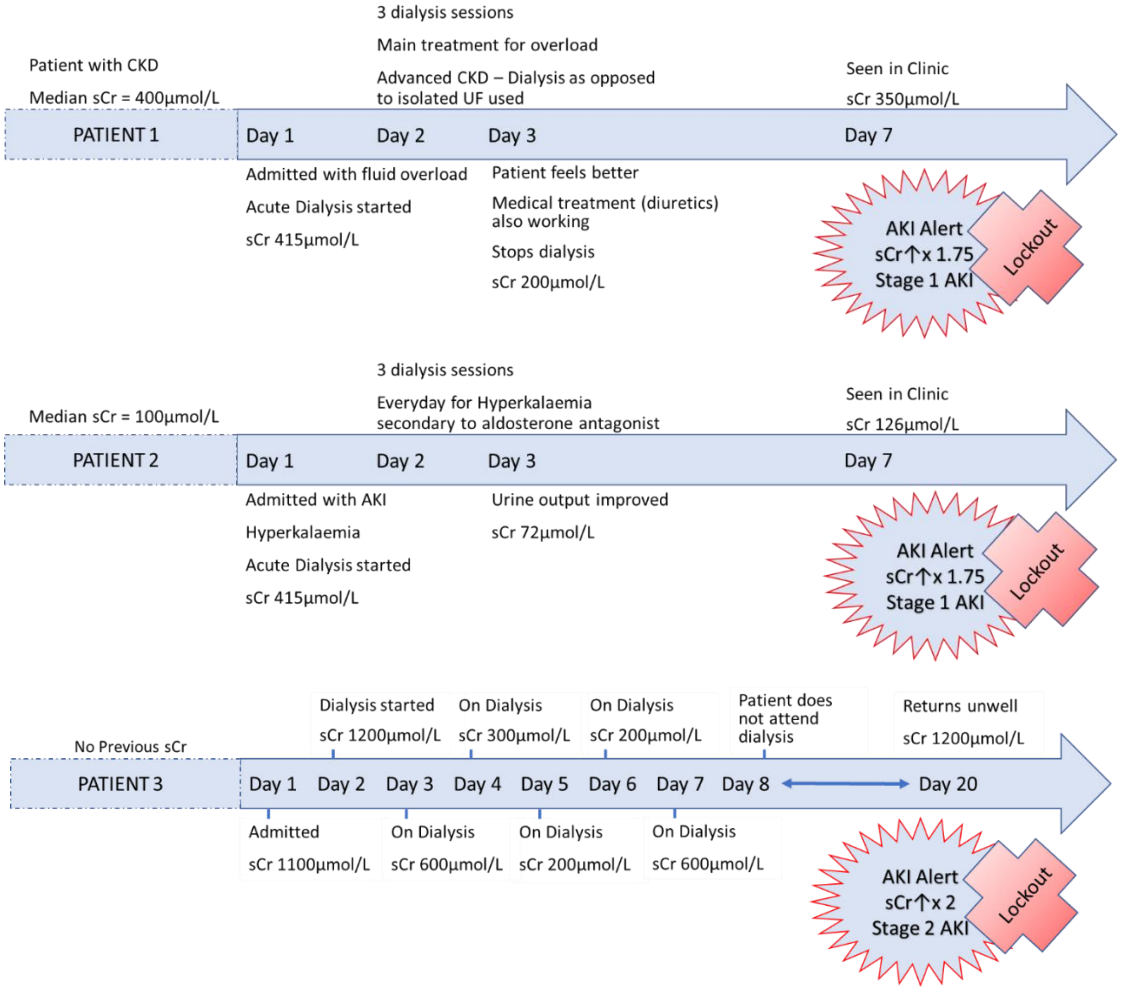


Figure 28 - Example of dialysis effect on AKI trigger

In these examples above, patient 1 shows a person with advanced chronic kidney disease (CKD) who has a short spell of dialysis to treat a CKD complication, they then stop dialysis. Without a lockout period, they would then be falsely labelled as AKI. The second patient has AKI requiring treatment, they then recover (using a definition in comparison to the baseline at the time of first AKI), however the dialysis artificially lowering their creatinine, so there is a 1.75 times increase compared to their 7-day baseline (lowest SCr in the last 7 days). Patient 3 is likely to be a 'crash lander' CKD patient. They have started on dialysis with a very high SCr, subsequently with the dialysis treatment the SCr comes down greatly. They then miss their dialysis sessions. In this example, they reattend 12 days later, so the algorithm reverts to an 8-365 day median approach. As a result, the algorithm will label them AKI 2. Interestingly in this patient's case, they may have AKI, it is unclear, but they will not have been labelled by AKI before day 20.

Acute Kidney Injury patient table

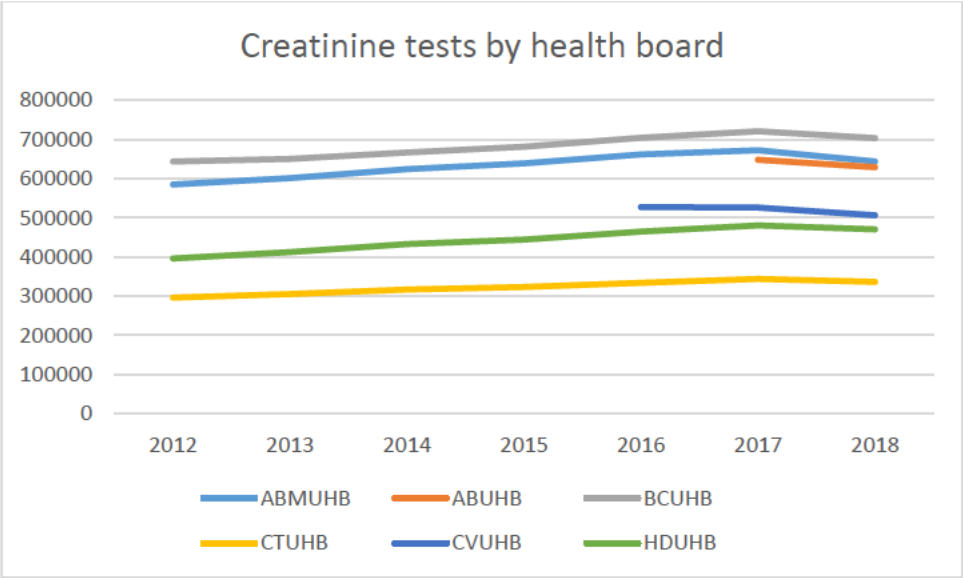
Running the AKI algorithm against the SCr values from the all Wales pathology table (PATH) allowed us to create a table of patients who would trigger an AKI alert. Once this was done, we used our dialysis table above to highlight patients who are known to be on chronic renal replacement. This created an AKI cohort, we then added in AKI alerts that were seen in clinical practice (WRRS alerts) which were recorded in the PATH table, linking them on the tests. The final AKI table then had the additional results from PEDW, WDS, WLGP, OPD, CCDS, ADDE for analysis.

AKI table Problems

There were a few problems that were spotted and corrected along the way. One problem that was spotted was a missing day (31/12/13). This came about as a date number was used instead of a date as shown above. This was used to speed up the AKI algorithm processing, however, using the calculation the date time number corresponded to the start of the 31/12/13 but not the end of the day 23:59 pm, therefore 1600 results were excluded leading to 80 missed alerts. This was spotted by plotting out the alerts by day and as a result was corrected, but it highlights the potential for errors caused by formatting and highlights the need for rigorous checks.

Testing frequency and AKI incidence

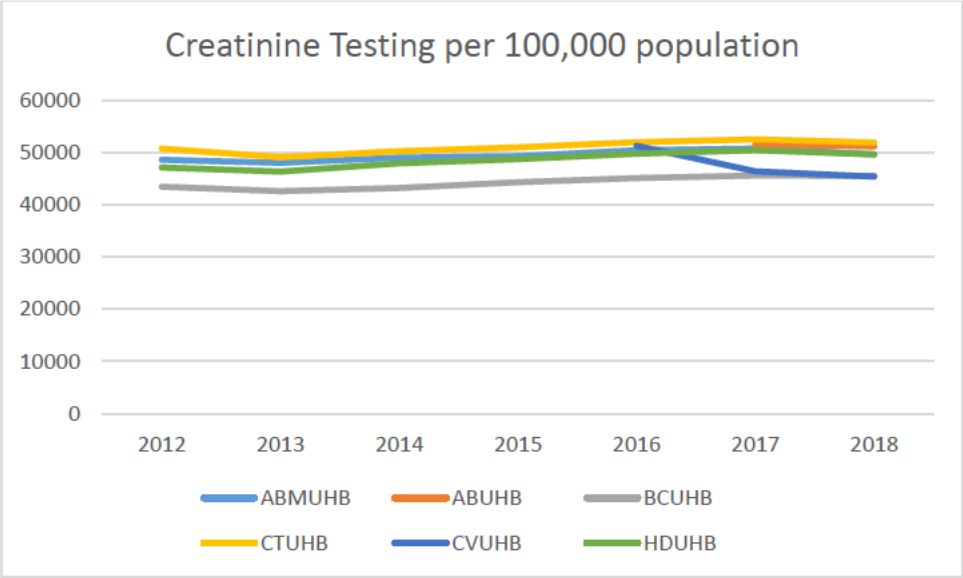
Using the creatinine cohort, I was able to identify those at risk of developing AKI by year. Across the health boards studied there are millions of creatinine results available. Some of these health boards have data for longer periods than others. The graph on the next page (Graph 44 – Creatinine tests by year and different health boards) shows the number of creatinine tests per year in the 6 Welsh health boards with biochemistry laboratories (Powys teaching health boards was excluded);



Graph 44 – Creatinine tests by year and different health boards

ABMUHB = Abertawe Bro Morgannwg University Health Board, ABUHB = Aneurin Bevan University Health Board, BCUHB = Betsi Cadwaladr University Health Board, CTUHB = Cwm Taf University Health Board, CVUHB = Cardiff and the Vale University Health Board, HDUHB = Hywel Dda University Health Board)

Using the ONS estimates of populations which splits them into local area, I have looked at the number of tests in adults (≥18 year of age) to show the creatinine tests per 100,000 in Wales.



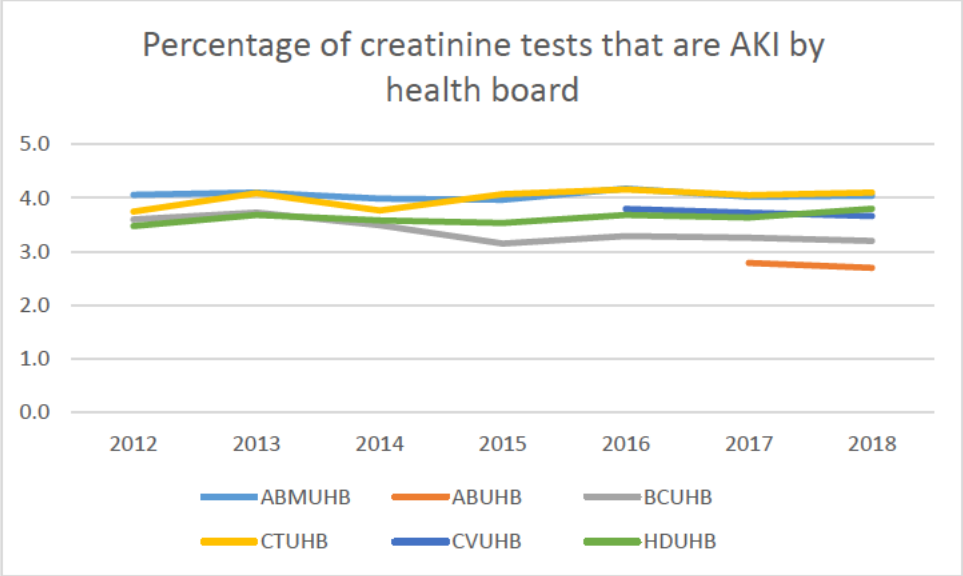
Graph 45 – Number of people with creatinine tests per year per 100,000

These tests are broadly similar across the regions, although the number of tests in BCUHB seems a little lower as does CV. This likely represents a problem with the method, in that local areas do not necessarily represent health boards, primary care practices or laboratories

boundaries. For example, a patient in Cowbridge, which is part of Cardiff and the Vale is likely to go to the Princess of Wales hospital Bridgend for renal outpatient appointments, which is part of ABMU (at the time studied), so unless they have a GP test then the test will be counted in ABMUHB bloods but not CVUHB thus lowering the testing incidence.

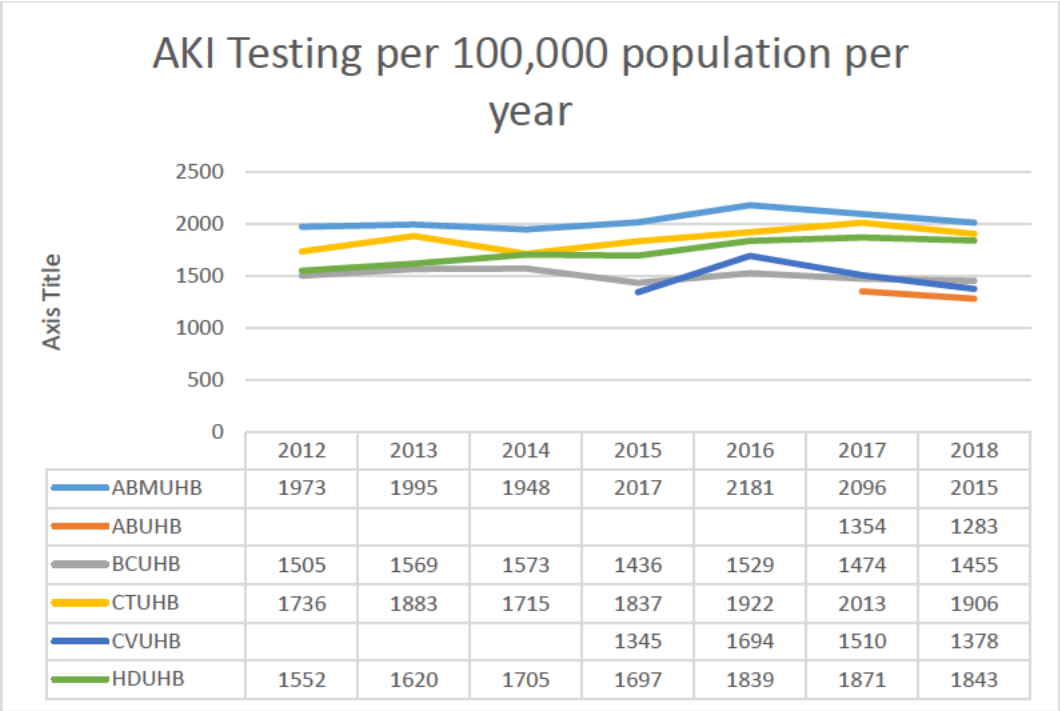
If we look at the whole of Wales, adjusting for when the data are available in different health boards, we see that between 45.8% and 49.1% of the adult Welsh population have creatinine tests each year and 1.6-2.1% will have a creatinine test with AKI (excluding Powys).

Of those SCr tests, some triggered AKI. The graph below shows the percentage of tests with AKI;



Graph 46 - Percentage of creatinine tests that are AKI by health board

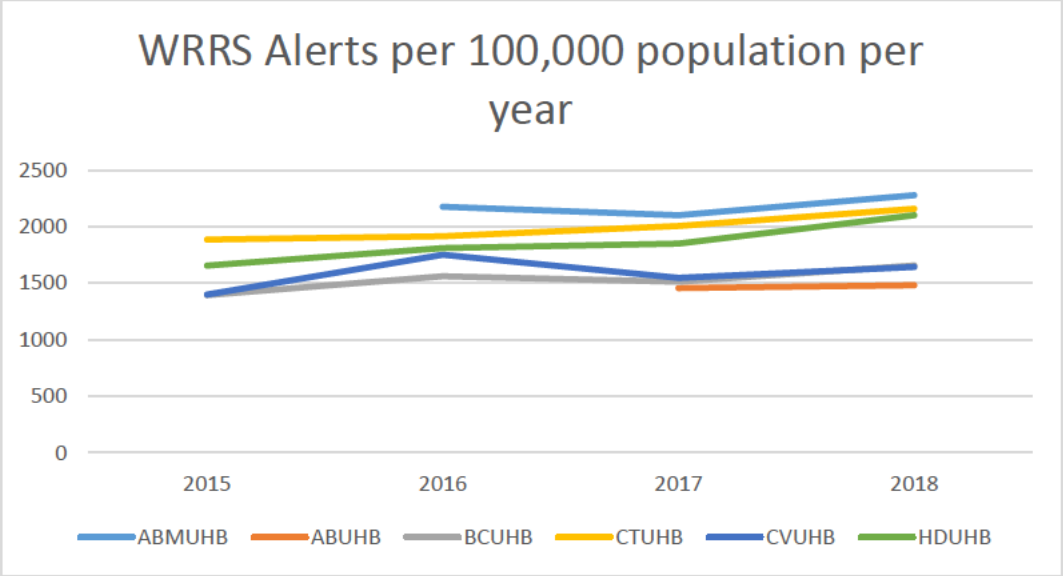
The incidence of AKI using our method of identifying it is shown below;



	2012	2013	2014	2015	2016	2017	2018
ABMUHB	1973	1995	1948	2017	2181	2096	2015
ABUHB						1354	1283
BCUHB	1505	1569	1573	1436	1529	1474	1455
CTUHB	1736	1883	1715	1837	1922	2013	1906
CVUHB				1345	1694	1510	1378
HDUHB	1552	1620	1705	1697	1839	1871	1843

Graph 47 - Incidence of AKI per 100,000 populations using our AKI cohort

This was very similar to the incidence of AKI using the electronic alerts sent in practice (WRRS alerts) as shown below;



Graph 48 - Incidence of AKI per 100,000 populations using electronic Alerts (WRRS alerts)

As with the population testing, the local areas used to define populations leads to overestimation and underestimation in some areas. Also, some places have tertiary services, such as ABMUHB which provides renal and tertiary cardiac services for ABMUHB, HDUHB, some of Powys and some of CTUHB which means the denominator may be understated.

Summary

In using the methods described in this chapter, we have been able to precisely identify patients with SCr tests that would trigger an AKI alert. Using the AWRD with the improved depth and quality, we are then able to accurately identify patients undergoing dialysis treatment so we can exclude them from the AKI cohort. When using timeline dialysis data in this manner, careful thought is required to apply an appropriate hierarchy beyond date alone, to allow for the creation of treatment spells and avoid premature termination of these spells. This AKI cohort can be used to describe the incidence of AKI over time and allows for further study of the electronic alerts (WRRS alerts) that have been introduced into clinical practice.

Chapter– 4 - Validation of electronic AKI Alerts

To understand the impact of these electronic AKI alerts, we must first understand whether they correctly identify AKI. We know that they are accurate at identifying AKI based on the KDIGO definitions for change in serum creatinine (SCr) in retrospective data (172), but are these definitions implemented accurately?

Introduction

Following the introduction of the KDIGO guidelines for AKI in 2012, a patient safety alert was issued by NHS England which led to the association for clinical biochemistry and laboratory medicine (ACB) developing an algorithm to aid the recognition of AKI (157). This algorithm was endorsed by NHS England (Figure 23 shown on page 136) was then applied to the Welsh Laboratory Information Management System (LIMS) and was introduced to Welsh hospitals in a staggered manner between 2014 and 2015.

Organisation	Date of adoption
Abertawe Bro Morgannwg UHB	Mar-15
Aneurin Bevan UHB	Mar-14
Betsi Cadwaladr UHB	Sep-14
Cardiff and Vale UHB	Nov-14
Cwm Taf UHB	Mar-14
Hywel Dda UHB	Mar-14
Powys Teaching HB	Oct-14
Velindre NHS Trust	Nov-14

Table 47 - Dates of electronic AKI alert implementation in Wales

The geography of these different health boards are shown in the next figure. Velindre NHS trust is specialist provider of cancer care in Wales and therefore it doesn't have a regional boundary. In 2019, there was a revision of the boundaries, but for the basis of these studies the old boundaries have been used;

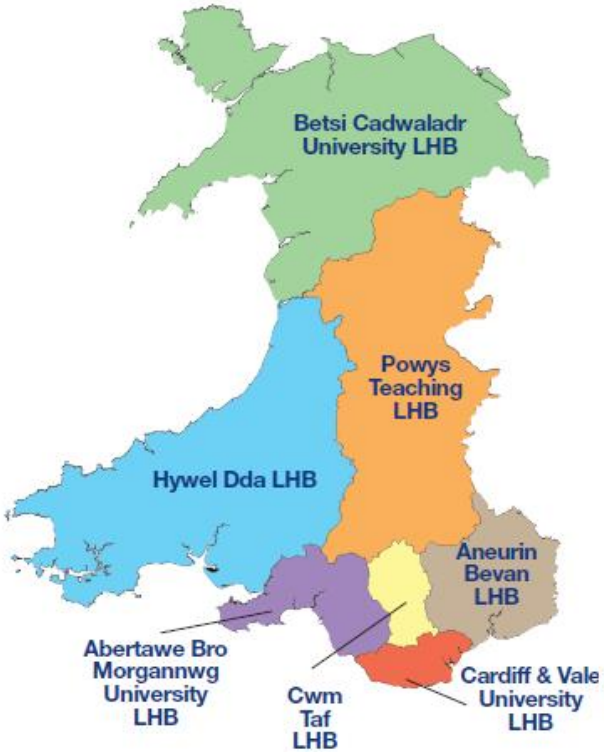


Figure 29 - Welsh health board boundaries 2009 to 2019

These alerts are attached to the urea and electrolyte profiles appearing on the user systems as a text message beneath the results. Two examples are displayed here;

Urea and electrolytes

		Result	Unit	Range
Sodium	L	132	mmol/L	(133 - 146)
Potassium	H	6.0	mmol/L	(3.5 - 5.3)
Urea	H	11.9	mmol/L	(2.5 - 7.8)
Creatinine	H	272	umol/L	(58 - 110)

AKI Alert
Acute Kidney Injury Alert. Creatinine increase over baseline value.

Figure 30 - Indigo Review© example of eAlert

This is in the former Abertawe University health board 'Indigo review' © system.

Result/Report origin: Morriston Hospital - Blood Sciences

UE	Urea and electrolytes (AUTHORISED [A])			
NA	Sodium	136	mmol/L	133-146
K	Potassium	5.8	mmol/L	H 3.5-5.3
Urea	Urea	8.4	mmol/L	H 2.5-7.8
CREAT	Creatinine	176	umol/L	H 58-110
	AKI Alert	Acute Kidney Injury Alert. Creatinine increase over		

value.

Figure 31 - Welsh clinical portal example of eAlert

This is the all Wales, Welsh Clinical Portal (WCP) which has now been adopted across Wales for reviewing results.

The alerts are generated based on changes in the serum creatinine (SCr) from a baseline, which is either the lowest SCr value in the 48 hours, lowest SCr in the last week or a median SCr of tests between 8 and 365 days. These alerts then require a review by a member of the laboratory staff prior to it being released to the clinicians. One of the reasons a review is required is to try and avoid falsely sending out alerts in dialysis patients who do not have AKI. However, the information available to the laboratory staff is usually very limited as the systems (in Wales at least) are not linked with dialysis data or hospital admissions data. In clinical practice, across several Welsh hospitals we have witnessed false positive alerts. We have also witnessed alerts being suppressed in patient with AKI, particularly when the patient is under a kidney specialist (Nephrologist) as the laboratory staff make the incorrect assumption that the patient is on dialysis. The degree of this problem has not been studied to our knowledge. We have re-created the AKI algorithm and used the all Wales renal dataset (AWRD) to create an AKI cohort allowing for comparison.

Aims

To assess the accuracy of the electronic AKI alerts in Wales.

Hypothesis

The Nationally implemented AKI algorithm will falsely identify AKI in some dialysis patients and will falsely suppress AKI alerts in some patients.

Method

The analysis is carried out in the SAIL databank using the Welsh Results Recording Service (WRRS) pathology data (PATH described on page 91) to create an AKI cohort. Only those 18 years of age or older at the time of their SCr test (at any point of the year) were included for analysis. For analysis, age at the time of their test was used. In this study we look at a cohort of patients and compared those patients identified as having AKI by two different implementations of the NHS England AKI algorithm (page 136). The first cohort is called **'Our AKI'** which uses the aforementioned algorithm reproduced in SAIL on PATH dataset SCr tests,

joining with the renal dataset (AWRD) to identify those patients on chronic dialysis and exclude them as AKI (as described in Chapter 3 – The Creation of AKI Cohort). This creates an accurate AKI cohort of patients, with knowledge of whether they are on dialysis at that point in time. The second cohort was the electronic alerts stored with in the PATH dataset which uses WRRS data and was therefore called '**WRRS Alert'**. These are the electronic alerts issued by the laboratories in practice and therefore have been reviewed by a clinician. Both alerts use the same SCr tests to identify AKI and in theory these should be the identifying the same number of AKI alerts. By using the records of suppressed alerts in WRRS, we are able to judge when an alert has not been sent out, i.e. suppressed. Using the two AKI groups, we can assess correlation by health board, investigating the number of alerts correctly sent out, incorrectly suppressed (false negatives) and incorrectly sent out (false positives).

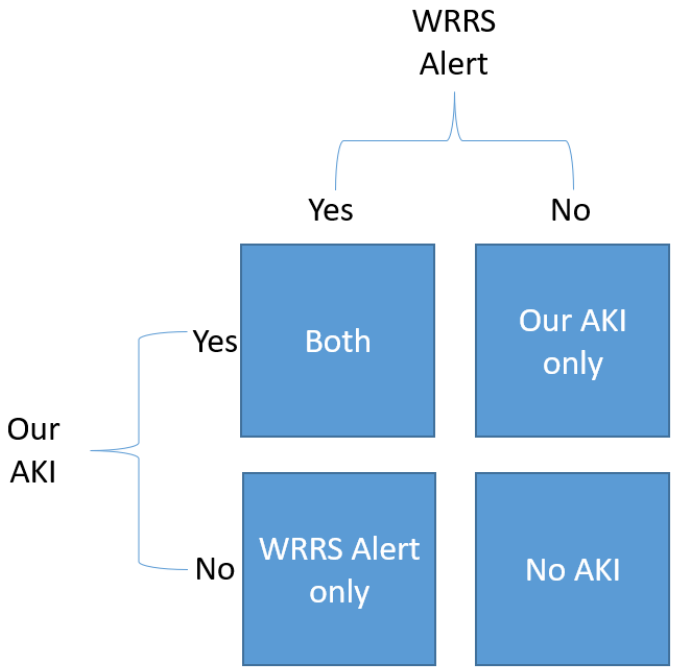


Figure 32 - AKI by our AKI and WRRS AKI alerts

The year 2017 was analysed as this was a year with the most complete data across the 6 main health boards. Powys teaching health board has not been assessed as this does not have its own biochemistry laboratory and as a result, blood tests are sent to multiple laboratories including some in England and therefore outside the capture of the PATH (WRRS) dataset. Charlson Score was created using PEDW ICD-10 hospital episode codes and primary care Read codes. The location of the test was defined as the location recorded on from the test sample

and then binned to areas (A&E, GP, Inpatient, Outpatient or other) as described on page 96 (Creating look up tables – WRRS_PROV_SITE_HB20181209).

Statistical analysis

IBM SPSS Statistics for Windows (IBM, V.24.0) was used for this quantitative analysis. I used descriptive statistics to summarise demographic characteristics and comorbidities. We calculated sensitivity, using chi squared (X^2) test comparing our AKI (reference standard) to the WRRS alerts. When the first AKI of the year was used, this was the initial test that triggered AKI, and the age at the time of this test was used.

WRRS alerts

The PATH (WRRS) table was added to SAIL initially in September 2018. This dataset contains the SCr and alerts from varying points in time (Table 18 on page 91). This initial dataset was then updated in March 2019 however, upon review it was clear that the alerts were not included in the update, so they were not present for 2018. This was likely due to the results containing text which meant that the SAIL data warehouse analysts would have removed the data for fear of de-anonymisation. At the same time there were no records of suppressed alerts, which appear on the clinician facing systems with the text report 'No AKI alert generated as Patient Type is Dialysis'. With this missing data, I set out to try and get these results included, and since the suppressed alerts used a default text response, there was no risk of identification of individuals from these records. This involved meeting with Gareth John (Improvement and innovations manager in NHS Wales Informatics Service) where we reviewed the raw data together to find these reports. We then imported this data, the first attempt however only included the alerts and suppressed alerts from 2018 onwards (the table was named WRRS_PATH_AKI_20191205) so a further upload of suppressed alerts before 2018 was arranged on the following day (the table was named WRRS_PATH_AKI_20191206).

Structure

Gareth Davies (SAIL analyst) used this PATH datasets to create a table with part of it structed in a similar way as shown below:

Person	Date	Creatinine	Dialysis	Our AKI	WRRS Alert	WRRS Suppressed	
1	01/01/2017	100	No	Not AKI	No Alert	No	True Positive
1	03/01/2017	160	No	Alert1	AKI	No	
2	01/01/2017	400	Yes	Not AKI	No Alert	No	False Positive
2	03/01/2017	600	Yes	Alert1	AKI	No	
3	01/01/2017	100	No	Not AKI	No Alert	No	False Negative
3	03/01/2017	210	No	Alert2	No Alert	Yes	
4	01/01/2017	395	Yes	Not AKI	No Alert	No	True Negative
4	03/01/2017	610	Yes	Alert1	No Alert	Yes	

Table 48 - AKI alerts example of validation

We used the 'Our AKI' to recognise AKI but exclude patients on dialysis, this way we can see those that would trigger if not recognised as being on dialysis. In this example, patient 1 was correctly identified as having AKI on the second test. Patient 2 was on dialysis and has therefore been incorrectly identified as having AKI, so it was a false positive alert. Patient 3 was not on dialysis, but the alert has been suppressed incorrectly therefore it was a false negative alert. Patient 4 was a patient on dialysis that has been recognised by the laboratory staff and therefore correctly suppressed.

Health Board Comparison

Due to concern from the senior SAIL data analyst team about potential performance based comparison, the health boards have been anonymised in the result sections. In different sections, the health boards are given different identities to help avoid identification.

Results

In 2017 there were 3,420,925 tests in 1,142,257 patients across Wales. The baseline and demographic details are out lined below, this includes all the health boards and areas, not just the ones studied;

	All	Our AKI	WRRS Alert AKI
Tests	3,420,925	138,913	95,084
People	1,142,257	40,512	39,941
Mean Age (Median)	64(67)	71 (74)	71 (74)
Mean Test Creatinine (Median)	96 (77)	258 (183)	223 (161)
Mean RV2 Baseline (Median)	99 (78)	154 (97)	134 (90)
Female Tests % (People %)	53 (55)	46 (52)	48 (53)
Transplant (People)	21,205 (1,812)	1,648 (300)	889 (257)
Renal Replacement Therapy (People)	60,899 (2,289)	18,845 (1,922)	8,767 (1,490)
Death at 30-days from test (%)	134,510 (3.9)	31,513 (22.7)	22,342 (23.5)
Charlson score (Median)	1 (1)	3 (3)	2 (3)
	Test Location		
A&E (%)	247,213 (7.2)	13,107 (9.4)	12,835 (13.5)
OPD (%)	510,301 (14.9)	15,610 (11.2)	8,437 (8.9)
Inpatient (%)	1,108,502 (32.4)	98,527 (70.9)	63,239 (66.5)
GP (%)	1,488,024 (43.5)	10,433 (7.5)	9,568 (10.1)
Other / Null Location (%)	66,885 (2)	1,236 (0.9)	1,005 (1.1)

Table 49 - Demographics table – Validation

RV2 is the name of the median baseline creatinine between 8-365 days; A&E = Accident and Emergency department; OPD = Outpatient department; GP = General practitioner.

Those that have AKI alerts (either method), are older, have a higher baseline SCr (RV2), more likely to be male, have a higher Charlson score and more likely to have a test from an inpatient location. The SCr testing by health boards is shown below;

	ABMUHB	ABUHB	BCUHB	CTUHB	CVUHB	HDUHB
Adult Tests	672,559	648,282	721,308	344,353	526,644	480,910
Adults Tested	216,891	239,454	253,934	124,111	181,889	156,600

Table 50 - Health Board SCr tests in 2017

ABMUHB = Abertawe Bro Morgannwg University Health Board, ABUHB = Aneurin Bevan University Health Board, BCUHB = Betsi Cadwaladr University Health Board, CTUHB = Cwm Taf University Health Board, CVUHB = Cardiff and the Vale University Health Board, HDUHB = Hywel Dda University Health Board)

Of these tests in the 6 main health boards, 119,703 were identified as AKI in 39,960 non-dialysis patients by our AKI code and there were 84,138 AKI WRRS alerts in 40,726 patients.

Sensitivity and Specificity of WRRS alerts

The number of AKI alerts by the different methods are seen in this table below;

Health Board	1	2	3	4	5	6	Total
Our AKI	13,976	27,069	18,072	17,481	19,622	23,483	119,703
WRRS Alerts	9,407	18,891	12,940	11,702	13,950	17,248	84,138
Our AKI individuals	4,759	8,962	6,290	5,812	5,920	8,217	39,960
WRRS Alert individuals	4,742	8,978	6,768	5,746	6,066	8,426	40,726

Table 51 - AKI by Our AKI algorithm and WRRS alerts by health board

As can be seen there was a difference between the number of AKI tests between the WRRS alerts and the AKI using our code, which was present across all the health boards. To compare the alerts methods, we need to check correlation, not just overall numbers. This next table (Table 52) uses all the AKI tests identified by our method ('Our AKI') to signify AKI as a standard and then compares them to the AKI alerts sent in practice ('WRRS Alerts');

	Our AKI method based on NHS England Algorithm	
	AKI	Not AKI
WRRS Alert	73,750	10,388
No WRRS Alert	45,953	3,263,965

Table 52 - Comparison of WRRS AKI alerts with the NHS England AKI algorithm alert's ('Our AKI')

Given that we understood the AKI algorithms to be the same (Our AKI NHS England method and the Welsh WRRS alerts) except for the dialysis recognition, then we would expect the sensitivity to be high. We would expect the specificity to be slightly lower than 100%, given our hypothesis that the WRRS Alerts will have some false positives in dialysis patients. When we perform sensitivity analysis, we can see that the sensitivity of the WRRS alerts was relatively low at 61.6% with a high specificity of 99.7% as expected. In the overall alerts the positive predictor value was 87.7% and the negative predictive value was 98.6%.

Comparison of AKI methods

The table below (Table 53) shows how I have analysed the next few results. This section looks to compare the two AKI methods. In the column, 'Our AKI' the comparison was based on the number of AKI results we have identified using our AKI code in SAIL. In the columns 'Ours not

AKI' and 'Ours not AKI (not dialysis)' the denominator was the WRRS alerts, displayed in the example below;

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	WRRS Alerts/Our AKI (Sensitivity)	Ours not AKI / WRRS Alerts	Ours not AKI (excluding dialysis tests)/ WRRS Alerts
No WRRS Alert	Not a WRRS Alerts/Our AKI		

Table 53 - Example of validation table

Combined health boards

As previously described only 61.6% of patients with AKI using our code had matching WRRS alerts (sensitivity) and 12.3% of the WRRS alerts did not have a matching alert by our code, however this dropped to only 4% when the dialysis patients were excluded (falsely positives).

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	61.6%	12.3%	4%
No WRRS Alert	38.4%		

Table 54 - Alert validation of all the alerts - 6 health boards combined

If we look at the first AKI of 2017, we see that the sensitivity improves significantly to 93%. The numbers not identified by our method and not on Dialysis remains similar at 6.6%, however.

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	93%	10.9%	6.6%
No WRRS Alert	7%		

Table 55 - Alert validation of the first alerts of 2–17 - 6 health boards combined

Health boards

When examining individual health boards, we see variation in the performance of the alerts, this section looks at them individually. The health boards remain anonymised using an alphabetical reference instead of a numerical.

Health board level - Sensitivity and Specificity of WRRS alerts

In the first table, we look at the sensitivity, specificity, positive predictive value and negative predictive value of the WRRS alerts by health board. Again, 'Our AKI' based on the NHS England algorithm with dialysis patients removed was used as the standard;

	Health Boards %					
	A	B	C	D	E	F
Sensitivity	62.2	62.2	61.7	63.3	58.5	62.1
Specificity	99.7	99.7	99.6	99.5	99.5	99.8
Positive Predictor Value	86.9	89.1	84	94.1	82.3	92.8
Negative Predictor Value	98.9	98.4	98.7	98.4	98.4	98.6

Table 56 - Sensitivity, Specificity, positive and negative predictive value of WRRS alerts by health boards when compared 'to 'Our AKI'

Health board level - Comparison of AKI methods

In the tables used in this section the first column was the alerts identified by our code in SAIL, the 2nd and 3rd column are the alerts identified by WRRS code but not by our code in SAIL, as shown in the example table (Table 53 - Example of validation table).

Health Board A

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	62.2%	10.9%	2.0%
No WRRS Alert	37.8%		

Table 57 -Health Board A Alert Validation

In this table we can see that 62.2% of the AKI tests using our method were also identified by the WRRS system (sensitivity) leaving 37.8% of the alerts as false negatives. When using the WRRS alerts as the denominator we saw that 10.9% of the WRRS alerts were not identified

by our method, and therefore for the basis of this study false positives. In those that were not identified by our code, 82% of these were false positives as the patients were on dialysis at the time, this explains the majority of this mismatch, with only 2% of the WRRS identified alerts not identified by our method when excluding dialysis patients. The false negatives are less easily explained as in this case here only 2.6% of those not identified by WRRS were in incorrectly supressed alerts, i.e. those patients wrongly thought to be on dialysis. This means that of the AKI tests not identified by WRRS, very few of them (2%) were not identified because they were wrongly suppressed, so there must be another reason (37.8%).

When reviewing individuals however, 95.5% of the patients identified by our AKI method also had a WRRS alert, so only 4.5% of those we identified as AKI had no alert sent at all to a clinician in 2017.

Health Board B

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	63.3%	5.9%	2.1%
No WRRS Alert	36.7%		

Table 58 - Health Board B Alert Validation

Health board B performs broadly similar to A. In this table we can see that the sensitivity of the WRRS alerts in identifying AKI in this health board was 63.3%, which was the best performance of the health boards. The WRRS Alerts resulted in 36.7% false negatives when compared to 'Our AKI'. When using the WRRS alerts as the denominator we saw that 5.9% of the WRRS alerts were not identified by our AKI method, and therefore for the basis of this study false positives. When the dialysis patients were removed, only 2.1% of the WRRS alerts were not identified using our code in health board B. This means that 64.4% of the false positives were due to dialysis blood tests. In the false negative group, which was again just over a third of our AKI, only a tiny 0.03% of the missing alerts are explained by incorrectly suppressed alerts, so again there appears to be other reason(s).

Nevertheless, again when we look at individuals, 96.5% of the people with AKI by our method also had an alert by the WRRS methods in 2017, suggesting that the missing alerts are occurring in patients with multiple alerts. Therefore, in health board B only 3.5% of those we identified as AKI by our method had no alert at all sent to a clinician in 2017.

Health Board C

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	62.2%	13.1%	9.5%
No WRRS Alert	37.8%		

Table 59 - Health Board C Alert Validation

The agreement of the two methods was like the previous two health boards with just under two thirds of our identified AKI tests have corresponding WRRS alerts. Of the false positives (13.1% of WRRS alerts) only 27.4% were in dialysis patients this time. This means that there are still 9.5% of the WRRS alerts not in identified by our method and are unexplained. Of our AKI not identified in WRRS (false negative), no alerts were inappropriately supressed. Therefore again, we have another reason for the missing alert.

In the same way as with the previously mentioned health boards, 95% of patients with an AKI identified by our method had an WRRS AKI alert in 2017, again suggesting that most of the missed alerts are in patients with multiple alerts.

Health Board D

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	58.5%	17.7%	1.4%
No WRRS Alert	41.5%		

Table 60 – Health Board D Alert Validation

This was the health board with the lowest agreement between our AKI and WRRS alerts. The sensitivity of the WRRS alerts here was only 58.5%. In our AKI without a corresponding WRRS alert only 1% of the alerts were incorrectly supressed. In the WRRS alerts not identified by

ours (17.7%), the majority were because the patients were on dialysis (91.8%) meaning that only 1.4% of those alerts in WRRS did not have AKI using our code.

Even though there was poor agreement, again the percentage of individuals with AKI by our method that had an WRRS alert was high at 95.3%. This means that most patients with an alert identified in SAIL also had an alert sent in clinical practice at some point in 2017.

Health Board E

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	62.1%	7.2%	2.2%
No WRRS Alert	37.9%		

Table 61 – Health Board E Alert Validation

Health board E had similar agreement to the first 3 health boards, with 62.1% of our AKI having a corresponding WRRS alert (sensitivity). Of the false positives alerts (7.2%), 69.8% were alerts in dialysis treatment periods. If you exclude these, it leaves 2.2% of those with WRRS alerts and not identified by us, that do not have a simple explanation. Of those with false negative alerts (37.9%), only 0.02% are due to incorrect suppression, again requiring further investigation.

In this health board, 95.8% of the people with an AKI alert by our method also had one by WRRS in 2017, fitting with the previously mentioned pattern appearing, that suggests that patients with multiple alerts are not having all their alerts identified.

Health Board F

Alerts	Our AKI	Our Not AKI	Our Not AKI (not dialysis)
WRRS AKI	61.7%	16%	6.7%
No WRRS Alert	38.3%		

Table 62 – Health Board F Alert Validation

In this final health board, the sensitivity of WRRS alerts remains just under two thirds, at 61.7%. Of the WRRS alerts, 16% were false positives of which 58.4% could be explained by

alerts being in patients on dialysis, but then 6.7% of all the WRRS alerts are not in ours AKI group and not during a dialysis spell. Of the false negatives (38.3%), only 0.5% are due to erroneously suppressed alerts.

In a similar way to the other health boards, 94.9% of individuals with AKI alerts by our method have an alert in WRRS in 2017.

Lack of agreement

This next section will explore the lack of agreement between our AKI group and WRRS alerts.

Health Board	1	2	3	4	5	6
Dialysis – False Positive % (N)	3.8 (360)	9 (1692)	3.6 (465)	5 (589)	16.2 (2264)	9.3 (1612)
Not dialysis – False Negative %	0.03	2.6	0	0	1	0.5

Table 63 – False positives and False negatives

This table shows the false positives patients on dialysis identified by WRRS as having AKI and the false negative tests incorrectly believed to be in patients on dialysis who had their WRRS alert suppressed. The overall number of false positives are displayed, but not for false negatives as some numbers are lower than <5 and therefore cannot be extracted from SAIL.

False Positives

In the WRRS alerts, 8.3% of all the alerts were in patients undergoing haemodialysis (false positives) and this accounts for 4.2% of the people with WRRS alerts. Across the health boards this ranged from 3.6-16.2% of the WRRS alerts. We expected that there were alerts sent in dialysis patient from our clinical experience, but this was 1 in 12 of all the WRRS alerts. These are unnecessary alerts with no clinical benefit, that are not in themselves directly harmful, however they do potentially promote alert fatigue.

If we excluded the false positives explained by dialysis, then we are left with 4% of the WRRS alerts that are not identified using our code. To explore these patients and missed alerts, I carried out a manual review of all the results from a sample of patients from each health board. Overall, I reviewed 2% of the missing alerts across the health board. In these patients

37% did not appear to have AKI from the blood tests available in the PATH dataset (WRRS). 3% of the reviewed alerts our algorithm did not recognise had recent reading with SCr levels below the lowest recordable reading such as <15, <18 or <20 (depending on the health board). We excluded these reading, but I suspect the LIMS managed them differently, potentially by using the highest possible number such as 14, 17 and 19 respectively. This problem was only apparent from the samples in 3 health boards and was not mentioned in the NHS England algorithm, so it raises the possibility of variable local implementation. 6% of the reviewed sample showed genuine AKIs missed by our algorithm, it was not clear why this was the case, but it appears some parts of their baseline calculations had become null in our table. This means that there was a problem with the table joining process for those patients as they did have previous tests and therefore should have had a baseline creatinine. This was a very small percentage of the overall numbers (if extrapolated it would be <0.25% of WRRS alerts) and did not appear to be the case in any of the false negative reviews (False Negatives). 13% of the patients did not have any previous results, this was a problem in health boards whose data was only available for later years and suggests that the local implementation of the algorithm allowed for use against old LIMS systems along with the newly implemented LIMS system. Finally, almost a third of those WRRS alerts missed by our AKI code had missed AKI due to the definition of day 7 and day 8. In our code we used the number of days between a date as the definition of the number of days where as WRRS used the difference between the date time, this effected the baseline values of the RV1 (0-7 days) and RV2 (8-365 days). In the example below if we compare the dates there are 8 days difference, but if we compared the date and time, it is 7.98 days and therefore the SCr of 100 would be counted as RV1 and this would be AKI.

Date	Creatinine	Date	Creatinine
01/06/2021 23:00	100	09/06/2021 22:30	140

Table 64 – Date difference implementation example

On re-reviewing the NHS England algorithm and KDIGO guidelines, I suspect the LIMS interpretations was what was intended, however as hours are not used, it does leave it to interpretation. NHS England AKI Algorithm (157) timing;

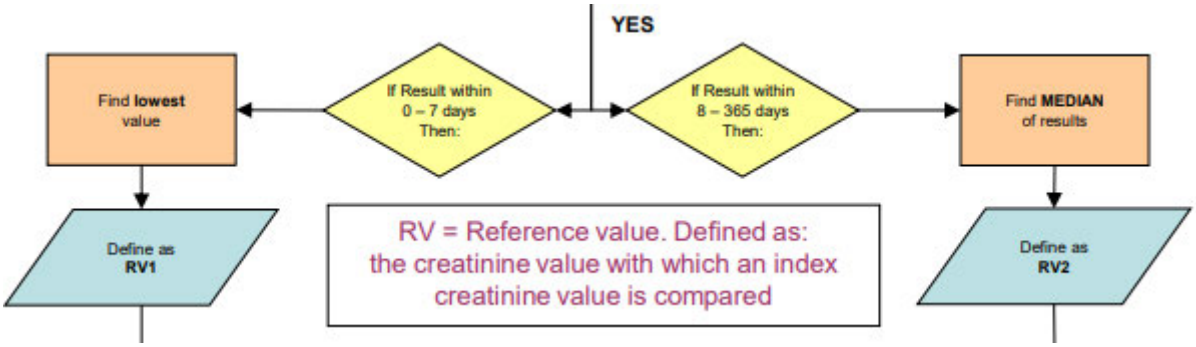


Figure 33 – NHS England RV1 and RV2 timing

The KDIGO guidelines (108) suggest that the creatinine rise should be known or presumed to have risen in the last 7 days

2.1.1: AKI is defined as any of the following (*Not Graded*):

- **Increase in SCr by ≥0.3 mg/dl (≥26.5 µmol/l) within 48 hours; or**
- **Increase in SCr to ≥1.5 times baseline, which is known or presumed to have occurred within the prior 7 days; or**
- **Urine volume <0.5 ml/kg/h for 6 hours.**

Figure 34 – KDIGO AKI baseline timing

This explains the mismatch with some of the patients in this cohort and shows some of the difficulties and variations in the interpretation of time between tests especially when a date time variable was used and it was particularly difficult if the true time of the test needs to be deduced as mentioned in chapter 3 (Test Timing).

False Negatives

There were 1,035 alerts (0.9%) incorrectly suppressed which was only 6.3% of the alerts missed by WRRS. This varied from 0-2.6% in the 6 main health boards. Given the numbers of alerts missed I looked at the unexplained patients in more detail. To do this I selected random rows (using random number generation to order rows) and manually reviewed 1% of the missing patients in each of the different health boards. As is already established, some patients were missing several alerts as a result, this meant that I reviewed 6.1% of all our AKI not with corresponding WRRS AKI alerts. The majority of these missing alerts I reviewed were clear AKI and often had other AKI alerts in close proximity, i.e. the day before or after. When reviewing these AKI tests, it was not clear what led to the alerts not being issued in the majority of cases. To try and help understand this I looked at the trigger for the AKI tests that were missed;

Missing AKI tests (False Negatives)	Baselines Methods (Percentage)					
Health Boards	**1**	**2**	**3**	**4**	**5**	**6**
Lowest Creatinine 0-7 days (RV1)	21.2	21.2	19.4	19.9	22.9	17.3
Median Creatinine 8-365 days (RV2)	69.7	62.8	72.6	69.5	65.8	74.0
Lowest Creatinine within 48 hours (RV3)	8.8	8.9	7.6	10.4	8.4	7.2
Both Lowest and Median (RV1 And RV2)	0.3	0.3	0.4	0.2	0.3	0.2

Table 65 – False Negative alert trigger rules

As was mentioned previously, some health boards had limited data prior to 2017, so they are likely to have missed some tests in the 8-365 median (RV2). In these health boards, understandably we see a higher percentage of that rule resulting in missed alerts (i.e. health boards 3 and 6 in Table 65 – False Negative alert trigger rules). Albeit one of those mentioned health boards had good historical data). In the health board without good historical data before 2017, the false positive analysis did suggest that the alerts algorithm in WRRS did have access to some blood results that we did not (i.e. not in PATH), however the review of false negative suggests that that was not always the case.

Another reason that came to light following the manual review was how the timing of the test were handled. It was apparent that the time that the specimen was received in the laboratory was used in WRRS instead of the time it was collected. I suspect this was a pragmatic decision as the time the bloods are taken are often not entered (18.4% of PAMO and PABR dataset). We on the other hand used the time collected as the main time and then the received time when that was not available, which was a logical pragmatic approach but albeit it was more complicated. Most of the missing alerts however were truly missing alerts and lacked an immediate explanation, nevertheless, in most cases there were alerts within 48 hours before or after the reviewed test.

True Negatives

It was not only important to look at the false negative and false positives but also when the alerts have behaved as intended. This table below shows how the anonymised health boards correctly identified patients on dialysis breaking it down into the number of people and tests. The numerical order of health boards has been changed in this table to avoid potential de-

anonymisation. This was because there are two outliers here, one health board has very few tests per dialysis patients which was likely a health board where dialysis patients get their tests sent to a neighbouring health board for the patient's routine monthly blood tests and another health board where the patients have the equivalent of two tests per month on dialysis which likely represents how the monthly dialysis blood tests are done.

	1	2	3	4	5	6
True Negatives	2462	9986	7862	4721	1178	6134
People	160	551	505	216	370	230
Dialysis Test Frequency (tests per patient in 2017)	15.4	18.1	15.6	21.9	3.2	26.7

Table 66 - True Negative (correctly identified dialysis patients)

First AKI

As outlined, most patients had an AKI test at some point during the year identified by both the WRRS alert and by our AKI methods. The aim of the alerts was to help identify AKI as it presents, therefore the initial AKI test could be thought of as the most important. Given this, I have looked at the percentage of initial AKI tests identified in the 6 health boards.

	1st AKI alerts - Percentage agreement			
Health Board	**Ours and WRRS (Sensitivity)**	**Ours but not WRRS**	**WRRS not ours**	**WRRS not ours excluding dialysis**
1	94.5	5.5	3.9	1.8
2	93	7	5.3	1.9
3	92	8	15.3	13.2
4	92.9	7.1	2.5	2.1
5	91.7	7.3	7.8	1.9
6	92.9	7.1	2.5	2.1

Table 67 - First AKI alert of 2017 - Agreement of alerts method

The sensitivity of the WRRS alerts in identify the initial AKI test was high across the health boards. All the health boards detected more than 90% of the first AKI tests as identified by our method. When we flip the denominator and look at the alerts missed by our code in non-dialysis patients, again we see that the numbers are very small, apart from in health board 3

which was one of the health boards with the least historical biochemistry data in the PATH dataset.

Mortality

One of the main drivers of concern regarding AKI was the associated mortality. Using the above data, I have calculated the mortality percentage by the different categorisation. The table shows the percentage 30-day mortality of all the patients with AKI, as well as those without AKI;

	30-day percentage mortality – from Test			
All AKI by Health Board	**Both % (N)**	**Ours only (N)**	**WRRS Only (N)**	**Not Both - not AKI (N)**
1	23.7 (1089)	26.4 (500)	19.3 (53)	1.9 (2361)
2	21.7 (1858)	25.8 (915)	25.3 (207)	2 (4420)
3	26.8 (1604)	27.9 (730)	14.6 (172)	1.8 (4228)
4	23.5 (1307)	27.7 (658)	11.8 (347)	2 (3084)
5	22 (1239)	24.3 (639)	16.1 (105)	1.7 (3176)
6	23.9 (1867)	27.3 (911)	14.1(163)	1.9 (4856)

Table 68 - 30-day mortality of all AKI tests by AKI identification

The suggestion from these results was that those tests missed by the WRRS alerts carry a higher percentage mortality and those missed by our method. The 30-day mortality percentage was much higher in AKI patients compared to the non-AKI population.

	30-day percentage mortality first AKI			
1st AKI by Health board	**Both (N)**	**Ours only (N)**	**WRRS Only (N)**	**WRRS Only not HD (N)**
1	19.7 (880)	21.8 (57)	11.7 (21)	15.7 (13)
2	16.6 (1376)	19.1 (119)	11.9 (55)	55 (16)
3	22 (1229)	17.4 (84)	11.5 (116)	116 (99)
4	18.5 (988)	19.5 (80)	16.1 (22)	22 (8)
5	17.3 (939)	17.1 (72)	9.6 (44)	44 (14)
6	19.5 (1442)	14.6 (98)	9.1 (69)	69 (56)

Table 69 - 30-day mortality from 1st AKI

In comparing percentage mortality between the first AKI alert and all the AKI alerts, we can see that the mortality gap diminishes overall. This was potentially due to patients with more

alerts having a higher mortality associated with them and these patients are better represented in our AKI. In this table (Table 69) we can see those in our AKI only (false negative) and those in both (true positives) have the highest 30-day mortality and those in WRRS only have the lowest. Interestingly, this gap narrows in some health boards when you exclude the dialysis patients, suggesting to me that there were some patients with possibly true and significant AKI that our AKI method did not pick up. Again, this may be because the LIMS running the WRRS AKI alerts had access to data not currently in PATH dataset (WRRS) in SAIL.

First and only AKI

Some patients did not have multiple alerts, the next table looks at patients who only had one alert;

30-day percentage mortality first and only AK[I]			
1st and only AKI by Health board	**Both AKI**	**Ours not WRRS**	**WRRS not Ours (not HD)**
1	17.1	18.9	9.1 (6.3)
2	12.9	17.9	15 (9.9)
3	19.7	13.2	13.2 (12.0)
4	14.5	15.1	15.8 (17.6)
5	15.9	17.1	11.5 (7.0)
6	17.8	14.6	10.3 (10.9)

Table 70 - First and only AKI alert 30-day mortality

This table shows the first and only AKI percentage mortality and supports this idea of the effect of multiple AKI alerts and increasing percentage mortality. Again, both the first and the first and only AKI results show a lower mortality percentage in those with WRRS alerts only, in all health boards except in health board 4. Some of the overall numbers in this section are very low, therefore the number of people dying was not displayed (N).

Discussion

To our knowledge this was the first study examining the accuracy of electronic alerts in clinical practice. The WRRS alerts which were seen by clinician do not always identify AKI as we would expect them to when compared to our version of the NHS England algorithm. It was apparent that some AKI alerts are missed (38.4% of all the alerts, with a test sensitivity of 61.6%), and the reason for this was not immediately clear. Through analysis it was apparent that these missing alerts appear to occur in patients with multiple AKI alerts. It was therefore

understandable that these patients seem to carry a high percentage mortality. The WRRS alert have a high specificity (99.7%) suggesting that there are few false positives when examining all the patients at risk of an AKI, however this was due to the high number of people tested. When we look at the first AKI of 2017, the mortality effect seems to diminish, suggesting that the increased associated mortality was related to multiple AKI alerts. It was evident that the minutia of the handling of test timing used to identify AKI varies slightly between our code and the code used in WRRS, nevertheless there are times that the WRRS algorithm should identify AKI but doesn't. It also appears to differ between the health boards, resulting in variations in the overall agreement, number of false positive and number of false negatives. One potential reason for this may be that the alerts require authorised SCr levels to be analysed for the AKI algorithm. Delay in this may affect the way or ability for the AKI alert to be calculated. Early in my research, I discussed this with the lead consultant in clinical biochemistry and metabolism in one of the health board, who told me that, at that health board these alerts need to be reviewed by a senior biochemist or clinician prior to release (authorisation). He also told me that there are occasions, particularly on weekends and bank holidays, where this may not happen for several hours or even days. It may be possible, that these delayed alerts may not get released and therefore do not appear in WRRS, particularly if there are other alerts for that patient being authorised at the same time. When discussing this with a clinical biochemistry scientist, she told me that there was a period where the alerts only ran on authorised creatinine, confirming this theory.

If we look at things pragmatically, the role of the alerts is to help identify AKI early, to institute actions. These alerts do not escalate or change if kidney function worsens, given this, there is a strong argument that the first AKI is the most important. For the first AKI in 2017 the concordance between our AKI and the WRRS alerts was good, however up to 7% of the alerts are still missed. This patient group have a 30-day mortality of 20.1% on average, compared to a 18.8% 30-day mortality when in both (Our AKI and WRRS) and 12.1% when in WRRS only (not including dialysis patients). If we work on an assumption that these alerts make a difference, then delaying these alerts may contribute to the difference in 30-day mortality. This assumption is explored in later chapters.

The agreement between our AKI and WRRS were similar to the 1st AKI alert in those patients that only had one alert in 2017, with 6.9% of alerts missed in WRRS alerts. This population as a whole had a lower 30-day mortality with a 30-day mortality of 16.2% when identified by both groups and 15.8% when identified by our code only (i.e. not in WRRS). This mortality was still much higher than the 30-day mortality following a blood test across the whole population which was between 1.7 and 2% across the health boards. It is likely that this group consists of two types of patient groups, one was patients having an AKI alert then dying before further testing and the others are those who recover immediately from the AKI alert, likely recover (as no further alerts) and therefore live beyond 30-days.

Despite the high specificity of the WRRS alerts, they do falsely identify AKI in patients on dialysis, this accounts for 8.3% of all the alerts sent by the laboratories. There appears to be a variation between the health boards as to the extent of this problem ranging between 3.6% and as high as 16.2% of the alerts in another health board. One reason for the variation may be the prevalence of dialysis blood tests within that health board and the ways in which the dialysis patients are identified. A health board without a renal ward, but with an offsite dialysis unit will find it easier to identify false positives and have a high positive predictive value (PPV) such as health board B with a PPV of 94.1%, whereas a health board with renal wards may falsely label AKI as dialysis patients and have a lower PPV such as health boards D and F (PPV 82.3% and 84% respectively). I have not explored the effect in detail, as it risks identifying the health boards which concerned the data guardians within SAIL at the point of extracting the data. As discussed earlier, there is little by way of direct harm in these false positives, but there is the potential for exacerbating alert fatigue in clinicians. There was also the potential effect that this could have on any publications that use alerts to identify AKI, if these false positives are not removed. This will be the case for outcomes such as mortality as we know that dialysis patients have a higher mortality than the general population, but they have a lower 30-day mortality than the true AKI population, as observed here.

Incorrectly suppressed alerts however, are more likely to carry the potential of direct harm. It seems that this was infrequently a problem and in some health boards it does not occur. When we have observed these suppressed alerts in clinical practice, the reason appears to be that the laboratory staff associate the requesting consultant with dialysis. In these cases, it

was because the consultant was a nephrologist who looks after dialysis patients. Nephrologists rely heavily on SCr in clinical practice and are specialists who manage or offer advice on patients with AKI, therefore suppressing these alerts may not have a large effect on the patient care. Nevertheless, the NECPOD report, 'Adding insult to injury' in 2009 (151) reported that AKI care even by nephrologist was suboptimal, therefore AKI recognition by nephrologist may not be as good as expected, and so alerts may help.

The comparison of alerts highlights the complexities of interpreting and implementing this AKI code to datasets. In creating the code, we had to make a number of assumptions, some of which appear to agree with the WRRS methods and others do not. The areas that did not match the WRRS method include the handling of less than results (e.g. <18 µmol/L). For ease of running the code we excluded results with text, whereas the WRRS algorithm seemed to count these results, the exact way was not clear, but I presume they used the highest next value such as 17 µmol/L in the aforementioned example. This makes sense, but it was not mentioned in the NHS England algorithm schema. Another variation was the handling of dates. Many SCr results (18.4% in WRRS dataset) do not have a recorded sample taken time as this requires the person drawing the blood to write it on the bottle, as a result a default time was used which appears to be 00:00. To avoid errors, it looks like the WRRS algorithm used time received in the laboratory (entered when the bloods are processed) as the date and time for the test. In practice this can vary by a day or even more particularly if from primary care. For our algorithm we used a few different steps to make the timing as accurate as possible. This was explained in more detail in the 3nd chapter (Test Timing on page 134), but simply, we used the date and time it was collected unless it was blank or default, in which case we used the time it was received in the laboratory. I believe this was a good method of handling this problem, but evidently it was not what the WRRS used and therefore it led to a fall in the agreement observed in this study. In some manually reviewed cases, this meant that the 48-hour window (lowest creatinine in 48 hours, also termed RV3) was wrongly missed by the WRRS system, and therefore the AKI was missed. Finally, the other reason for missing some alerts by the WRRS method compared to our AKI was the handling of day 7. For our AKI we used the day difference between the dates as 7 days, whereas WRRS seemed to use the hours difference for 7 days (shown in Table 64 – Date difference implementation example). This means that we handled patients differently, mainly affecting our 0-7 day lowest

creatinine but also our RV2 in a small number of patients. Without seeing the algorithm used, it seems these variations are very difficult to prevent, nevertheless. The main cause for the mismatches overall seems to be false positive alerts in dialysis patients, and the alerts missed by WRRS often after or between other WRRS AKI alerts.

In the case of WRRS alerts not in ours, part of this could be explained by missing historical results in two health boards, and therefore some of the 8-365 medians (RV2) were not accurate in SAIL and evidently the LIMS used for the alerts had access to results outside this. This was shown in SAIL by patients with alerts without any previous results when manually reviewed.

It should also be noted that both our AKI and the WRRS alerts will miss AKI that was identified by a clinician (171). An example of this would be if someone presents with a high SCr but then their test improves.

The answer

After years of trying to understand the variation between our AKI and WRRS, I happened to stumble across the reason for the variation. In June 2022, a leading Welsh biochemical scientist (Rachel Still) asked for my opinion on potential changes to the AKI electronic alerts, as Wales was due to move to a new all Wales laboratory information management system (LIMS). In this meeting, it was highlighted that there are three implementation adaptations to the NHS England algorithm, and it was wondered if we should continue with them.

1. Alert exclusions such as renal and dialysis tests
2. Different advice logic potential based on patient type (GP versus IP)
3. The EQACV (External quality assurance creatinine value) was incorporated to prevent alert fatigue

The most important rule here is the 3rd one, the EQACV, this was what led to the variation observed. The external quality assurances are produced to attempt to minimise variation and allow for accurate and precise analysis using comparisons of different sites (i.e. laboratories). In the context of serum creatinine testing, as I understand it, there was a 3% variation in test results. The EQACV introduced in Wales, looked to make allowances for the variation by introducing a rule that supressed alerts if it was within 2 times the 3% variation (i.e. creatinine

levels within 6% of the most recent test). I cannot find any literature record of these variation, or when the decision was to implement them. I received the schematic views of the adjustments, that had the aim of avoiding repetitive alerts and therefore alert fatigue called 'EQACV';

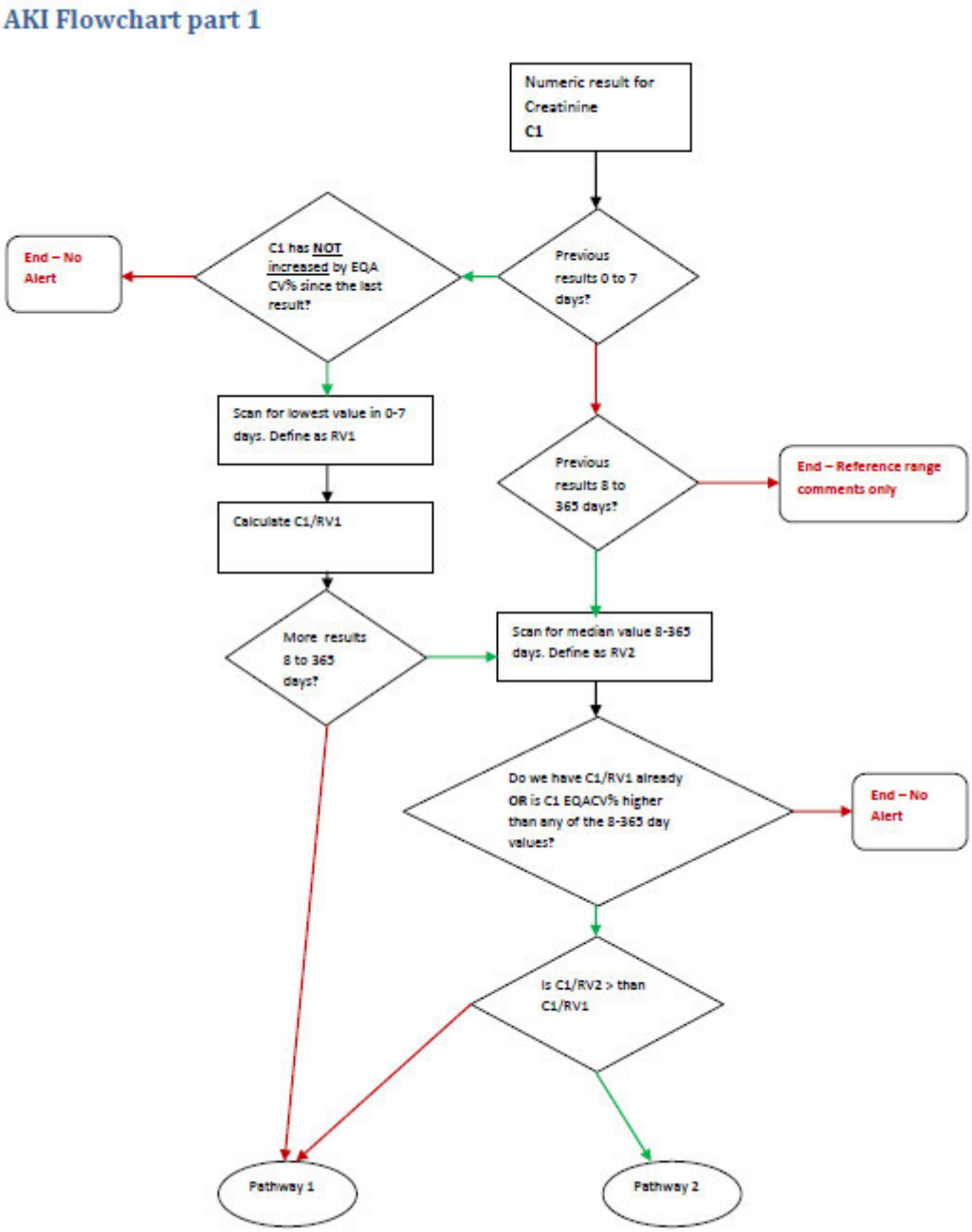


Figure 35 - Welsh AKI algorithm variation 1

This algorithm then fed into another one;

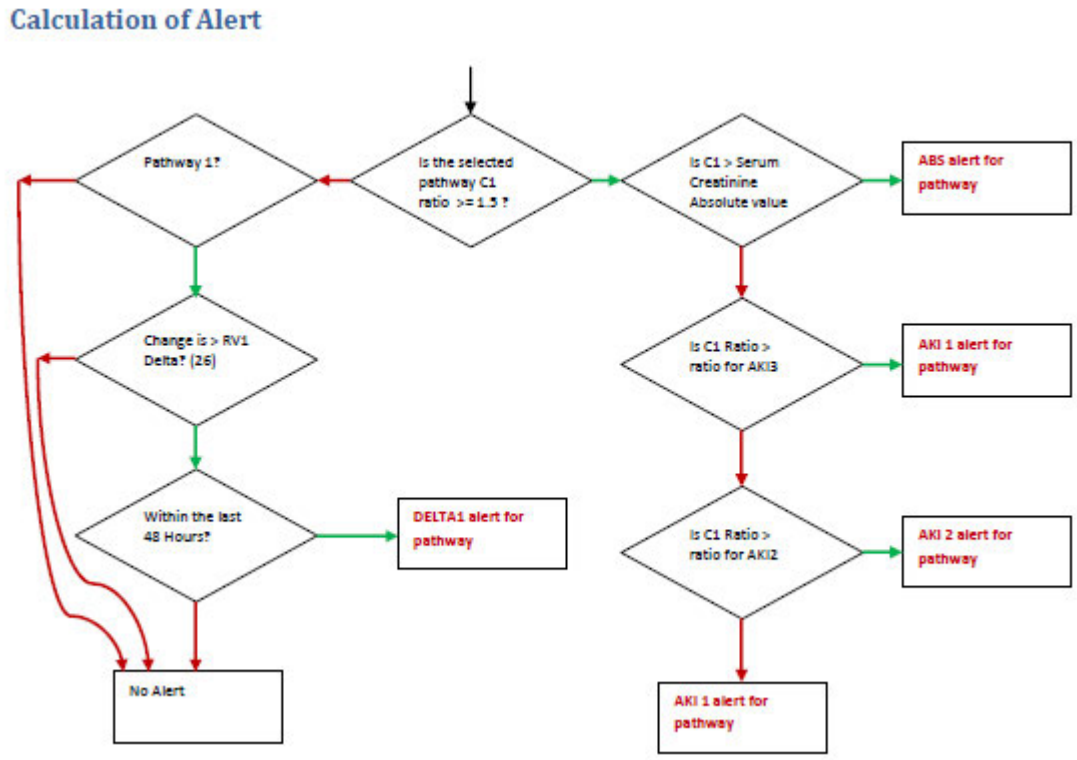


Figure 36 - Welsh AKI algorithm variation 2

The original intention of this code was to avoid repeated alerts, but it has been identified by those at digital Health and Care Wales (DHCW which was previously the NHS Wales Informatics service – NWIS) that there was the potential to miss patients with creeping creatinine values as shown in an example that they provided;

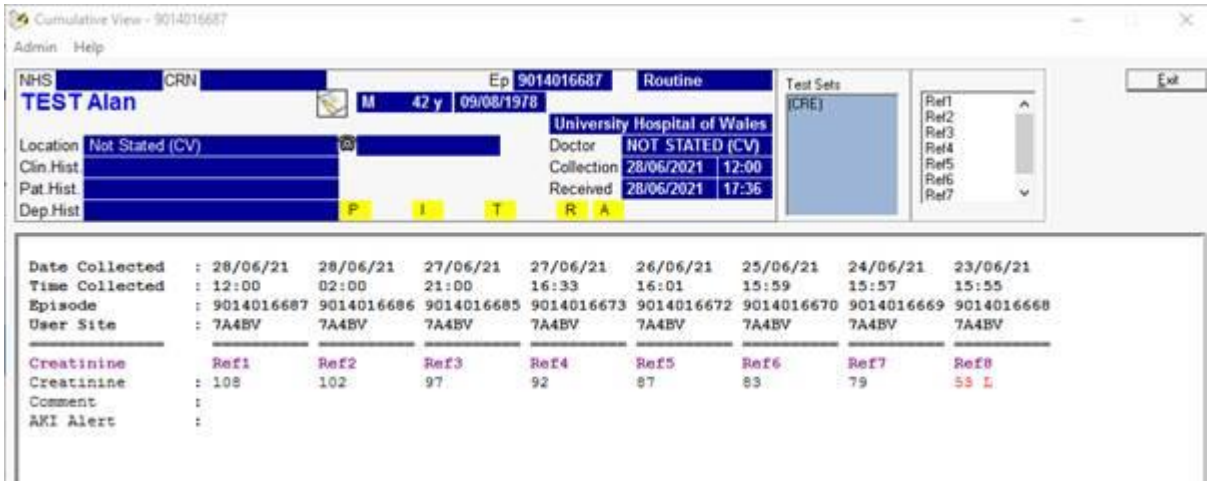


Figure 37 - Creeping creatinine example from DHCW - 1

In this example, several of these tests should trigger AKI but they do not. These are shown more clearly in the next table, again supplied by DCHW;

Episode	date/time	creatinine	Previous Cre	Diff from 1st	Diff from last	C1RV1 ratio	RV1>1.5	AKI alert	Alert expecte	Comment
9014016668	23/06/2021	53	NA	0	0			No		No PREV
9014016669	24/06/2021	79	53	26	26	1.49	No	No	No	Not >26 in 48 hours
9014016670	25/06/2021	83	79	30	4	1.57	Yes	No	No	>26 (30) in 48 hours
9014016672	26/06/2021	87	83	34	4	1.64	Yes	No	R1AKI1	>26 (30) in 48 hours
9014016673	27/06/2021	92	87	38	5	1.74	Yes	No	R1AKI1	RV<1.5 and >2.0
9014016685	27/06/2021	97	92	44	5	1.83	Yes	No	R1AKI1	RV<1.5 and >2.0
9014016686	28/06/2021	102	97	49	5	1.92	Yes	No	R1AKI1	RV<1.5 and >2.0
9014016687	28/06/2021	108	102	55	6	2.04	Yes	No	R1AKI2	RV >2

Figure 38 - Creeping creatinine example from DHCW - 2

As highlighted here, this rule even misses AKI stage 2. The term used in these e-mails was 'Creeping creatinine', which means that those with a creatinine that was increasing test on test (<6% per test) would not trigger AKI. The software engineers also highlight that the code was only run against authorised creatinine values which was my suspicion. These rules of course make perfect sense with the results that I have found. What was remarkable about this variation was that there was no mention of this, that I can find anywhere. The Welsh AKI steering group that was crucial in setting up the alerts refer specifically to the NHS England algorithm in their multiple publications (153, 169, 190, 195, 252, 253) and at no point mention creeping creatinine. On top of that, this AKI steering group also published an article in 2016 which states;

''Although alert fatigue may be avoided by suppression of some alerts to reduce the number of alerts issued, the data also suggest that this would lead to the exclusion of a number of high-risk patients.'' (169)

This makes me believe that they were not aware of deviation from the NHS England algorithm, but it raises the question of who drove this variation. Having worked for 6 years now on this type of coding, this would have taken considerable work from Stephen Winder and his team at DCHW. I have left this section separate from the others, as it was only later in the research that this answer has come to light, despite a lot of effort along the way and as a result it was only after writing my entire thesis, that this was evident. Prior to working on the AKI algorithm with Gareth Davies (my analyst in SAIL), I had spoken to multiple biochemist and biochemist IT staff to try and aid my understanding, but they were not aware of this.

AKI table error

To create this cohort, we need to use multiple sources of raw data which then creates feeder tables which supply the data for the final table. This increases the possibility of errors. This was the case in first analysis of this data. I spotted the error by manually reviewing the patients that triggered alerts by our code but did not appear in the WRRS data. In manually reviewing them the raw data of 25 patients per health board I spotted that our table had dropped some tests. In working with GD (analyst) we were able to spot the cause and correct it. Repeating the manual review in the final results helped ruled out the presence of this error in the corrected table. Nevertheless, a small number of patients with AKI were not identified by our algorithm due to dropped baseline results, however this was only 3% of those with WRRS alerts and not our AKI, so will have a minimal effect on later chapters.

Other missing alerts

It was observed that alerts were suppressed in some patients in practice with the comment, 'No AKI alert generated as Patient Type is Dialysis' and sometimes this was incorrectly applied to non-dialysis patients. In September 2022, I witnessed an example in clinical practice of a true AKI SCr result without a WRRS AKI alert, not effected by the additional rule and without a suppressed comment. This test was done in my name (Kidney specialist). The reason this alert was not sent was not clear as it does not fit with any of the problems, I have identified to date and raises the question as to whether there was another method of suppressing alerts, without the commonly seen comment. This has been highlighted to those in charge of the alerts, including those who suppress the alerts in my hospital, and they were unaware of how this may have taken place. They will investigate this deviation.

Conclusion

When reviewing the whole populations at risk of AKI, the WRRS alerts are mostly sent out correctly with a high specificity (99.7%), but AKI was often missed with a sensitivity of just 61.6% compared to the NHS England AKI algorithm. The number of alerts falsely suppressed are very small (false negative), but 1 in 12 of the WRRS alerts that are sent out for AKI are in dialysis patients (false positive). These false positive alerts may lead to alert fatigue, which could affect the impact that correctly issued alerts have on the clinicians. In patients who have multiple alerts for AKI, some alerts appear to be missed by the laboratory system, these patients carry a high associated 30-day mortality in this studied cohort. These alerts appear to have been intentionally left out by a step added to the NHS England algorithm looking to prevent alert fatigue however they lead to missed AKI in those with creeping creatinine values. This extra rule was not widely described and means that we cannot directly compare finding from our electronic alerts in Wales (WRRS alerts) to that of England or Scotland. Despite the introduction of an all Wales LIMS to manage the SCr and send the alerts, there appears to be variation in the implementation of these alerts between the health boards.

Chapter 5 - AKI alerts comparison with Coding

Introduction

Hospital admission diagnostic coding has been widely used for the identification of acute kidney injury (AKI) (119, 129, 138, 140, 143, 144, 254). Comparisons between creatinine-based identification of AKI and hospital coding have been carried out, including with temporal trends, however there have been variations in the findings (116, 119, 138, 144). For a hospital episode of AKI to be coded as AKI in the United Kingdom, the clinical coders need to read documentation of AKI in the medical records or the discharge summary. In some countries, such as the United States of America, coding is crucial for medical billing, and is therefore under greater scrutiny.

Hypothesis

1. An increase in the identification of AKI over time
2. SCr identifies a greater number of patients with AKI than coding

Method

The serum creatinine-based AKI cohort created for the previous chapter was used for comparison with hospital coding identification of AKI when the patient had an alert as an inpatient. The serum creatinine-based AKI cohort includes whether or not a WRRS alert was sent to the clinicians. The period studied was between 2010 and 2018. Only the health boards with biochemistry laboratories and therefore creatinine data were studied, and the time frame availability of this data varied, so comparisons were carried out over the following periods;

Health Boards	Year studied
Abertawe Bro Morgannwg University Health Board (ABMUHB)	2012 - 2018
Aneurin Bevan University Health Board (ABMUHB)	2016 - 2018
Betsi Cadwallader University Health Board (BCUHB)	2012 - 2018
Cardiff and the Vale University Health Board (CVUHB)	2015 - 2018
Cwm Taf University Health Board (CTUHB)	2010 -2018
Hywel Dda University Health Board (HDUHB)	2010 - 2018

Table 71 - Health board coding studied periods

Inpatient spells were identified by the test date falling between the start and end of a hospital admission spell. AKI was identified by coding using any derivatives of the ICD-10 code N17 in

any diagnostic positions (primary or secondary). To compare the AKI coding with SCr identified AKI, patients admitted for emergencies (admission method coded '21', '22', '23', '24', '25', '27', '28', '29') and intended to be admitted (intended management coded '1','2') were used to exclude day cases and elective procedures. For each health board I examined the temporal trend of the coding. Hospital mortality was identified by the discharge method code of 4 'patient died'.

Results

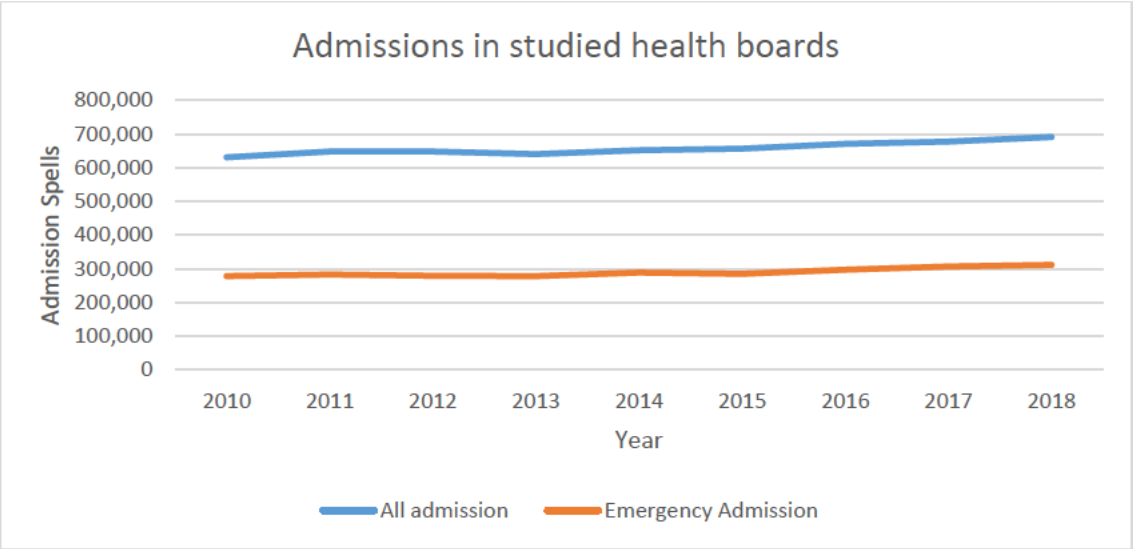
Over the period studied (2010-2018) there were 5,910,078 inpatient spells in 1,643,740 people. Of these admissions 2.5% (116) had ICD-10 coding for AKI, this increased to 5.2% when examining emergency admission.

2010 to 2018 Admissions	All Admissions	Emergency Admissions	AKI Coded	Emergency Admissions AKI Coded
Admissions	5,910,078	2,602,131	149,116	135,284
People	1,643,740	1,030,264	101,903	97,387
Female % of Individuals	56	54	47	47
Female % of Admissions	58	54	46	46
Mean Age (Standard Deviation)	57 (21.1)	60 (21.7)	76 (13.9)	76 (14)
Median Age	61	65	79	79
Mean Length of Stay (Standard Deviation)	5 (21.7)	8 (24.7)	18.5 (24.7)	17.5 (23)
Median Length of Stay	1	2	11	10
Death at discharge %	2.4	4.9	23.8	24.2

Table 72 - Admission demographics

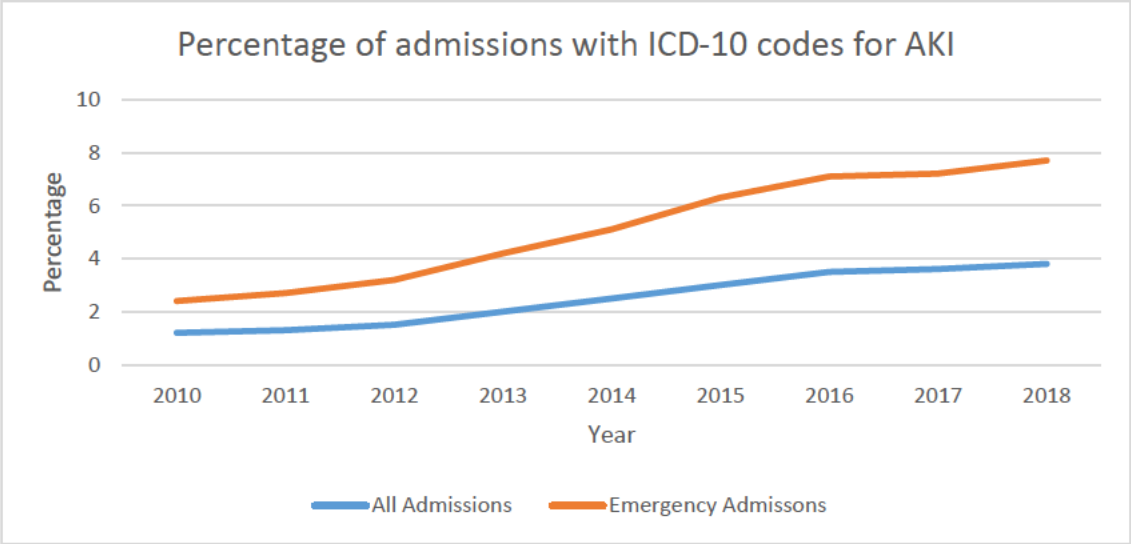
Those with AKI coding were more likely to be male and older than those admissions without AKI. The AKI cohort also have a longer average length of stay and a much higher inpatient mortality than the overall group.

Between 2010 and 2018 there was a 9.5% increase in all hospital admissions and a 11.9% increase in emergency admissions in these health boards;



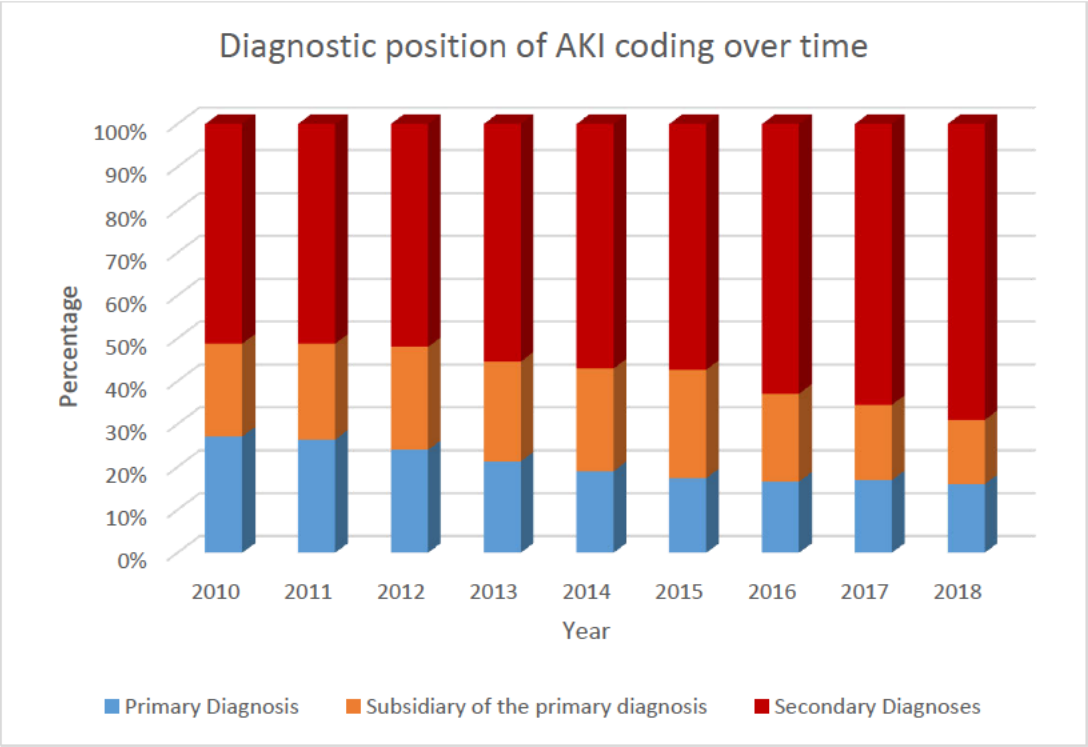
Graph 49 - Admissions in the health boards by year

Over this time period we have seen a large increase in the proportion of these admissions being coded for AKI, with emergency admissions coded rising from 2.4% to 7.7%;



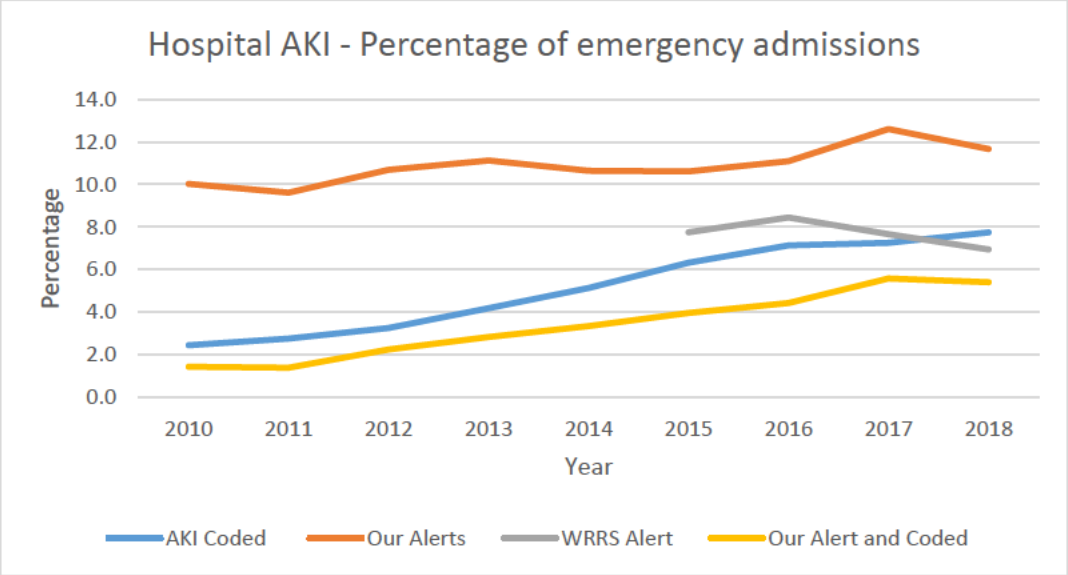
Graph 50 - AKI hospital admission coding

With this increase we see a change in the coding diagnostic position for AKI, with AKI the primary diagnosis in 27.1% of AKI coded patients in 2010 compared to 16.2% in 2018. These changes are gradual, as shown in this graph;



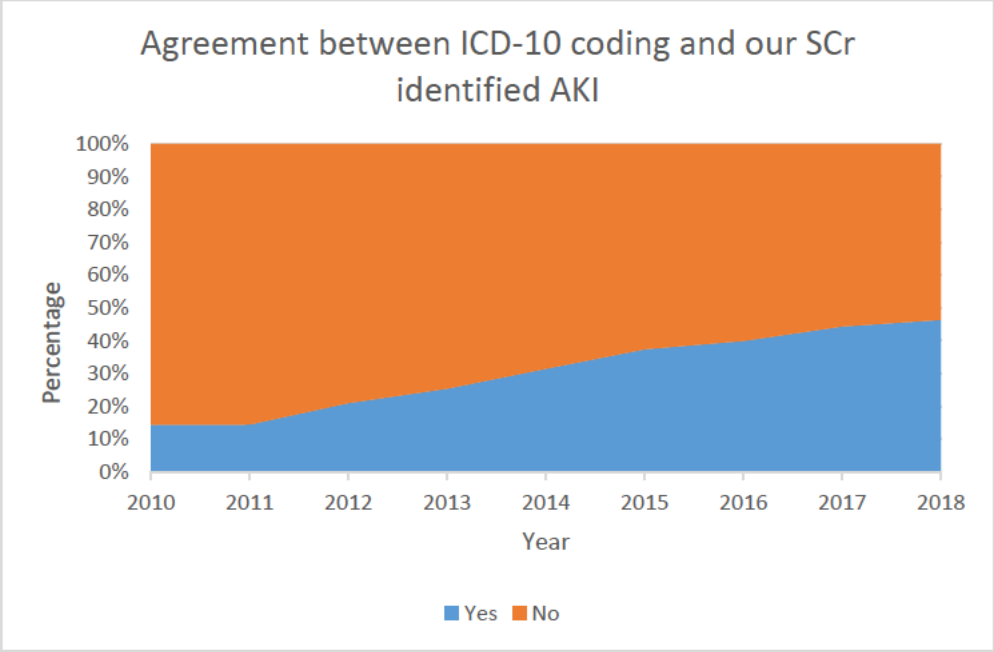
Graph 51 - AKI Diagnostic position by year

With the increase of AKI coding over time, it was important to understand whether this represents a genuine increase in AKI or a change in coding practice. The graph below compares the overall percentages of emergency admissions with AKI coding and those identified by biochemistry data. In this graph 'our alerts' are the AKI episodes we identify by the creation of the previously mentioned AKI algorithm in SAIL, the WRRS alert are the alerts available clinically, introduced across the Welsh health boards between 2013 and 2015;



Graph 52 - AKI coding comparison with creatinine identified AKI

This graph shows, that when using our AKI (Our alerts), there has been a gradual increase in the proportion of patients having AKI in an emergency admission from 10% in 2010 to 12% in 2018. The increase in diagnostic coding however has been even greater than this from 2.4% to 7.7%. Interestingly, a significant proportion of those patients coded for AKI are not AKI by our method as seen by the difference between 'AKI coded' and 'Our Alert and Coded'. It was apparent that only 46% of those identified as AKI by SCr (Our Alerts) have hospital coding for AKI in 2018 when you would expect it to be 64% if you consider that in that year, of the emergency admissions, 12% were identified as AKI by 'our alerts' and 7.7% had AKI coding. This means that some of those coded for AKI must not have AKI by our methods, this is explored in a later chapter. Overall, the association between our AKI and AKI coding does increase with time in spite of this.



Graph 53 - Agreement of AKI coding with our serum creatinine identified AKI by year

The next table shows a comparison of the AKI patients during this period.

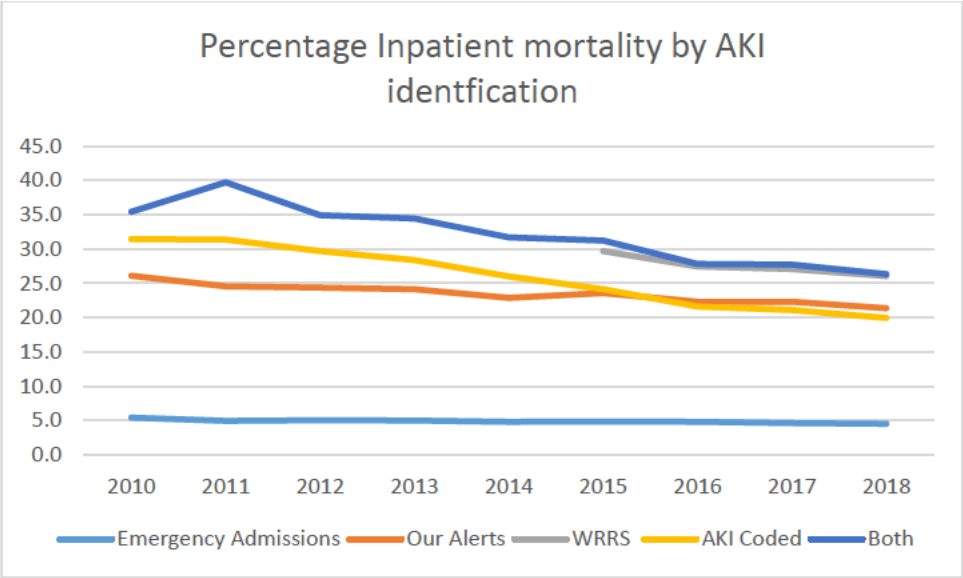
	Our AKI	Coded	Not Coded
Admission	181,820	63,315	118,505
People	129,383	52,178	92,277
Female (%)	92,423 (51)	29,780 (47)	62,643 (53)
Mean Age (Median)	73 (76)	75 (78)	71 (75)
Transplant (%)	1,501 (0.8)	478 (0.8)	1,023 (0.9)
Mean 1st AKI Alert Creatinine (Median)	183 (148)	244 (196)	151 (128)
Peak AKI 1 Stage (%)	115,243 (63)	28,277 (45)	86,966 (73)
Peak AKI 2 Stage (%)	36,017 (20)	15,377 (24)	20,639 (17)
Peak AKI 3 Stage (%)	30,560 (17)	19,661 (31)	10,900 (9)
Death Discharge (%)	41,930 (23)	18,778 (30)	23,152 (20)
Length of stay (mean)	19.5 (11)	19.7 (12)	19.3 (11)
	Location of first alert		
Inpatient (%)	132,432 (73)	42,408 (67)	90,024 (76)
A&E (%)	41,301 (23)	17,335 (27)	23,966 (20)
OPD (%)	3,986 (2)	1,527 (2)	2,459 (2)
GP (%)	3,195 (2)	1,736 (3)	1,459 (1)
Others/Null (%)	906	309	597

Table 73 - Comparison of those with AKI with and without ICD-10 coding for AKI

This table shows that the AKI patients coded were older, a greater proportion were male, they were more likely to have a more severe peak AKI, a longer hospital stay and more likely to die. A greater proportion also had their first AKI alert in A+E. These findings suggest a more severe illness and a presenting complaint involving AKI in those with AKI Coding.

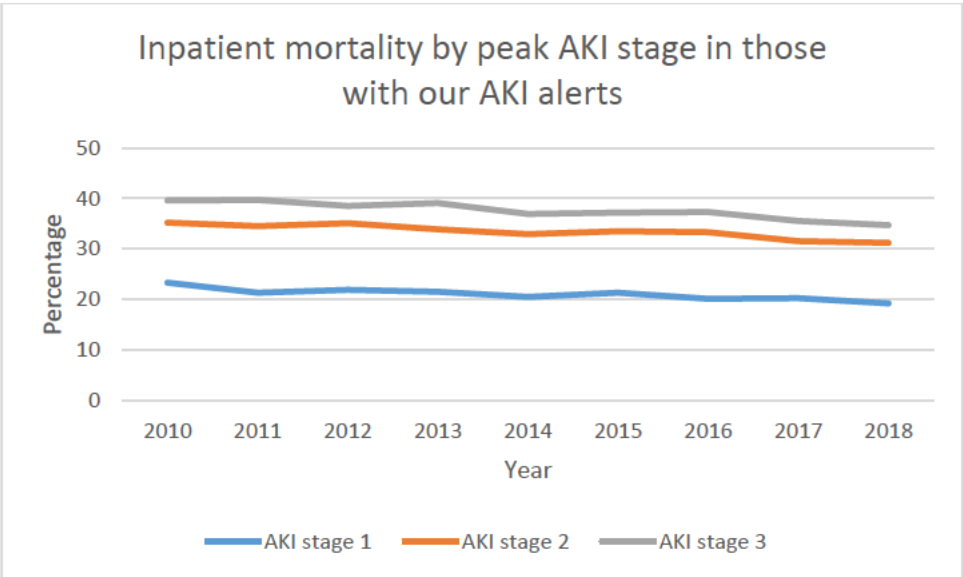
When comparing to our identified AKI ('Our AKI') the overall sensitivity of coding was 34.8% with a specificity of 98.7%. The positive predictive value was 64.7% with a negative predictive value of 95.6%.

If we look at the mortality trends over time in these AKI cohorts, it further clarifies this point;



Graph 54 - Hospital mortality in those with AKI by coding and by other methods (WRRS alerts and by our AKI method called 'Our alerts')

This graph shows a fall in inpatient emergency admission mortality over time from 5.4% in 2010 to 4.5%, there are lots of potential variables leading to this (better palliative care, improved hospital care, better treatment etc). This reduction in mortality is seen in all the AKI groups, but the greatest improvement was observed in the AKI coded group, again there are many potential reasons for this, but the most obvious and most likely was that the increased coding was now identifying less severe AKI compared to 2010. Nevertheless, it was promising that there may be improving AKI outcomes over time as suggested by 'Our Alerts' group. The graph below shows the inpatient mortality by AKI stage in those with AKI alerts by our method;

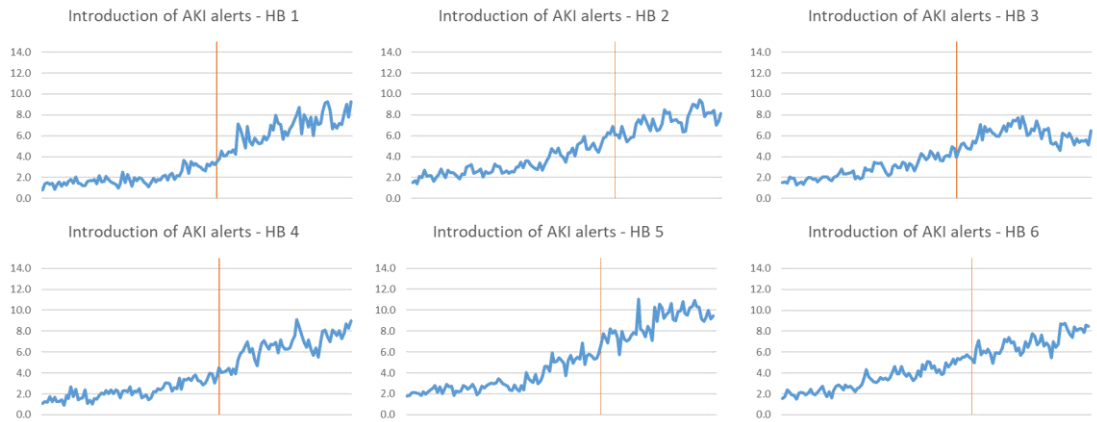


Graph 55 - Mortality by stage of AKI in coding cohort

As expected, the greater the AKI peak (stage 3 being the worst), the higher the hospital mortality. We again see an improving hospital mortality across all the group between 2010 and 2018.

Effect of WRRS alerts

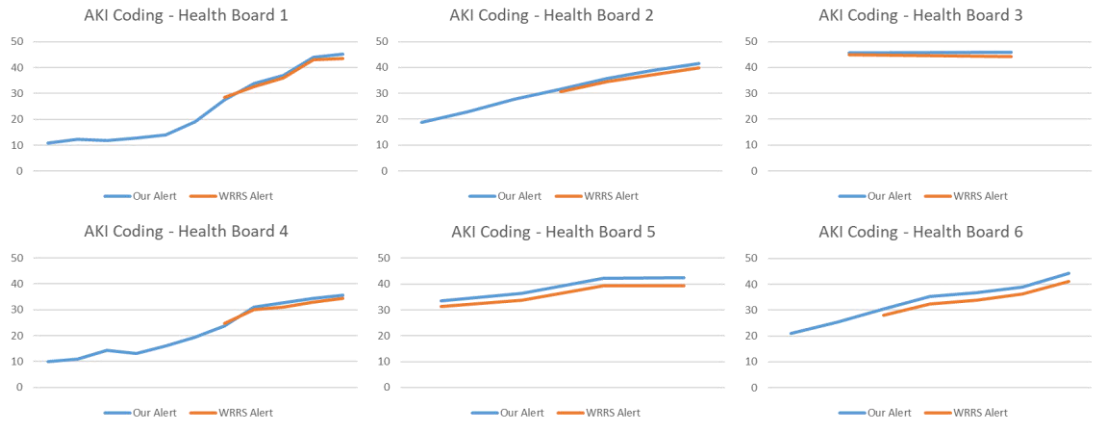
The electronic AKI alerts seen in clinical practice (WRRS alerts) were introduced to improve recognition of AKI. The graph below explores the introduction of these alerts and the changes in coding practices. To maintain the anonymity of the health boards and the coding variations the time points in the x axis have been removed. The graphs show the percentage of emergency admissions coded by year with the introduction of the alerts shown by the orange line;



Graph 56 - Coding for AKI and the introduction of AKI alerts by health board

In all these health boards the number of admissions coded with AKI increased with time, there may be slight changes in the trajectory, but there are no striking differences.

If we then look at the percentage of our AKI ('our alerts') and WRRS alerts coded over time in the different health boards, where there was biochemistry data before the introduction of the alerts, it was only health board 4 that shows a possible jump in trajectory of the proportion of coding beyond the background increase (Graph 57 - Coding for AKI and WRRS AKI alerts by health board). In these cases the WRRS alert beginning represents the introduction of alerts.



Graph 57 - Coding for AKI and WRRS AKI alerts by health board

AKI coding but no alert

An unexpected finding was the finding of patients coded for AKI without having AKI alerts. The table below looks at this cohort who have had blood tests in more detail;

Coded patients without AKI alert	Blood test no alert
Admission	34,556
People	28,771
Female (%)	15,702 (45.4)
Mean Age (Median)	77 (81)
Transplant (%)	243 (0.7)
Dialysis (%)	828 (2.4)
Mean Creatinine (Median)	164 (135)
Death Discharge (%)	3,849 (11.1)
Mean Length of stay (median)	14.2 (8)
Location of first blood test	
Inpatient (%)	20,067 (58.1)
A&E (%)	12,695 (36.7)
OPD (%)	899 (2.6)
GP (%)	721 (2.1)
Others/Null (%)	174 (0.5)

Table 74- Those coded for AKI but without biochemical AKI

From Table 74 we can see that those AKI coded patients without AKI by our algorithm had less severe illness (reduced mortality and length of stay). Some of the patients were on dialysis at the start of the admission (first blood test was used) and the median creatinine measurement tells us that many had abnormally high levels which could be chronic kidney disease (CKD) or AKI.

Some patients do not appear to have blood tests at all yet are coded for AKI. On reviewing these patients, I suspect some did have a blood test, but they are not available in SAIL. The health boards and time periods of these missing results are well spread with no obvious individual cause. This group has a high hospital mortality but a lower length of stay. I am suspicious that some of these patients may have had tests initially as 'unknown' patients and therefore were not linked to NHS number. The table below shows this population;

	No Creatinine Test
Admission	3,972
People	3,482
Death Discharge %	28.9%
Female (%)	1,798 (45.3%)
Mean Age (Median)	76 (79)
Mean Length of stay (median)	9.5 (4)

Table 75 - Those coded for AKI but without creatinine test

Discussion

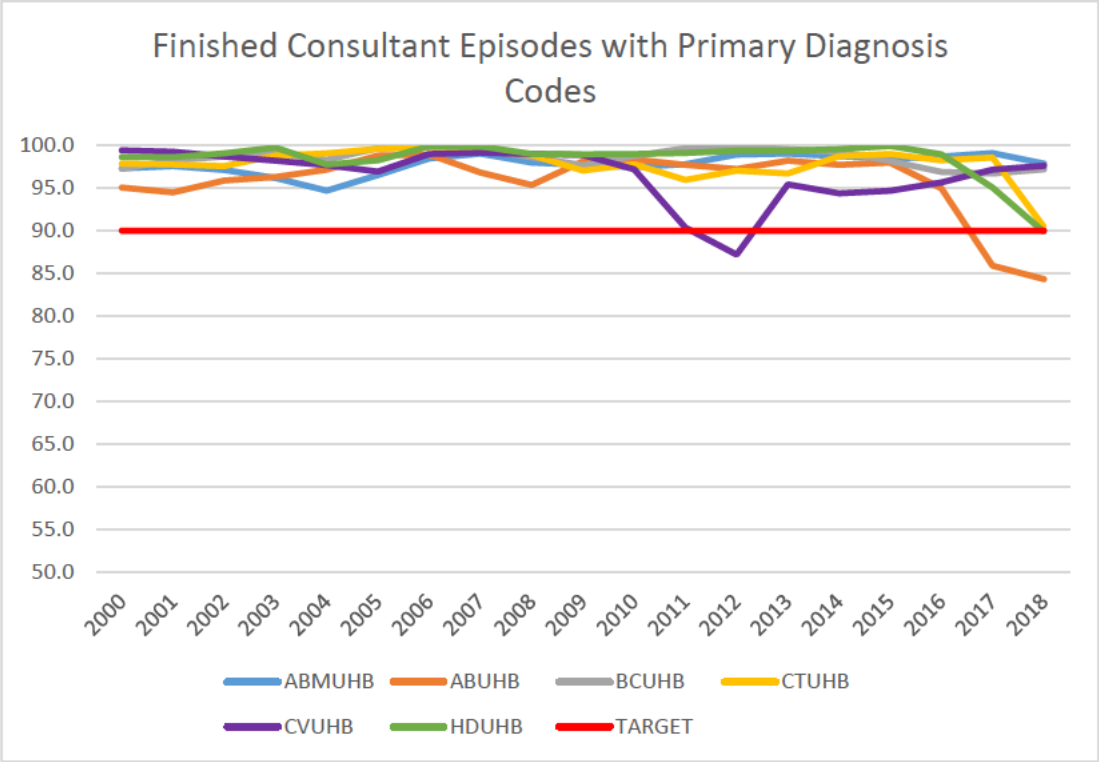
Over the last decade there has been a significant increase in the ICD-10 coding for AKI which was above the rate of increase of AKI diagnosed by serum creatinine changes, nevertheless coding still identifies fewer AKI admissions. If we look at the whole population, the sensitivity of coding was poor at 34.8% and this was similar to the findings of other studies as shown in Table 12 on page 57 and summarised in Waikar et al's paper from 2009 (125). It has a lower positive predictive value than expected which may be due to the repeat coding of previous episodes. This has been suggested in other studies (120, 142, 145). The improvements in proportion of patients identified as having AKI by coding predates the introduction of electronic AKI alerts (WRRS alerts). The factors that could lead to an increase in the likelihood of coding for AKI include;

The disease

We can see by our serum creatinine method (our alerts) that there was an increase in patients with AKI, however this was at a lower rate than coding, with a 20% vs 220% increase between 2010 and 2018. Therefore, this was likely to be only a minor factor.

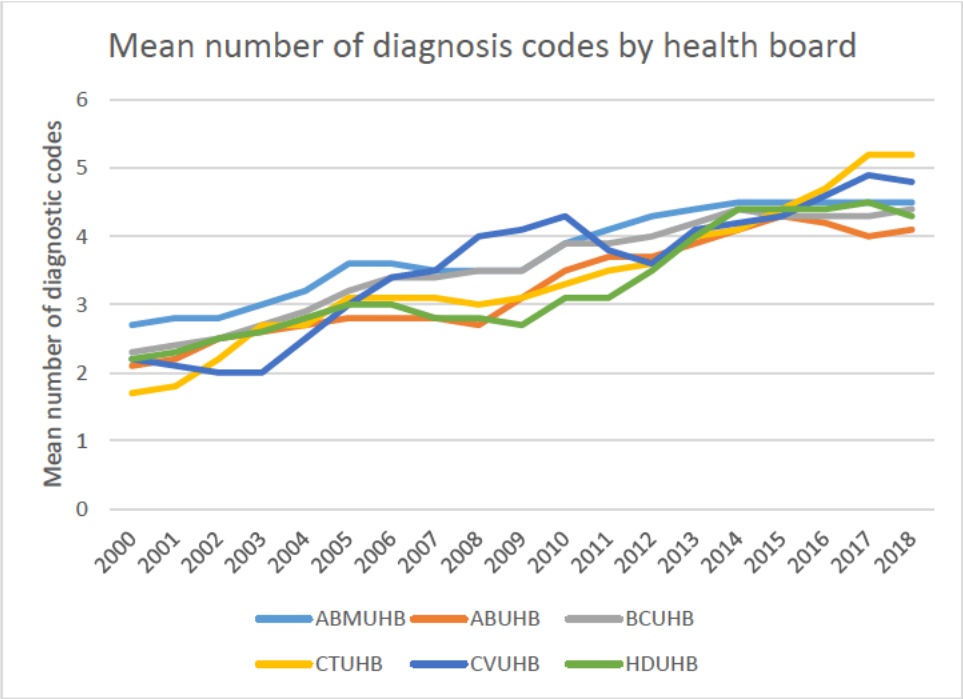
Coding practices

It could be an improvement in the completeness of coding. As part of the dataset analysis, I looked at the completeness of coding in PEDW over time.



Graph 58 - Finished consultant episodes with primary diagnosis

As can be seen in this graph, the coding completeness has been largely static and meeting targets in this dataset, therefore this was not an explanation of the increase. However, we have seen an increase in the average number of codes per episode over the last few years (coding depth). This in itself, has several possible explanations, such as patients with more complex, more comorbid conditions. I suspect that this was the case to a degree, but it was also likely an effect of a drive to code more conditions, possibly as a result of the coding audit such as the 2014 audit (246) and preceding audits.



Graph 59 - Mean number of diagnostic codes

This increase in the depth of coding will have increased the likelihood of AKI coding and this is highlighted by the increase in secondary diagnosis position of AKI code from 51% in 2010 to 69% in 2018.

The recognition

It was likely that the recognition of AKI has improved during this period. Until 2004 there was no agreed definition of AKI or acute renal failure as it was called then. Since then, there have been 3 iterations of a consensus definition. As such the condition has developed more of an identity and with this it was likely that recording of this condition has increased in patients case notes. The introduction of electronic AKI alerts (WRRS alerts) was implemented to improve recognition of AKI and these may well have help sustain the improvements made in the preceding years. There was however no clear jump in coding overall following their introduction. An interesting finding of this study was that those patients identified by coding were more likely to have their first blood tests in A+E compared to those not coded 27% vs 20%. This suggests that the coded population are more likely to present with AKI. This makes sense clinically, as often diagnosis lists are written at the beginning of an admission.

Documentation

Over the period studied, there may have been some improvement in clinical documentation. Certainly, some discharge summaries in 2010 were handwritten, therefore not available to the clinical coders or of insufficient quality to read (they would receive a carbon copy). In recent years the discharge summaries have become electronic and have now become standardised across Wales. There are some areas within Wales using partial electronic medical records, including for clinical notes, but this remains the minority and most areas continue to use paper patient files. Electronic medical records are easier for coders to review.

Health boards

There are variations when comparing the health boards, with one health board still only identifying 35.6% of the SCr identified AKIs, compared to 3 health boards above 45% in 2018. This variation suggests that the reason was more than just clinician recognition, as due to the alerts it should be similar across the health board. This may well reflect clinical coding differences.

Limitations of coding

Hospital ICD-10 coding for AKI identifies patients with a higher hospital mortality than those identified by creatinine alone, nevertheless over the period studied this gap has narrowed and hospital mortality has reduced. In fact, the mortality across all groups has improved, including in those with AKI stage 3 which may suggest improved care, treatment improvements or equally could reflect changes in discharge practice (i.e. palliative care). Nevertheless, coding was missing a significant number of patients with AKI and 1 in 5 of these missed patients died during their admission. This may reflect a lack of clinician recognition of the condition. Most of the patients missed by coding appear to have a less severe condition, nevertheless AKI identified by our AKI and/or WRRS alerts, identify a group of patients with a hospital mortality far higher than that of the average emergency admission mortality. I found that a third of patients with AKI stage 3 were missed by coding. This group has an inpatient mortality of 35-40%, so it was worrying that these are not identified. In spite of this, coding recognised a very high risk cohort and for retrospective research it was a useful group to study. However, this coding cohort cannot be used for prospective or interventional studies.

There was also great variation with coding year on year, as shown in this Welsh example, which may be comparable with other parts of the UK and some other countries but may not be as comparable for other countries where monetary renumeration was more closely linked to coding. It also means that publications using coding requiring care regarding chronology and interpretation. These findings suggest that studies based solely on ICD-10 coding select a cohort of AKI with a high mortality but miss over half of inpatient AKI.

Coded for AKI but without AKI by SCr methods

There are a number of reasons people may have coding for AKI but not detected by our alert algorithm. This can be split in to two categories, those with blood test results in SAIL and those without. For those with bloods a few reasons come to mind. It is known that patients can present with very high creatinine values that then improve, and due to the lack of baseline they don't get identified by algorithm as having AKI, nevertheless a clinician may recognise this as AKI from an acute illness or the subsequent improvement and document this in the notes. Another potential reason was the coding of historic diagnosis of AKI, this might be highlighted best by the patients coded for AKI but on dialysis. Their hospital admission may be falsely coded for AKI based on their past medical history of AKI. This is understandable as clinical coders are encouraged to code comorbidities. There was also the possibility that some patients were transferred in with AKI. Some tertiary services are based outside Wales, such as cardiac surgery services in North Wales, these patients may have their AKI test in England prior to convalescence or rehab in Wales. We know tertiary care like cardiac surgery carries a high risk of AKI (255). Some patients may have falsely been identified as AKI when on dialysis by the WRRS alerts, as described in the validation chapter (Chapter 4 page 160).

Limitations of the study

Our SCr AKI cohort identifies patients with AKI that falls between an admission start date and end date, this means that some patients with AKI before admission are not identified. If we include all the clinical coding for AKI and not just the ones we recognised as AKI using SCr methods ('Our Alert), then the overall numbers of coded AKI appear better. Nevertheless, coding still only represents two thirds of the number of AKI admissions that are identified by SCr ('Our Alerts'). As mentioned, some AKI episodes may start outside our biochemistry cohort. At the end of the study (2016-2018) this would only be Welsh blood tests carried out in England, but prior to that it could be Aneurin Bevan or Cardiff and the Vale health boards. As mentioned, the 'Our Alerts' group do not identify those presenting with AKI if no recent creatinine and then they subsequently improve. Some of the patients not coded for AKI in 2018 may have been missed as the data used was from 2019 and we have observed that some patients are coded well after their discharge, however this will represent a small number as the 3 month target of completeness of coding is 95% (246) and this was largely achieved (Graph 20).

Conclusion

Admissions with hospital coding for AKI are associated with a high mortality and prolonged length of stay. When compared to AKI algorithms based on serum creatinine, coding identifies a proportion of patients with a low sensitivity of 34.8%. Nevertheless, over the period of the study the correlation between the two methods has improved. The inpatient mortality for patients recorded as having AKI using coding has improved which was likely to be due to the identification of a less severely unwell cohort, nevertheless there has been a downward trend to the mortality even in the creatinine group. Coding has been used for the study of AKI, but it must be used in caution due to low sensitivity in identifying AKI compared to serum creatinine methods which are commonly used in prospective and interventional studies. Coding selects a more severely unwell group and may miss some of those who may benefit more from interventions. Coding has also varied significantly over time, therefore the use for studies investigating temporal changes, will likely identify changes in coding practice and not the disease. Nevertheless, the discrepancy between coding and AKI based on creatinine has

narrowed with time, and coding cohorts are readily available for studies of this high-risk group.

Chapter 6 - Impact of electronic AKI Alerts

Introduction

The outcome of patients suffering with acute kidney injury (AKI) is poor, with an increased mortality rate, an increased length of hospital stay and an increased risk of developing chronic kidney disease, including the need for renal replacement therapy (54, 118, 123, 153). In 2009 the NCEPOD report into the recognition and management of AKI in the United Kingdom found poor care (151). As a result, electronic alerts were introduced with the aim to improve identification and therefore the treatment of AKI (117). These alerts were introduced in Wales in a staggered approach with the introduction of an all Wales Laboratory Information System (AWLIMS), across 2014 and 2015. The impact of these type of alerts has been looked at in randomised control trials (183) and there have been reviews in individual hospitals (188, 256, 257), but there has not been a large scale, multiple centre retrospective analysis comparing the period before and after their introduction.

Aims

To assess whether there was an improvement in mortality rates, recovery from AKI, and a reduction in need for future renal replacement therapy following the introduction of electronic Alerts for AKI.

Hypothesis

Electronic AKI alerts improve 30-day mortality in patients with AKI.

Method

The study compares adult (≥18 years of age) patients with AKI before and after the introduction of the electronic AKI alerts. To do this I used the blood test results from the Welsh Result Reports Service (WRRS) stored as the PATH dataset (pathology) and the All Wales Renal Dataset (AWRD) within SAIL. Within the WRRS dataset are serum creatinine (SCr) results and the AKI alerts. Unfortunately, Cardiff and the Vale and Aneurin Bevan university health boards did not have sufficient biochemistry results for the period before the introduction of alerts, this was despite efforts to try and gain the data, therefore they were

not studied. Powys health board does not have its own biochemistry laboratory, therefore it was not studied, however some patients from this health board would have been included if they had tests which were sent to the other health boards. Velindre University NHS trust is an oncology service for Wales and the test for patients receiving its care are mostly included in the other health board results. The regions studied are university health boards; Betsi Cadwaladr, Cwm Taf, Hywel Dda and Abertawe Bro Morgannwg.

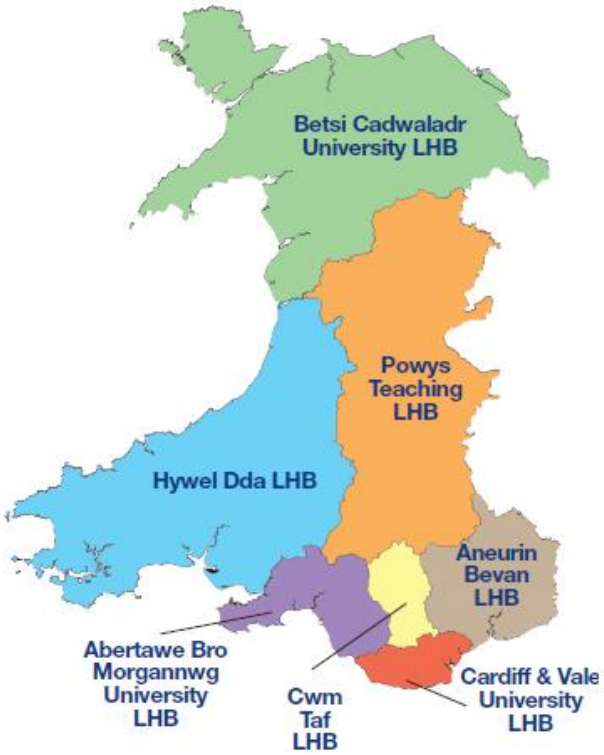


Figure 39 - Welsh health boards 2013-2016

This covers 11 of the 15 teaching or district general hospital within Wales at the time the alerts were introduced, along with some smaller hospitals. Prior to the introduction of the eAlerts, a reproduction of the NHS England AKI alerts algorithm within SAIL was created by Gareth Davies (analyst working on this project) with my help, which was used to identify AKI (Chapter 3 – The Creation of AKI Cohort). This was created based on the NHS England AKI algorithm which at the time of the study was thought to be the same algorithm applied in Wales and therefore seen in the WRRS dataset that sends AKI alerts to clinicians. As mentioned in the in chapter 4 (Chapter– 4 - Validation of electronic AKI Alerts), there was a difference between the AKI–numbers identified by our replication of the NHS England AKI algorithm and the alerts sent in clinical practice (WRRS alerts). This was due to several

reasons, but the main reason which was only identified after this study, when I discovered that there were some additional rules added to the NHS England algorithm with the aim of reducing the number of alerts. Another reason for the variation was that our AKI code allows for an accurate removal of dialysis patients using the all Wales renal dataset (AWRD). As the result the post eAlert introduction group has two parts, those with the eAlerts in WRRS and those with AKI by our code. The 'Our AKI before' and 'Our AKI After' are directly comparable. The WRRS alerts group matches 'Our AKI after' 61.6% of all the alerts and 93% of the first alerts in 2017;

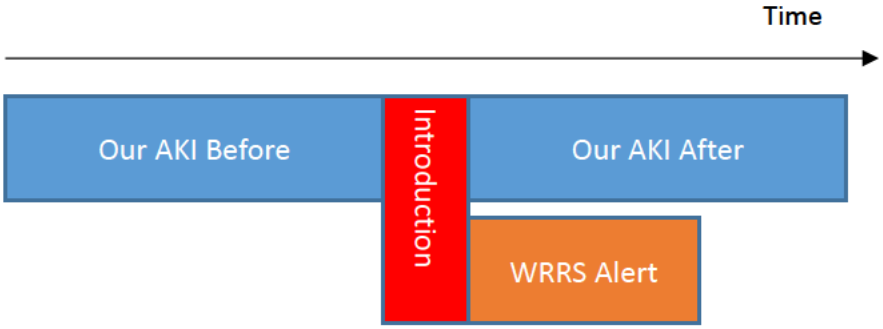


Figure 40 - Schematic of electronic alerts

These AKI cohorts were compared for a year before and after the introduction of the eAlerts with the month of the introduction excluded. This time period was pragmatically chosen to allow for the inclusion of the most health boards (i.e. 4) which have the pre-alert introduction data for 2 years (allowing for the baseline creatinine) and to capture a large number of patients. At the time of the planning of this research there were no similarly designed trials to call upon, which compared electronic alerts. The periods covered in the different health boards are shown in the image below;

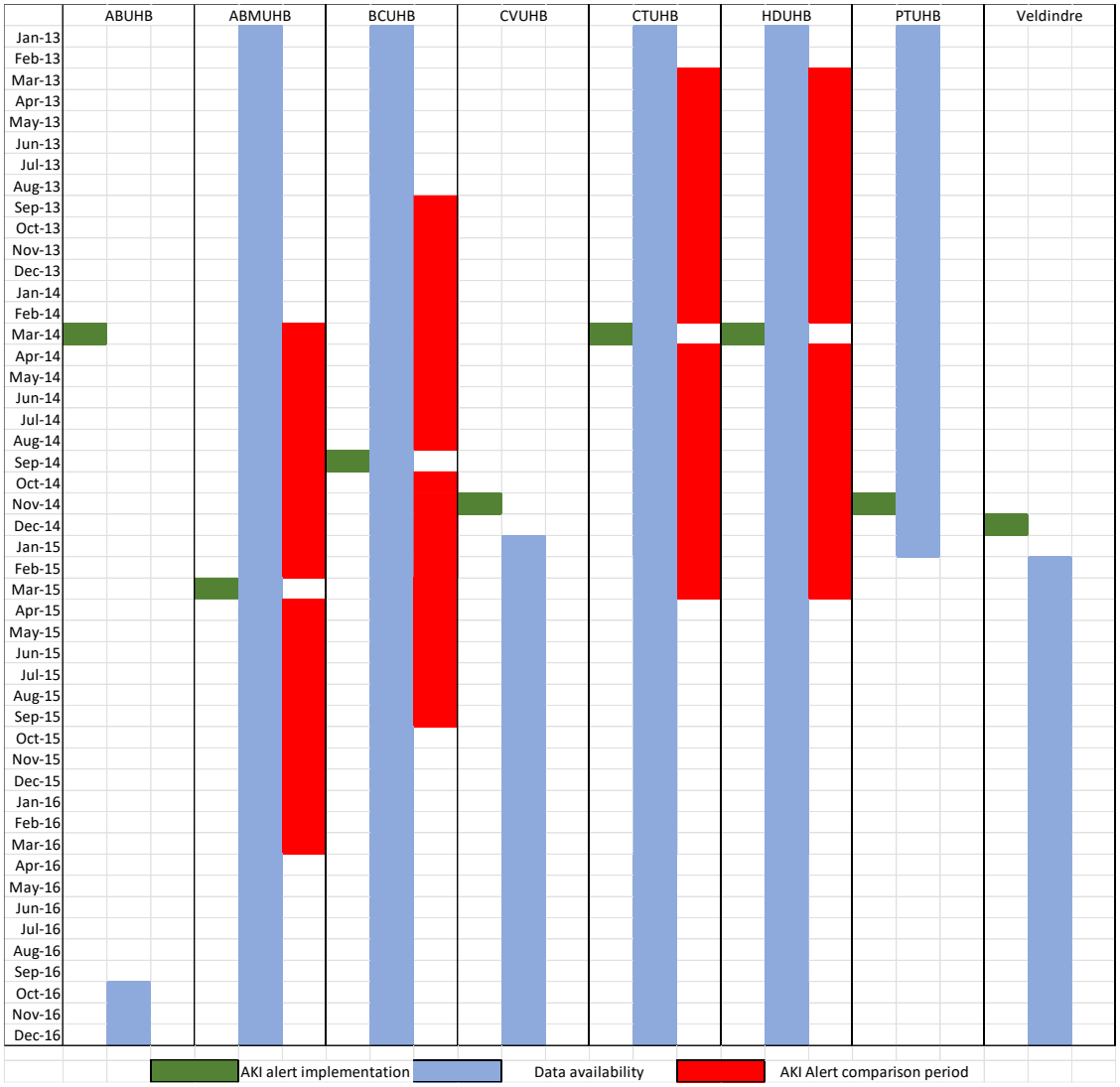


Figure 41 - Timing of eAlert introduction in Welsh health boards

Key –AB–HB - Aneurin Bevan University Health Board, ABM–HB - Abertawe Bro Morgannwg University Health Board, BC–HB - Betsi Cadwaladr University Health Board, CVUHB - Cardiff and the Vale University Health Board, CTUHB – Cwm Taf University Health Board, HD–HB - Hywel Dda University Health Board, PT–HB - Powys Teaching Health board, Velindre NHS Trust.

In this figure above, the green cell represents the introduction of electronic alerts within that health board. The blue represents good quality biochemistry data identified by comparing the number of tests by month to the mean over the subsequent year and included if there was a <5% variability. The red colour represents the periods studied (change over month not included).

The data used includes demographic and outcome data which was collected from several sources within SAIL; the age, gender and death dates are collected from the Welsh Demographic service dataset (WDS) with the death date also collected from the Office of National Statistics (ONS) death dataset called ADDE in SAIL. There are times where the two

death date sources do not match, usually having a mismatch of one day, in these cases WDS was preferentially chosen as it was the most complete.

The Patient Episode Database for Wales (PEDW) was used to obtain information of any admission at the time of the AKI, this included coding for AKI in any diagnostic position and length of stay information. To do this, patient episode and spell information was collected. The critical care dataset (CCDS) was then used to ascertain the information regarding admission to critical care and renal replacement whilst on the intensive care units. Level 3 care was defined as "Level 3 critical care – patients requiring advanced respiratory support alone or basic respiratory support together with support of at least two organ systems. This level includes all complex patients requiring support for multi-organ failure" taken from the NHS Data Dictionary(258).

To allow for the adjustment of comorbidities, data was collected for Charlson comorbidities variables and a score tallied using the technique described in these SAIL papers (248, 259). The Charlson components were identified using the PEDW and the primary care datasets within SAIL.

Charlson Comorbidity Index	Score
Myocardial Infarction	1
Congestive Cardiac Failure	1
Peripheral Vascular Disease	1
Cerebrovascular Disease	1
Dementia	1
Chronic Pulmonary Disease	1
Rheumatologic Disease	1
Peptic Ulcer Disease	1
Liver Disease	1
Diabetes Mellitus (controlled)	1
Diabetes Mellitus (uncontrolled)	2
Hemiplegia/Paraplegia	2
Renal Disease	2
Malignancy (localised)	2
Malignancy (Metastatic)	6
Leukaemia	2
Lymphoma	2
Acquired Immunodeficiency Syndrome	6

Table 76 - Charlson Comorbidity Index

The primary care dataset does not cover the whole population studied therefore there will be some patients whose comorbidities are underrepresented; however, this remains equal across the comparison groups before and after the alerts introduction as shown in Graph 23.

Recovery from AKI was identified using the lowest creatinine within 90 days of the AKI triggering test (index) as used by Lafrance et al (260), and was present if the lowest creatinine does not trigger AKI compared to index baselines values as used by Holmes et al(253) (i.e. RV1, RV2 and RV3). It was analysed for the first AKI of the year only.

Information on the current and future need for dialysis was gathered from linkage to the AWRD and follow up appointments in outpatient were gathered from the outpatient dataset. When someone has an AKI alert they may go on to have further alerts. Given that the primary outcome studied was mortality from the alert, I have analysed the **first** AKI within each period studied (1 year before and the 1 year after alert introduction). It was likely that some individuals are present in both groups. These outcomes are also assessed by individual health board based on the location of the test to see if there are different outcomes in the different health boards.

In comparing a year before and after the introduction of alerts, there are some difficulties encountered, in that there was the potential that the after group reflects a more recent group and therefore might represent an overall change in practice, nevertheless, the staggered introduction of the alert does help to minimise this effect. This was because some health boards overlap different cohorts with different parts of other health boards (i.e. before and after), visualised in Figure 41.

Mortality was assessed using the WDS date of death as the primary death date, but where this was unavailable and there was a death date in the ONS ADDE dataset, that was used. Overall mortality following an AKI alert was calculated, but the main analysis looks at death following first AKI alert at 30-days and 1 year to avoid multiple events (alerts) impacting the mortality figures. Mortality was displayed as a percentage, with the denominator as AKI alerts or 1st AKI episode (correlates with individuals).

Statistics

Statistical analysis was carried out using SPSS using descriptive statistics to summarise demographic characteristics and comorbidities. Comparison of outcomes was performed using logistic regression analysis and comparison of the mean was done using independent t test.

Result

All Tests

Across the four health boards there were 2,014,501 SCr tests (693,228 individuals) in the year before the alert introduction and the 2,081,269 test after (709,951 individuals). Of these tests 3.8% of the tests before (75,889) and 3.6% after (75,958) the introductions of alerts triggered AKI by our algorithm. Over half of these tests were in women. Table 77 shows the breakdown of the whole population at risk of having an AKI alert (i.e. those that are tested, people can have AKI without being tested, but they need a test to have an alert);

Pooled Health Boards	**Year Before Alert Introduction**	**Year After Alert Introduction**
All SCr Tests	2,014,501	2,081,269
Individuals with tests	693,228	709,951
Testing frequency	2.9	2.9
Mean Age (Median)	65 (67)	65 (68)
Female	379,914 (54.8%)	389,418 (54.9%)
Mean Creatinine (Median)	96 (79)	95 (78)
AKI alerts	75,889 (3.8%)	75,958 (3.6%)
Death < 30-days	84,938 (4.2%)	89,258 (4.3%)
Death < 1-year	295,663 (14.7%)	310,786 (14.9%)
	Location of Test	
Inpatient	647,148 (32.1%)	648,066 (31.1%)
A&E	168,804 (8.4%)	174,666 (8.4%)
GP	916,717 (45.5%)	921,301 (44.3%)
OPD	266,103 (13.2%)	304,306 (14.6%)
Other	15,729 (0.8%)	32,930 (1.6%)

Table 77 - Demographics of those with tests before and after alert introduction

If we compare the overall tested population to those triggering AKI in Table 78 using our algorithm, we can see that the average age was older, average creatinine was understandably higher and the tests are far more likely to be taken as an inpatient. It however remains similar with the gender proportions.

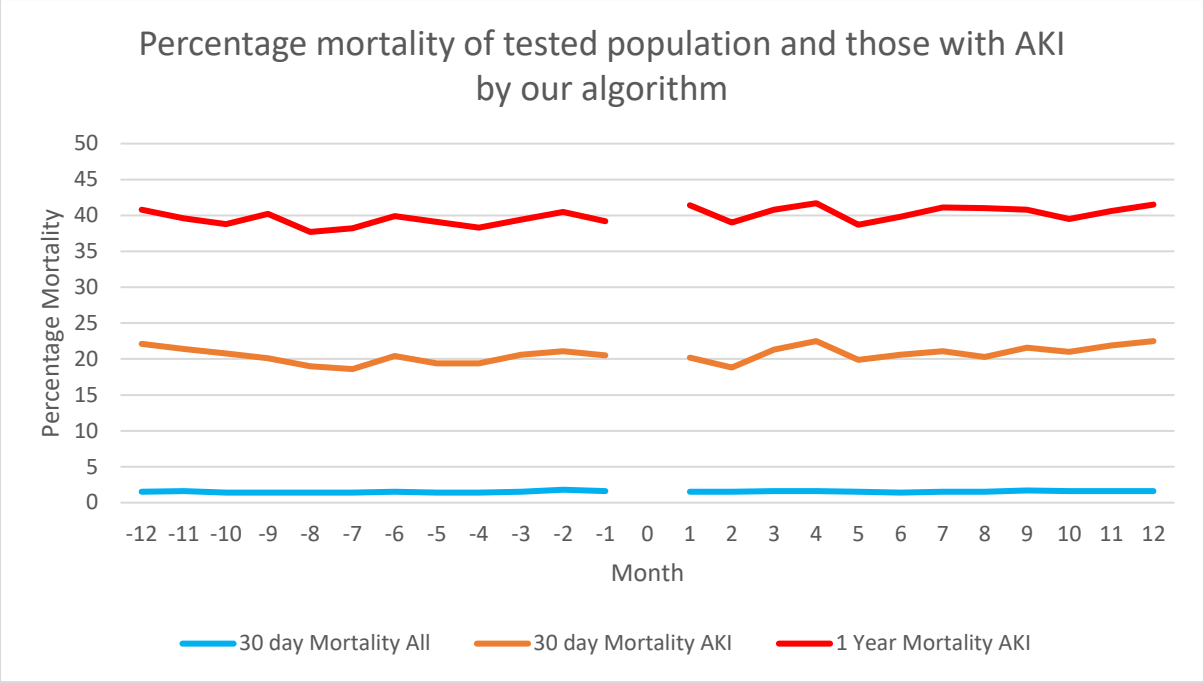
Pooled Health Boards	AKI Before Alert Introduction	AKI After Alert Introduction
All	75,889	75,958
Individuals	26,258	25,991
Mean Age (Median)	72 (75)	72 (75)
Female	14,517 (55.3%)	14,182 (54.6%)
Mean Creatinine (Median)	207 (166)	205 (165)
Alert stage 1	47,895 (63.1%)	48,223 (63.5%)
Alert stage 2	14,686 (19.4%)	14,676 (19.3%)
Alert stage3	13,308 (17.5%)	13,059 (17.2%)
Death < 30-days	18,944 (25%)	19,277 (25.4%)
Death < 1-year	35,555 (46.9%)	35,734 (47%)
	Location of Test	
Inpatient	56,575 (74.5%)	55,515 (73.1%)
A&E	8,532 (11.2%)	8,873 (11.7%)
GP	6,976 (9.2%)	6,447 (8.5%)
OPD	3,504 (4.6%)	4,390 (5.8%)
Other	302 (0.4%)	733 (1%)

Table 78 - AKI results before and after eAlert introduction using our AKI algorithm

The percentage of those that die within 30-days or a year also was much higher in this AKI group compared to the population that have a creatinine test in these years. The problem with understanding the mortality in these two tables is that we are on occasion counting patients more than once, in fact, you may expect that it is more likely that a patient who dies during a year would have more tests than someone that does not. For example, someone who has 30 tests in a year and dies, their death will be counted 30 times. For this reason, to deal with the effect of multiple events, the mortality following the first AKI test for the period should be studied. First, I look at the overall mortality;

Mortality

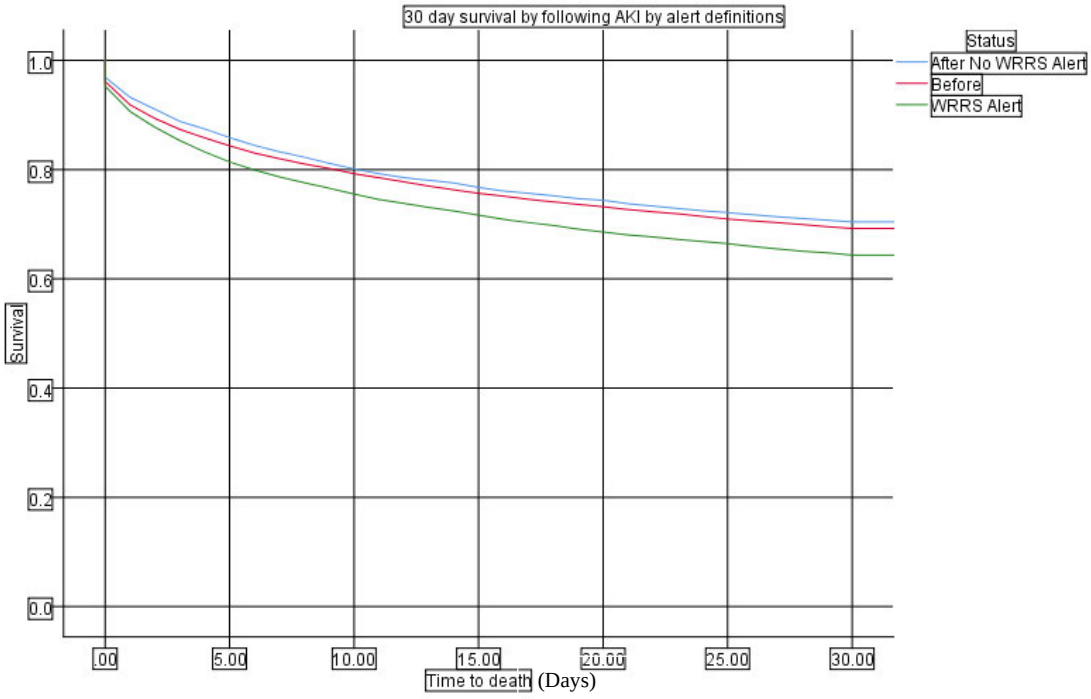
Mortality is an outcome important to both patients and clinicians following AKI. It was hoped that the introduction of electronic alerts would improve mortality. To understand the effect the alerts have on mortality, we first need to understand if there was any changes in the general population. The graph below shows the percentage mortality of **individuals** with AKI using our application of the algorithm and the general population who have a blood test that month around the introduction of the alerts (month 0).



Graph 60 - Mortality percentage before and after eAlert introduction

As can be seen here, there are some fluctuations in the percentage mortality by a small amount across the period, but the before and after group are comparable.

The Kaplan-Meier survival curve below shows the 30-day unadjusted survival following the 1st AKI episode of the period.



Graph 61- 30-day survival in those with AKI identified by our algorithm and WRRS alerts

This unadjusted analysis suggests that the survival following the introduction of the alerts was unchanged when comparing our AKI tests (our AKI before alerts) and our AKI with no WRRS alert after, however it does show a reduced 30-day survival in those with a WRRS alerts.
I used logistic regression analysis to compare our AKI groups before and after the eAlerts introduction and this showed that there was no significant difference between the two groups in this univariate logistic regression analysis;

Mortality	Our AKI Before alerts	Our AKI After alerts	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	Standard Error	p value
30-days	24.9%	25.4%	1.02	0.99	1.05	0.01	0.61
1-year	46.8%	47.0%	1.01	0.99	1.03	0.01	0.44

Table 79 - Mortality following an SCr test triggering AKI as identified by our algorithm before and after eAlert introduction

If we compare our AKI before and WRRS after however, as suggested in the Kaplan-Meier curve, there appears to be a significant increase in the 30-day mortality in the WRRS group.

Mortality	Our AKI Before alerts	WRRS Alerts After	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	Standard Error	p value
30-days	24.9%	26.8%	1.1	1.07	1.13	0.01	<0.01
1-year	46.8%	47.4%	1.02	1.00	1.05	0.01	0.05

Table 80 - Mortality following an SCr test triggering AKI as identified by our algorithm before and WRRS eAlert after the introduction of eAlert into clinical practice

When it comes to the 1-year mortality however, we have less confidence that what we are seeing was not due to chance (p 0.054), nevertheless it does give a trend towards an increased mortality in the WRRS group.

First AKI

This table below looks at the baseline characteristics for the first AKI of the year, comparing the 3 groups.

Baseline	Our AKI before Alerts	Our AKI after Alerts	WRRS Alerts After
Age (mean)	71.3	71.2	71.2
AKI Creatinine (mean)	161.9	161.3	159.2
Baseline eGFR (RV2 mean)	75.9	76.6	77.1
Female (%)	55.3	54.2	55.1
AKI Stage 1 (%)	79.2	78.8	77.8
AKI Stage 2 (%)	13.5	13.5	14.5
AKI Stage 3 (%)	7.2	7.6	7.7
Triggered by RV1 Rule(%)	24.4	24.6	29.5
Triggered by RV2 Rule(%)	63.9	64.0	61.3
Triggered by RV3 Rule(%)	11.7	11.4	9.2
Inpatient (%)	68.3	67.1	70.3
Admission Test Day (%)	23.5	22.8	23.2
Primary Care Data Available (%)	82.8	84.0	83.4
No comorbidity data (%)	9.5	9.1	9.7
Charlson score 0 (%)	16.5	15.9	15.8
Charlson score 1-3 (%)	48.3	47.5	48.4
Charlson score 4-6 (%)	21.0	22.0	21.4
Charlson score ≥7 (%)	4.7	5.5	4.7
	History of		
Myocardial Infarction (%)	12.7	12.7	12.3
Congestive Cardiac Failure (%)	16.9	17.8	16.7
Diabetes Mellitus (%)	30.8	32.5	31.6
Chronic Kidney disease (%)	4.4	4.3	3.7
Cancer (%)	21.5	21.7	21.4
Kidney Transplant (%)	0.3	0.5	0.4

Table 81 - Comparison of those with AKI before and after alert introduction including those with eAlerts

Key - RV1 is lowest 0-7 days, RV2 is median value 8-365 days and RV3 is lowest in 48 hours.

Broadly these 3 groups are similar, however the WRRS group appears to identify a high proportion of inpatients (70.3%) in comparison to those identified by our AKI algorithm (67.1%). It also has fewer patients with chronic kidney disease (CKD), which was likely due to the code variation added into avoid repeat alerts where there needs to be a >6% increase from the previous test, this may also explain why there are fewer RV2 based alerts in the WRRS group.

AKI outcomes from first AKI

To get an accurate picture and avoid bias of the outcomes when multiple events (AKI tests) are possible I have looked at the first AKI of the year studied (year before and year after alert introduction). The table below looks at the unadjusted outcomes using logistic regression analysis following the first AKI the patients suffered in the studies periods. For the comparisons of the mean independent t test was used;

Outcomes	Our AKI Before alerts	Our AKI After alerts	P value (Before vs After)	WRRS alerts after	P value (Before vs WRRS)
30-day Mortality	18.6%	19.3%	0.08	19.7%	0.01
1-year Mortality	36.8%	37.9%	0.01	37.5%	0.12
Recovery	72.8%	74.2%	<0.01	75%	<0.01
Recovery and 30-day survival	65.2%	66.2%	0.01	67.1%	<0.01
Future Dialysis Treatment	2.3%	2.9%	<0.01	2.3%	0.65
Critical Care Admission	5.1%	6.6%	<0.01	7.1%	<0.01
Critical Care RRT	0.8%	1.3%	<0.01	1.3%	<0.01
Length of Level 3 care days Mean (Median)	5.8 (4)	6 (4)	0.62	5.5 (4)	0.69
Admitted to hospital same day	23.5%	22.8%	0.07	23.2%	0.46
Coded for AKI	15.3%	19.0%	<0.01	19.2%	<0.01
Length of Hospital stay in those admitted Mean (Median)	20.2 (11)	21.6 (12)	<0.01	21.5 (11)	<0.01
Progression of AKI to Stage 3	14.0%	14.5%	0.1	14.6%	0.06
Clinic Review After AKI	3.3%	3.3%	0.93	2.7%	<0.01
Percentage of New Clinic Reviews After AKI	18.7%	18.5%	0.87	17.3%	0.34

Table 82 - AKI univariate outcomes in AKI identified by our algorithm before and after eAlert introduction and with WRRS eAlert

We observe an increase in 30-day mortality when comparing the before and WRRS groups (p = 0.01) as well as an increase in the mortality in our group after, however the p value does not reach the traditional confidence threshold of <0.05 (p = 0.08). However, when examining the 1-year mortality there was a significant increase in mortality in our AKI after (p = 0.01) but not with the WRRS alerts (p = 0.12).

Recovery and future dialysis

Another important outcome following AKI is the recovery of renal function. For this we look for the lowest creatinine in 90 days after the AKI and whether it no longer triggers AKI. In

order for the outcome to be relevant, we are looking for recovery and survival for 30-days. This excludes those that have a lower creatinine and die from being included as a positive outcome. Here we observe an improvement in the unadjusted recovery after the introduction of the alerts, with the largest percentage seen in the WRRS alert group (p <0.01). However, following the introduction of the alerts we have seen no change in the number of patients needing future dialysis when comparing our AKI before and the WRRS alerts (p 0.65), but there was an increase in the number of people requiring future dialysis when comparing our AKI before and after (p <0.01). There were no significant differences in the number of patients reaching AKI stage 3 following an initial alert of a lower stage.

Critical care admissions

There was an increase in the number of patients requiring admission to critical care and then receiving renal replacement therapy following the alert introduction. However, the was no major change in the duration of time patients were on level 3 ICU support.

ICD-10 Coding for AKI and admission

There was no significant difference in the number of patients admitted on the day of their first AKI test, but we did see an increase in the mean length of stay, and in the median length of stay when comparing our AKI before and after AKI. There was an 25% increase in the proportion of those with AKI being coded during their admission for AKI which was a positive finding. There has been a been a year on year increase in coding for AKI, but 2013-2015 are the periods with 3 of the 4 highest percentage increase as shown below;

Year	Percentage increase in AKI coding year on year
2012	50%
2013	19%
2014	24%
2015	19.4%
2016	8.1%
2017	10%
2018	4.5%

Table 83 - Percentage increase in AKI ICD-10 hospital coding compared to our algorithm

Renal follow up

In the WRRS group, there was a reduced proportion of patients seen in renal outpatients follow up compared to the other groups ($p < 0.01$), however this may in part be caused by the survival differences observed. Due to the low numbers, there was no discernible difference in the proportion of patients seen as a new clinic referral following the introduction of AKI alerts.

Multivariate analysis -All

There are several factors that appear to be associated with survival following AKI, correction for these factors was crucial in understanding if there was a true variation in survival before and after the introduction of the WRRS alerts. The factors that appear to be important identified when using univariate analysis are; age, gender, Charlson score categorised to ≥3, chronic kidney disease stage 4 or greater, critical care admission, critical care renal replacement.

Univariate analysis of these factors was shown in the table below;

30-day mortality - Variables	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	Standard Error	P Value
Age	1.04	1.04	1.04	0.001	<0.001
Gender	0.78	0.75	0.81	0.022	<0.001
Charlson Score > 3	1.76	1.71	1.81	0.015	<0.001
Critical Renal Replacement Therapy	2.84	2.39	3.38	0.088	<0.001
Critical Care Admission	2.22	2.05	2.4	0.04	<0.001
CKD4 or worse	1.5	1.38	1.64	0.043	<0.001
Individual Charlson Comorbidities					
MI	1.37	1.29	1.45	0.031	<0.001
CCF	1.72	1.63	1.81	0.027	<0.001
Diabetes Mellitus	1.26	1.21	1.32	0.023	<0.001
Cancer	1.55	1.47	1.63	0.025	<0.001
Renal Charlson Code	1.26	1.14	1.4	0.051	<0.001

Table 84 - Logistic Regression analysis of individual variables influencing 30-day mortality

Using these factors, I ran logistic regression analysis with these variables;

		WRRS alerts vs our AKI before		
WRRS vs before	**Odds Ratio**	**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**	**P value**
30-day mortality (negative outcome)	1.06	1.00	1.12	0.03
1-year mortality (negative outcome)	1.04	0.99	1.09	0.11
Recovery (Positive outcome)	1.13	1.08	1.18	<0.01
Recovery and Alive (Positive outcome)	1.10	1.06	1.15	<0.01
Future Dialysis (negative outcome)	1.05	0.91	1.21	0.49

Table 85 - AKI multivariate regression outcomes in AKI identified by our algorithm before and WRRS eAlert after introduction Number = 38,936 Missing 13,313

In this analysis we are reviewing the **WRRS alerts** comparing it to our AKI before. For negative outcomes, we would want a protective odds ratio (i.e. <1) and for positive outcomes we would want a odds ratio > 1, meaning the outcome was more likely. We can see that even after correction the WRRS cohort appears to have an increased 30-day mortality, however this was not still the case at 1-year. We see that the ratio of those recovering and alive at 30-days improves (driven by the recovery improvement), but this did not translate into a reduction in need of future dialysis treatment. As mentioned, there was a difficulty with directly comparing these two groups, therefore when we compare **our AKI before** and **after** we do not see a statistically significant survival difference. We see fewer people recovering in the before alerts group, however we also see fewer people requiring dialysis in this group.

	Our AKI before vs our AKI after			
Before vs after	**Odds Ratio**	**Lower 95% Confidence Interval**	**Upper 95% Confidence Interval**	**P value**
30-day mortality (negative outcome)	0.98	0.93	1.03	0.37
1-year mortality (negative outcome)	0.96	0.92	1.00	0.06
Recovery (Positive outcome)	0.93	0.9	0.97	<0.01
Recovery and Alive (Positive outcome)	0.95	0.92	0.99	0.01
Future Dialysis (negative outcome)	0.83	0.74	0.94	<0.01

Table 86 - AKI multivariate regression outcomes in AKI identified by our algorithm before and after AKI eAlert introduction Number = 45,361 Missing 6,888

In this comparison, of the AKI identified by our version of the NHS England algorithm for identifying AKI before and after the introduction of the clinical AKI alerts, we see that the corrected mortality at 30-days and 1-year was not statistically significantly different between the two groups. We did see a lower recovery, and lower recovery and alive at 30-days in the before group, but the before group appeared to have a reduced need for future dialysis.

Health Board Comparison

To better understand the effects of the electronic alerts we need to see if there was any regional variation. To allow for the extraction health board level data from SAIL we have been asked to anonymise the health boards. The Table 87 shows the baseline characteristics comparing the 4 health boards before and after. In this table we can see differences between the health boards with variations in the age and the locations of the tests, this may explain in part some of the discrepancies of the impact findings. The table shown on the next page (Table 87) shows a variation in the number of patients with renal transplants, this was likely explained by those health boards with higher percentage of transplant having inpatient nephrology care.

	A Before	A After	F Before	F After	B Before	B After	E Before	E After
SCr Tests	624,680	642,844	664,598	679,854	308,734	320,924	416,489	437,647
Individuals	204,245	208,214	237,475	242,903	114,911	117,752	144,474	148,539
AKI Alerts	25,188	25,843	22,979	21,951	12,398	12,373	15,277	15,760
People	8,284	8,681	8,643	8,030	4,348	4,092	5,096	5,290
Mean Age (Median)	72 (75)	71 (75)	72 (75)	72 (75)	70 (74)	70 (73)	73 (76)	73 (76)
Female (%)	12,400 (49.2%)	12,788 (49.5%)	11,606 (50.5%)	10,863 (49.5%)	6,063 (48.9%)	6,455 (52.2%)	7,646 (50%)	7,853 (49.8%)
Mean AKI Creatinine (Median)	201 (163)	200 (159)	205 (160)	208 (164)	214 (172)	207 (168)	217 (172)	210 (172)
Alert Stage 1	16,226 (64.4%)	16,901 (65.4%)	14,809 (64.4%)	13,540 (61.7%)	7,648 (61.7%)	7,777 (62.9%)	9,200 (60.2%)	9,982 (63.3%)
Alert Stage 2	4,972 (19.7%)	4,870 (18.8%)	4,264 (18.6%)	4,289 (19.5%)	2,481 (20%)	2,475 (20%)	2,960 (19.4%)	3,040 (19.3%)
Alert Stage 3	3,990 (15.8%)	4,072 (15.8%)	3,906 (17%)	4,122 (18.8%)	2,269 (18.3%)	2,121 (17.1%)	3,117 (20.4%)	2,738 (17.4%)
Inpatient	19,830 (78.7%)	19,445 (75.2%)	17,296 (75.3%)	16,007 (72.9%)	8,890 (71.7%)	9,391 (75.9%)	10,540 (69%)	10,645 (67.5%)
A&E	2,319 (9.2%)	2,551 (9.9%)	2,106 (9.2%)	2,698 (12.3%)	2,127 (17.2%)	1,653 (13.4%)	1,975 (12.9%)	1,969 (12.5%)
GP	1,882 (7.5%)	1,861 (7.2%)	2,462 (10.7%)	1,987 (9.1%)	853 (6.9%)	757 (6.1%)	1,758 (11.5%)	1,840 (11.7%)
OPD	1,102 (4.4%)	1,517 (5.9%)	1,047 (4.6%)	1,234 (5.6%)	439 (3.5%)	489 (4%)	914 (6%)	1,150 (7.3%)
Other	55 (0.2%)	469 (1.8%)	68 (0.1%)	25 (0.1%)	89 (0.7%)	83 (0.7%)	90 (0.6%)	156 (1%)
Transplant	178 (0.7%)	222 (0.9%)	130 (0.6%)	128 (0.6%)	11 (0.1%)	39 (0.3%)	38 (0.2%)	113 (0.7%)
WRRS Alert	0	13,781 (53.3%)	0	11,318 (51.6%)	0	7,464 (60.3%)	0	8,956 (56.8%)
Suppressed	0	698	0	44	0	0	0	5
Charlson Score (Mean)	3	3	3	3	3	3	3	3

Table 87 - Health board comparison before and after eAlert introduction

Health Board Outcomes 1st AKI

To understand any differences seen, it was important to look at the individual health boards studied to look at whether the trends are consistent. The results in the next large table shows the previously studied outcomes in the different health boards, comparing the before and after by AKI alerts and also the before with the WRRS alerts following the first episode of AKI.

Health Boards	A					F					B					E				
	Before	After	p value	After WRRS	p value	Before	After	p value	After WRRS	p value	Before	After	p value	After WRRS	p value	Before	After	p value	After WRRS	p value
Number	8187	8590		5501		8637	8027		5639		4345	4089		3452		5089	5285		4275	
30-days Mortality	18.4%	17.6%	0.18	14.9%	<0.01	18.9%	20.6%	<0.01	22.6	<0.01	21.2%	21.1%	0.85	22.3%	0.24	18.7%	18.5%	0.81	19.9%	0.16
1-year Mortality	37.1%	36.1%	0.16	30.7%	<0.01	35.8%	39.1%	<0.01	41.1%	<0.01	38.1%	39.4%	0.23	40.7%	<0.01	36.8%	37.8%	0.32	39.1%	<0.01
Recovery	75.5%	75.7%	0.68	77.6%	<0.01	72.3%	72.5%	0.73	73.3%	0.19	69.9%	74.7%	<0.01	74.8%	<0.01	71.7%	73.9%	0.13	74.1%	0.01
Recovery and alive	67.5%	68.1%	0.46	71.3%	<0.01	65.1%	64.6%	0.49	64.9%	0.88	61.8%	66.0%	<0.01	65.8%	<0.01	64.4%	65.9%	0.10	65.7%	0.19
Future Dialysis	4.1%	5.8%	<0.01	4.8%	0.07	1.1%	1.1%	0.67	0.9	0.29	1.2%	1.3%	0.42	1%	0.65	2.7%	2.1%	0.05	1.9%	0.01
CC Admission	5.4%	6.7%	<0.01	7%	<0.01	3.2%	6%	<0.01	6.7%	<0.01	5.8%	6.5%	0.23	6.6%	0.17	7.1%	7.6%	0.36	7.9%	0.17
CC RRT	0.8%	1.5%	<0.01	1.40%	<0.01	0.4%	0.9%	<0.01	0.9%	<0.01	1.6%	1.8%	0.48	1.7%	0.55	0.9%	1.2%	0.12	1.3%	0.37
CC LV3 LOS x̄ (median)	7.7 (6)	8.4 (7)	0.91	7.2 (6)	0.07	4.7 (4)	4.6 (4)	0.82	4.7 (4)	0.67	5.9 (4)	4.5 (3)	0.12	4.6 (3)	0.28	4.3 (5)	5.2 (4)	0.2	5.2 (4)	0.16
Same day admission	20.3%	19%	0.04	18.1%	<0.01	22.7%	23.8%	0.1	23.5	0.24	29.1%	27.7%	0.17	28.4%	0.49	25.2%	23.7%	0.75	25.1%	0.90
AKI Coding	25.2%	30.4%	<0.01	27.3%	<0.01	25.5%	29.6%	<0.01	29	<0.01	17.8%	27.7%	<0.01	28.4%	<0.01	16.9%	23.5%	<0.01	24%	<0.01
Hospital LOS x̄ (median)	23 (13)	26.4 (15)	<0.01	26.3 (14)	<0.01	18.4 (11)	18.6 (11)	0.25	19 (11)	0.09	16.6 (10)	19.6 (11)	<0.01	20.2 (10)	<0.01	19.5 (12)	18.9 (12)	0.28	19.3 (12)	0.79
Progression to AKI 3 ¶	14.4%	14.5%	0.88	14%	0.45	12.3%	14.3%	<0.01	14.4%	<0.01	14.9%	14.2%	0.39	14.7%	0.88	15.5%	15.1%	0.53	15.7%	0.82
OPD After	3.8%	5.5%	<0.01	3.7%	0.92	2.8%	3.4%	0.03	2.6	0.41	3.2%	4%	0.06	2.1%	0.01	2.2%	2.3%	0.86	2%	0.52
OPD New $	21.1%	20.8%	0.88	21.5%	0.87	12.9%	10%	0.08	8.5%	0.02	16.8%	20.1%	0.36	18.1%	0.76	33.6%	34.1%	0.91	31.4%	0.65

Table 88 - Health board univariate outcome comparison of the first AKI from before and after AKI eAlert introduction and also the before group with those that had WRRS alerts

* = Recovery and 30-day survival, ¶ Progression to stage 3 AKI, CC = Critical Care, LV3 = Level 3,
RRT = Renal replacement therapy, LOS = Length of stay, x̄ = mean, OPD = Outpatient Department appointment $ = Percentage of renal OPD appointments after AKI that are new

This table shows the effects that patient selection has on AKI outcomes following the 1st episode of AKI in the period. The four health boards studied have different tertiary services, only one has a combination of cardiac surgery and nephrology. One has a higher percentage of dialysis following AKI, likely the result of a tertiary service for other health boards and these variations need to be recognised when examining the outcomes;

Mortality

In health board A, we see a significant fall in the 30-day and 1-year mortality in this unadjusted analysis, this was the only health board that shows an improvement in mortality following the first episode of AKI and the mortality was much lower in this health board. It may be that patient selection leads in part to this effect, but it requires greater exploration. Health board F and E show an increased percentage of 30-days and 1-year mortality when comparing before to WRRS alert identified AKI, this was also the case in F when reviewing our AKI after, however there was no change between our AKI before and after in E. Health board B on the other hand was unchanged throughout, except an increased 1-year mortality in the WRRS group.

Recovery and dialysis

For recovery and 30-day survival, there was an improvement in the health boards A and B following the introduction of alerts, which was a percentage change of more than 5%. In health boards E and F, there were no changes.

When examining future dialysis health board E showed a difference with a decrease in the patients needing future dialysis in both our AKI after group and the WRRS alert group. The other health boards showed no difference when comparing our AKI to WRRS, however health board A, did show a significant increase in the need for future dialysis when comparing between our AKI groups but not with WRRS. Only health board F saw a change in the progression of AKI with an increase in the number of patients progressing to stage 3 AKI, the others were unchanged.

Admissions

In health boards A and F, we saw an increase in the need for critical care admission and critical care renal replacement therapy in both comparisons, there were no differences in the other health boards. There was a decrease in the number of patients admitted on the day of the AKI alert in health board A in both comparisons, but there was no significant change in the other health boards. We did not see any improvement in the length of stay in any health board, in fact it increased in health boards A, F and B. The length of admission went up by more than a day in comparisons with WRRS in health boards A and B. All the health boards saw improvements in coding and only B saw a change in outpatient follow up referrals where it saw a fall in outpatient reviews after AKI.

Health Board Multivariate

In our unadjusted analysis, we observed an improvement in the mortality in health board A and a worsening in health board F, however as with overall comparison, we need to review to see if this difference remains following correction for some key factors.

The table below looks at the 30-day survival comparing our AKI before to WRRS after correcting for age, gender, Charlson score categorised to ≥3 (or not), chronic kidney disease stage 4 or greater, critical care admission, critical care renal replacement;

WRRS alerts and 30-day mortality		95% Confidence Intervals		
Health Board	**Odds Ratio**	**Lower**	**Upper**	**p Value**
A	0.82	0.74	0.90	<0.01
F	1.29	1.18	1.42	<0.01
B	1.04	0.92	1.17	0.52
E	1.10	0.99	1.24	0.09

Table 89 - Health board multivariate 30-day mortality comparing our identified AKI with WRRS eAlerts following eAlert introduction

Correcting for age, gender, Charlson score ≥3, critical care admission and critical care renal replacement

In this table we can see that the improvement in 30-day mortality observed in health board A following the introduction of the WRRS alerts remains following regression analysis (Odds ratio 0.82). Likewise, the worsening in mortality observed in health board F remains (Odds ratio 1.29). The other two health boards show no significant difference in 30-day mortality.

WRRS alerts and 1-year mortality		95% Confidence Intervals		
Health Board	**Odds Ratio**	**Lower**	**Upper**	**p Value**
A	0.78	0.72	0.84	<0.01
F	1.23	1.1	1.33	<0.01
B	1.07	0.96	1.18	0.24
E	1.15	1.05	1.27	<0.01

Table 90 - Health board multivariate 1-year mortality comparing our identified AKI with WRRS eAlerts following eAlert introduction

Correcting for age, gender, Charlson score ≥3, critical care admission and critical care renal replacement

The exact same findings in health boards A, F and B are then observed in the 1-year survival, however in health board E we now observe an increased 1-year mortality.

Heart Failure

In observing a general lack of improvement following the introduction of the AKI alerts, I wondered if it may be a case that the care improved in some patients but worsened in others. One potential cohort that this may apply to was those with heart failure. Careful adjustment and treatment is required for AKI in this cohort, and too aggressive fluid replacement can result in harm from worsening of their heart failure (261). This table shows the make up of our cohort with previous primary care or hospital coding for heart failure;

AKI Individuals	Before %	After %	WRRS %
Heart Failure	16.9	17.8	19.1
Not Heart Failure	83.1	82.2	80.9

Table 91 - Percentage of patients with known heart failure by AKI group our AKI before and after eAlert introduction and WRRS alerts

In this table we can see that the WRRS group has a higher proportion of patients with heart failure. If we then look at the 30-day mortality before and following the alert introduction;

30-day mortality	Before %	After %	P value	WRRS %	P value
Heart Failure	26.1	26.8	0.48	23.4	<0.01
Not Heart Failure	17.1	17.6	0.18	18.1	0.01

Table 92 - 30-day mortality in patients with AKI comparing those with pre-existing heart failure to those without

Interestingly, we see an improved 30-day mortality in this heart failure cohort following WRRS AKI alerts but a worsening in those with WRRS alerts without heart failure. This heart failure group has a higher 30 mortality than those without it. When comparing our AKI groups of before and after alerts, there were no mortality differences.

Health Boards	30-day Mortality	Our Alert before %	Our Alert After %	P value	WRRS Alert %	P value	In GP data %	Heart Failure %
A	**HF**	25	30	<0.01	29	0.04	94.4	17.2
	NOT HF	17.6	18.9	0.05	17.2	0.55		
F	**HF**	23.1	20.5	0.08	19.6	0.02	75.6	19.9
	NOT HF	13	13.6	0.25	13.2	0.77		
B	**HF**	23.1	22.3	0.69	21.8	0.52	85.2	21.5
	NOT HF	14.4	14.4	0.68	14.1	0.98		
E	**HF**	23	26.1	0.11	25.2	0.28	77	19
	NOT HF	16.3	16.4	0.94	15.2	0.19		

Table 93 - Heart failure (HF) mortality with AKI by health board

If we then look at the health boards individually, we see great variation in the mortality again, this was most striking in health board A, which sees an increase in 30-day mortality from 25 to 29% in the heart failure group. This was the health board with the most complete coding, given the 94.4% primary coverage of this population. This was contrary to the pooled mortality data, and this was the health board with the lowest mortality as a whole, shown in Health Board Multivariate section. Health board F shows a significant decrease in mortality on the other hand. It was not possible to know if this was a direct impact of the alert or other changes.

If we use regression analysis correcting for the same factors outlined earlier, we do see that with the exclusion of the heart failure patients, observed differences no longer remain statistically significant, this was shown by the table below.

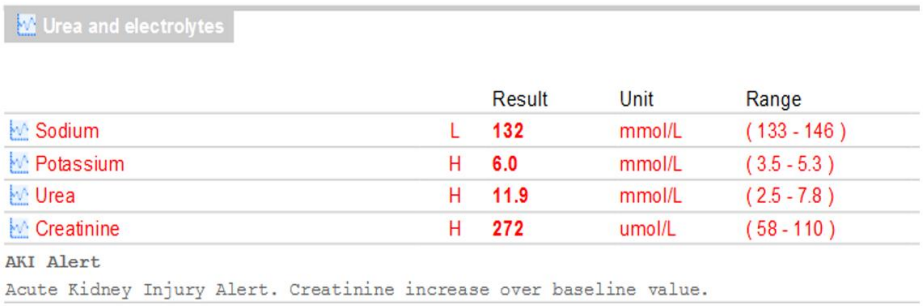
WRRS mortality	OR	Lower CI	Upper CI	P value
Heart Failure included	1.06	1.00	1.12	0.03
Heart Failure excluded	1.06	1.00	1.12	0.05

Table 94 - Multivariate analysis in those with heart failure and with heart failure patients excluded comparing WRRS with our identified AKI

Discussion

The electronic alerts for AKI were introduced with the aims of improving outcomes such as mortality (117). This analysis suggests that in the large this has not been achieved and was in keeping with some studies investigating alerts including to randomised controlled trials (183, 262) as well as a similarly designed trial from Dundee (263). There are a number of reasons that this may be the case, some of which we will explore. One of the reasons may be that the two groups, our AKI and WRRS alerts are not directly comparable. As shown in the previous chapter (Chapter 4), there was a correlation between our AKI and WRRS in under two thirds of the alerts. In this study we used the first alert of the period and in this case 72.6% of the alerts in the after group had WRRS alerts. This proportion was lower than in the validation chapter (94.6%), but this may be explained by the differences in need of an authorised SCr to trigger an alert in 2013-2015 which I believe to have been rectified by 2017 (validation study -Chapter 4). In this case the mortality of those patients not in WRRS alerts was slightly lower than those in WRRS 18.1% vs 19.7%. This means, that there was the potential that we are examining a more unwell group in the WRRS group. This was backed up by more patients in WRRS having an AKI stage > 1 with their first alert, 22.2% vs 21.1% in our AKI after group and more patients having heart failure (19.1% in WRRS vs 17.3% as a whole - Heart Failure). There was also a high percentage of patients as an inpatient on the day of their first alert, 70.3% vs 68.3%. Nevertheless, if there were a sufficient change in the mortality following the alert introduction, we would expect to see an improvement in the comparable group of our AKI before and after. It was clear however, from this analysis that not all health boards exhibit the same findings. This variability raises the possibility of variation in implementation of the alerts. With multivariate analysis only one health board shows an increased mortality, and one shows an improved mortality at both 30-days and one year. The health board (A) with the improved mortality, does not carry out any interventions beyond the passive eAlert, there has been AKI teaching aimed at junior doctors and undergraduates but there have been no interruptive interventions such as phoning through results or AKI bundles (i.e. a set of actions and interventions instigated following an AKI alert such as those used by Selby et al (264) or Sykes et al (265)). We have already witnessed that laboratories attempt to suppress alerts in patients that it believes were on dialysis, with varying degrees of accuracy. The electronic alerts are passive in the majority of health boards, appearing at the bottom of the blood results on the different systems. However, I understand that one health board has a more

interruptive approach by directly phoning through AKI alerts to the clinicians in patients with stage 2 and 3 AKI (Cwm Taf Alerts rules). Interestingly, this health board did not observe an improved 30 or 1-year mortality despite this effort. It was possible that the passive alerts are still missed by clinicians as they are not the most prominent.


Urea and electrolytes

		Result	Unit	Range
Sodium	L	132	mmol/L	(133 - 146)
Potassium	H	6.0	mmol/L	(3.5 - 5.3)
Urea	H	11.9	mmol/L	(2.5 - 7.8)
Creatinine	H	272	umol/L	(58 - 110)

AKI Alert
Acute Kidney Injury Alert. Creatinine increase over baseline value.

Figure 42 - Electronic AKI alerts

The example here shows an abnormal set of urea and electrolyte blood results, as all the figures are outside the range, they are red (instead of black), the electronic AKI alert appears below this, but was certainly less striking and has the potential to be overlooked. The alerts do not display the stage of AKI or identify progression of AKI stage, which could help clinicians those at most risk of harm.

The variations observed have many other potential causes beyond the AKI alerts and their implementations. For example, some of the health boards included have inpatient tertiary services such as cardiac surgery, tertiary cardiology, inpatient cancer services and inpatient nephrology care. All of these will result in increased frequency of AKI and will also affect survival following AKI, so it is important that we consider these when interpreting the data. For example health board A had 178 AKI alerts in transplant patients in the before group compared to 11 in health B. A health board that provides a large area and other health boards with tertiary service may see more AKI and AKI that patients are more likely to survive, as they will select patients for transfer that are more likely to survive. Other health board variations include the availability of comorbidity data, there was variation in the hospital coding, as shown in the methods chapter (Data Quality page 105) and there was variation in the primary care data available (Primary Care GP dataset – WLGP page 108), from 75.6 (health board F) to 94.4 (health board A). Without going into the individual figures (due to the risk of identifying the health boards), it was likely that comorbidities are underrepresented in health

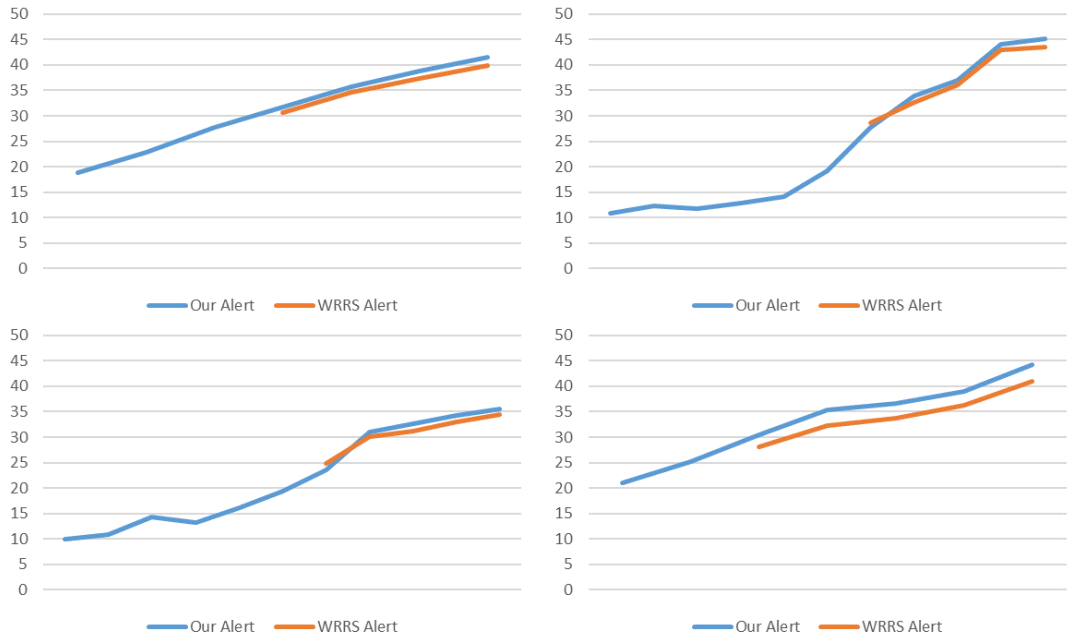
board F compared to A, as health board F has a lower depth of coding and lower GP representation in SAIL compared to A.

There is the possibility that alerts led to improvement in care for some patients but worsened the care in others as there is no single treatment for AKI. From clinical practice I have observed direct patient harm when patients have been treated blindly with intravenous fluids for AKI without prior thought. In some cases there is harm from the stopping of important medication perceived to be 'nephrotoxic'. This may explain the observations seen in health board A in patients with heart failure, where there was an increased mortality, despite a lower mortality in the health board F and as a collective. The alerts have a document attached to them that aims to help guide the users in the management of AKI, but this may not be utilised as frequently as expected. The NCEPOD report into AKI recognised that not only was the recognition of AKI poor, but so was the management (151). As is often the case in clinical medicine, AKI is a heterogenous condition with many potential causes, so care needs to be individualised following its recognition. When reviewing patients with AKI and pre-existing heart failure in isolation, the 30-day mortality did not significantly increase but when we excluded these patients from the regression analysis of comparing our AKI with those that had WRRS alerts the statistical difference disappeared (Table 94), suggesting that including these patients did have an effect on the overall 30-day mortality outcome.

Interestingly, despite the lack of effect on mortality as a whole, there does appear to be a positive effect on recovery which was even the case with the combination of recovery and 30-day survival, despite the fact that individually 30-day survival was lower in the WRRS alerts group. This is similar to finding of Park et al (266) who found an improved 30-day recovery but no improvement in 30-day mortality. This means that when examining the lowest SCr of 90 days post AKI and observing if it no longer triggers AKI using the index SCr's baselines (RV1, RV2 or RV3), the WRRS alerts appear to improve the number of patients achieving this. Although this is promising, despite this improved recovery, there was no difference in future need for dialysis in the WRRS group and comparing our AKI before and after, it appears that there was an increase in the need for dialysis in the after group. There is the potential that this fits in with the hypothesis of potential harm in some patients, i.e. the potential of overtreating with fluids carries harms or it could again suggest that WRRS selects more unwell

patients. As SCr is a concentration test, there is the potential of lowering creatinine by increasing the volume or water within blood without a change in the kidney function. This would mean that a patient has an improvement in their SCr, transiently meeting a recovery definition but without an improved kidney survival outcome. It also likely that some of the WRRS alerts are in patient on dialysis, therefore the recovery tests may represent tests after recent dialysis treatment. Given the lack of benefit in need for dialysis and mortality, the recovery aspect therefore is unlikely to confer any significant clinical benefit. This is further compounded by the increased incidence of critical care admission and critical care renal replacement in the WRRS and our AKI after group. This may play a role in the recovery aspect too, as a low creatinine due to intensive care renal replacement therapy may lead to a false identification of recovery. It was unclear if the increased number of intensive care admissions was the effect of improved recognitions of AKI or harms following the management of AKI.

We did observe an improvement in coding for AKI over this period, but it was unclear how much of this improvement can be attributable to eAlerts as there was an increasing trend prior to the eAlerts as shown in the previous coding chapter and in Table 83. The picture below is taken from Graph 57 on page 197 and has been limited to the 4 health boards in this study. It shows that there has been a gradual increase in the percentage of AKI coding in the health boards studied over time compared to our AKI in blue, the WRRS alert introduction continues along this increase but not necessarily beyond that of the previous years. There was potentially an increase in the gradient in the bottom two graphs followed by a levelling off, which may suggest some initial impact;



Graph 62 - Health board comparison of percentage of patients with ICD-10 coding for AKI compared to our recognition of AKI (our alerts) and WRRS alerts.

The X axis represents time, but the values have been removed to avoid health board identification. If there was a greater recognition, you may expect that to translate into more patients being followed up by nephrology, nevertheless, the number of patients followed up in the next year remains low with no discernible change in the proportion of new outpatient reviews.

There was an increased length of stay in the WRRS group which was a concerning feature, again there was the potential that this could be caused by over treating the AKI and merits further study given the patient morbidity impact as well as the economic impact.

This study also shows that the alerts missed by the Welsh alert variations, with this rule of >6% change from the previous test, misses AKI in patients with a high mortality (1-year mortality our AKI after 37.9% vs 37.5% WRRS) that go on to need dialysis (Our AKI after 2.9% vs 2.3% WRRS) when you consider that the WRRS alerts are a selection of Our AKI after alerts.

Conclusion

There does not appear to be an overall improvement in 30-day or 1-year mortality following the introduction of electronic alerts. There appears to be an improvement in recovery at 90-

days, the significance of this was unclear, but it may not be important as it does not appear to prevent the requirement of critical care admissions or dialysis treatment. There are potential signals to harm such as increased length of hospital admission, this may be the result of the groups not being completely comparable, however this remains the case when comparing like for like as seen in our AKI groups. If there really was harm, it was not the alerts or recognition of AKI itself that was doing it and more the actions that it initiates not being appropriate. Careful thought and research is required to try and improve care in patients with AKI. One health board showed improved 30-day and 1-year survival which provides hope, although the reason for this improvement was unclear.

Chapter 7 - Prescriptions and reviews in primary care following AKI

Introduction

Acute kidney injury (AKI) is common in hospital admissions and is associated with a high risk of inpatient mortality (153, 172). It has been described that the observed increased mortality continues after admission for up to one year (118). In the management of AKI it is suggested that some medications are temporarily stopped to improve the kidney function (216), however some of these medications are important to help cardiac function (206). This may be related to the finding that 25% of unplanned readmissions following an admission have hospital coding for pulmonary oedema (210). The evidence of which medications should be stopped and which medications should not remains debated (206). Non-steroidal anti-inflammatory (NSAIDS) medications can cause AKI by a number of methods, and therefore the argument for stopping and cessation these medications is strong (178). Other medications, such as angiotensin converting enzyme inhibitors (ACEi) and the similar agents angiotensin receptor blockers (ARBs), along with diuretics require a more individualised approach, as they may need to be stopped, suspended or even started during AKI (205, 206). There is great interest in the diagnosis, management and outcomes of patients in the hospital environment but little is known about what happens after discharge from hospital (267). The communication between primary and secondary care remains poor (219), but efforts have been made in some areas such as England to improve this (222, 268). Clinical prescriptions review by primary care following an episode of AKI are recommended (202, 206, 222) but the implementation is not well described (269).

Aims

To assess changes in primary care prescribing practice and medical reviews following AKI and whether this was influenced by having an AKI electronic alert.

To assess the hospital discharge summaries in a selection of patient AKI for medication changes and communication of the diagnosis of AKI.

Hypothesis

Increased medication reviews following AKI and a reduction in use of nephrotoxic and renally cleared medications.

Methods

The study was carried out using the serum creatinine-based (SCr) AKI cohort from the previous chapter (Chapter 3 – The Creation of AKI Cohort). These alerts are distinguished between before and after the introduction of the electronic alerts seen in clinical practice called WRRS alerts in this study. There are 3 groups, one before the introduction of electronic alerts created by our algorithm within SAIL ('our AKI before') and two groups after the introduction of electronic alerts which was AKI patients identified by our algorithm in SAIL ('our AKI after') and the other was the alerts seen in clinical practice stored within the WRRS results called 'WRRS alerts'.

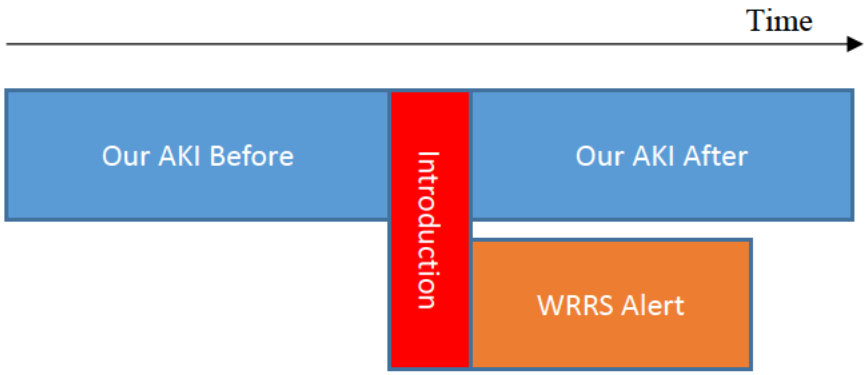


Figure 43 - Alerts

As previously clarified, there was overlap in the two after groups with WRRS alerts matching 72.6% of the after group. Due to the availability of pre-alert data, only patients in the four health boards with data were selected, they are Betsi Cadwaladr, Cwm Taf, Hywel Dda and Abertawe Bro Morgannwg university health boards. This was 4 of the 6 main health boards in Wales that have a biochemistry laboratory (Powys and Velindre do not). The time period studied in these regions was 1-year before and 1-year after the introduction of the electronic alerts in that health board, excluding the month of implementation, this ranged from 2013 to 2016 and was outlined in Figure 44.

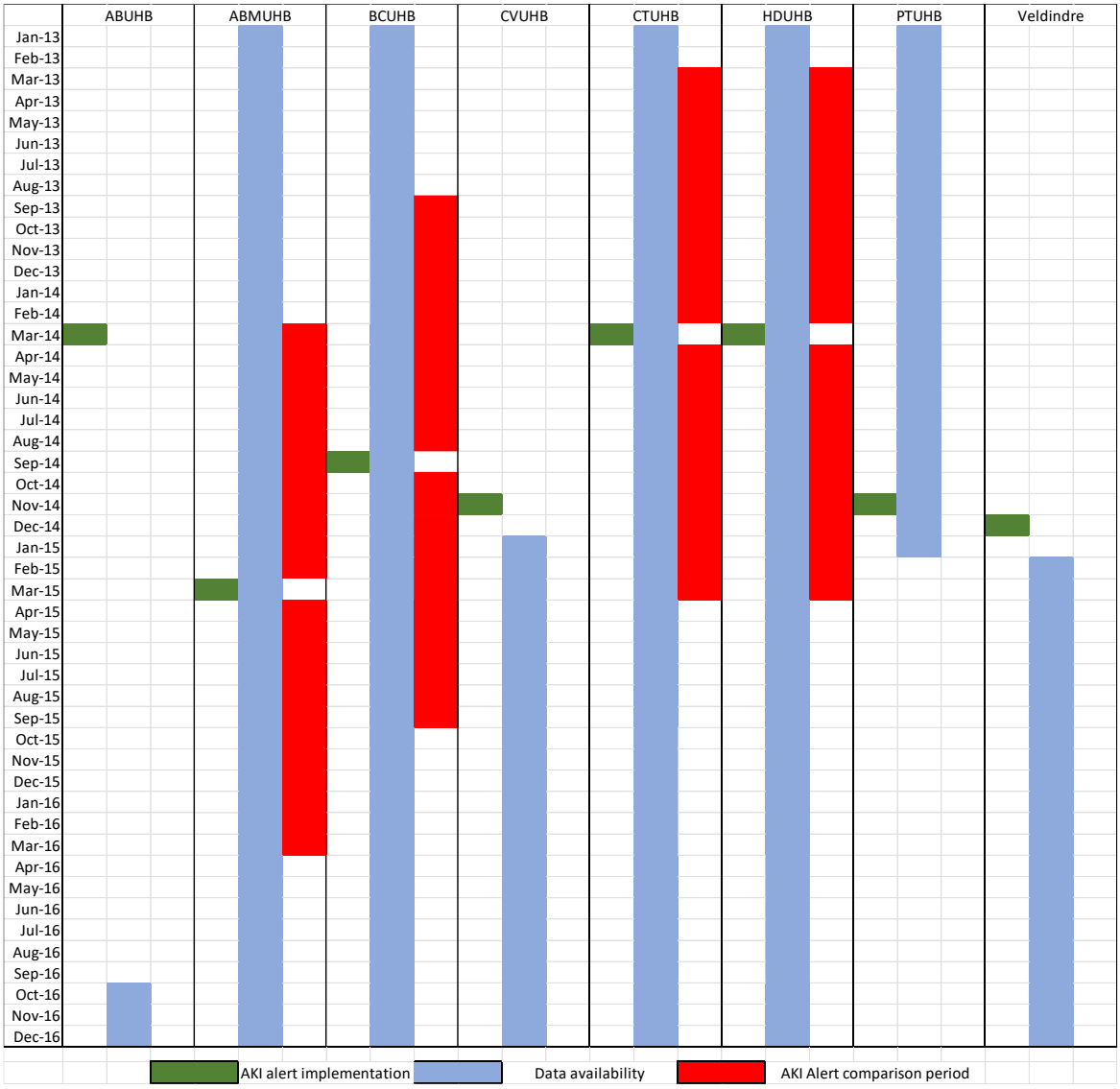


Figure 44 - Health boards alerts

Using these alerts, I assessed the 90-days before and after the alerts for prescriptions and medical reviews using Read code event records from the primary care dataset within SAIL. Read code entries are called events within SAIL and are in the same format. Therefore I used a primary care event to signify a entry. The Read codes used are included in the appendix on page 329 (Read Codes). If a single entry was made for that Read code during that period, then it was counted that that event had occurred for that patient. A Read code ('event') entry for a drug was used to define a prescription of that drug. A single Read code entry for medication review, blood pressure, acute kidney Injury, urine analysis and serum creatinine were also used to signify that these were preformed from primary care. This 90-day period was used to avoid missing patients who are given 3 month supplies of medication and to minimise the risk of identifying those previously prescribed a medication which has since been stopped. In an

initial pilot study using AKI hospital coding to identify an AKI cohort I compared different periods of time for prescriptions which was shown in the appendix (ICD-10 coded AKI pilot study on page 334). For the analysis, only those in the primary care dataset were used and for the after groups (After AKI and WRRS) only those alive at 30-days and in the primary care dataset were included. The AKI cohort was created using biochemistry and renal replacement data in SAIL by myself and Gareth Davies an analyst as described on page 132 (Chapter 3 – The Creation of AKI Cohort). The code used to compare the effect of AKI on primary care events was written by myself in Structured Query Language (SQL) code using IBM DB2 tables and eclipse software within SAIL. For comparisons of prescription frequencies before and after AKI, Pearson's chi square test was used.

Medication Studied

The table below shows the different medications analysed and why description of their use before and after AKI is interesting;

Medications	Indications	Role in study
Proton Pump Inhibitors (PPI)	Used for stomach acid suppression.	Implicated in AKI causation in some cases(270).
Histamine 2 Receptor Antagonist (H2 Antagonist)	Used for stomach acid suppression.	Comparator and alternative to PPI.
Non-steroidal Anti-inflammatoy Drugs (NSAID)	Used as analgesic / anti-pyretic.	Can cause AKI and almost without exception should be stopped and not restarted following AKI(231).
Paracetamol	Used as analgesic / anti-pyretic.	Comparator and alternative to NSAIDs. Can cause AKI in overdose
Aspirin	Primarily used for its anti-platelet (anti-coagulation) effect. Can be used as analgesic / anti-pyretic.	Can be implicated in AKI in high dose. Mostly used in lower dose that is not implicated in causing AKI(271).

Angiotensin Converting Enzyme Inhibitor (ACEi) / Angiotensin Receptor Blockers (ARB)	Anti-hypertensive, also important role in treating heart failure and proteinuria (improving long term kidney outcomes).	Can affect the physiology (compensation) within the kidney in acute illness (such as sepsis). Can also cause/worsen high potassium, which is also frequently a problem in AKI. In most cases (not all) temporary suspension is recommended. Failure to restart after AKI has the potential to harm(205, 206).
Calcium Channel Blocker	Primarily used as an anti-hypertensive	Comparator and alternative to ACEi/ARB for blood pressure control. Not commonly directly implicated in AKI.
Beta Blocker	Primarily used as anti-hypertensive or anti-anginal	Comparator and alternative to ACEi/ARB for blood pressure control. Not commonly directly implicated in AKI.
Statin	Used to lower cholesterol – to help prevent strokes and heart attacks (amongst others)	Linked with Rhabdomyolysis which can cause AKI. This is a rare association.
Loop Diuretics	Diuretics used mainly for salt and water retention – in conditions such as Heart Failure and Chronic Kidney Disease (CKD).	Can cause dehydration and therefore AKI. Sometimes are needed to treat AKI (Right sided heart failure). Sometimes started appropriately after AKI.
Thiazide Diuretics	Main use as anti-hypertensive. Can be potent diuretics	Can cause dehydration and therefore AKI. Sometimes are needed to treat AKI (Right sided heart failure). Sometimes started appropriately after AKI.
Potassium Sparing Diuretics	Main use as anti-hypertensive, treatment	Can cause dehydration and therefore AKI. Sometimes are needed to treat AKI (Right

	of heart failure or in liver disease.	sided heart failure). Sometimes started appropriately after AKI.
Metformin	Main use in Diabetes Mellitus (specifically, type 2).	Can cause complications (lactic Acidosis) in AKI and CKD so often stopped.
Sulphonylureas	Oral Hypoglycaemic used in Type 2 Diabetes Mellitus	Increase risk of hypoglycaemia in AKI so may be stopped.
Insulin	Subcutaneous glucose lowering hormone. Used in Diabetes Mellitus (both types)	Comparator and alternative to Metformin and Sulphonylureas. Not commonly directly implicated in AKI.

Table 95 - Medications studied and their roles in the study

A key question when investigating what primary care do following a hospital admission with AKI, is do they even know about the episode? The communication between primary and secondary care is usually in the form of a letter in the UK as historically neither have access to the other's system. To explore this communication, I also carried out an audit of these communications in Morriston Hospital in Swansea. The methods used for this small study are described later in this chapter. This audit looks to provide greater depth to this study, taking a single centre cohort of Welsh hospitalised patients with AKI and examining the communication with primary care and the medication changes at discharge.

Results

There were 52,249 patients with one or more episodes of AKI in the time period of 1-year before and after the introduction of electronic AKI alerts. 35,377 (67.7%) of these patients were inpatients on the day of their first AKI alert. 43,599 (83.4%) patients had primary care data and 42,947 (82.2%) had a primary care Read code entry (event) in the 90-days before their AKI. Of these same patients with events before, 34,876 were alive at 30-days after the AKI and had a primary care event within the next 90-day (81.2% of those alive after 30-days). Table 96 shows the demographics and finding in these group;

	Event 90-days before AKI (percentage of all AKI)	Event 90-days after AKI and alive 30-days (Percentage of all AKI alive at 30-days)
Patient with AKI	52,249	42,933
AKI with Primary Care event	42,947 (82.2%)	34,876 (81.2%)
AKI with Primary Care event and admitted	29,011 (66.6%)	22,395 (62.9%)
Female	53.4%	54.%
Mean Age (Median)	71 (75)	73 (77)
Mean SCr (Median)	160 (133)	155 (129)
Mean RV1 Baseline SCr (Median)	75 (68)	77 (71)
Mean RV2 Baseline SCr (Median)	77 (70)	73 (68)
Mean length of stay (Median)	20 (11)	21 (12)
Initial Alert Stage 1	34,062 (79.3%)	28,568 (81.9%)
Initial Alert Stage 2	5,723 (13.3%)	4,085 (11.7%)
Initial Alert Stage 3	3,162 (7.4%)	2,223 (6.4%)
Future Dialysis	1,101 (2.6%)	957 (2.7%)
Transplant	174 (0.4%)	158 (0.5%)
Critical Care Admission	2,335 (5.4%)	1,572 (4.5%)
Critical Care Renal Replacement Therapy	386 (0.9%)	233 (0.7%)
First test as inpatient	23,022 (53.6%)	17,966 (51.5%)
First test in A&E	9,272 (21.6%)	7,033 (20.2%)
First Test in Primary Care	7,306 (17%)	6,821 (19.6%)
First Test in Outpatient department	3,006 (7%)	2,770 (7.9%)
First Test in other area	271 (0.6%)	286 (0.8%)

Table 96 - Primary care baseline information – from 1st AKI test

Table 96 - Primary care baseline information – from 1st AKI test shows that the patients who are alive at 30-days after their AKI and had a Read code event were older age, more stage 1 AKI on presentation, less likely to have been admitted to critical care and more likely to have their first AKI blood test from primary care. If we look specifically at the subgroup of patients with WRRS alerts of which there are 18,867 patients, we find a higher proportion have primary care data and primary care events 88.1% and 86.8% respectively. The table below shows the demographics of this WRRS cohort comparing those with events before and those alive with events afterwards;

WRRS cohort	Event 90-days before AKI	Event 90-days after AKI and alive 30-days
AKI with Primary Care event	16,374 (86.8)	13,032 (83.7%)
AKI with Primary Care event and admitted	11,612 (61.5)	8,877 (57%)
Mean Age (Median)	72 (75)	70 (74)
Mean SCr (Median)	157 (132)	152 (128)
Mean RV1 Baseline SCr (Median)	76 (70)	78 (72)
Mean RV2 Baseline SCr (Median)	75 (77)	79 (72)
Mean length of stay (Median)	21 (12)	23 (13)
Initial Alert Stage 1	12,747 (77.8%)	10,523 (80.7%)
Initial Alert Stage 2	2,394 (14.6%)	1,686 (12.9%)
Initial Alert Stage 3	1,233 (7.5%)	823 (6.3%)
Future Dialysis	393 (2.4%)	325 (2.5%)
Transplant	66 (0.4%)	60 (0.5%)
Critical Care Admission	1,081 (6.6%)	713 (5.5%)
Critical Care Renal Replacement Therapy	188 (1.1%)	108 (0.8%)
First test as inpatient	9,223 (56.3%)	7,126 (54.7%)
First test in A&E	3,527 (21.5%)	2,610 (20%)
First Test in Primary Care	2,284 (13.9%)	2,110 (16.2%)
First Test in Outpatient department	1,162 (7.1%)	1,042 (8%)
First Test in other area	178 (1.1%)	144 (1.1%)

Table 97 - WRRS primary care cohort – from 1st AKI test

As mentioned, this group was broadly similar, albeit it has selected a group of patients that was more likely to be admitted to intensive care, have a high 1st stage alert and more likely to be an inpatient at the time of first alert. Those that survive to 30-days and have primary care data were similar to the previously described differences, however these WRRS alert patients that survived were younger in comparison to the overall group. It is important to highlight that the patients in the before and after group are the same AKI cohort, but for the after group, those that died before 30-days were excluded.

When reviewing the combined AKI cohort with primary care event data of 42,947 patients, we can see that with many medications there was a reduction in the prescription following the AKI episode;

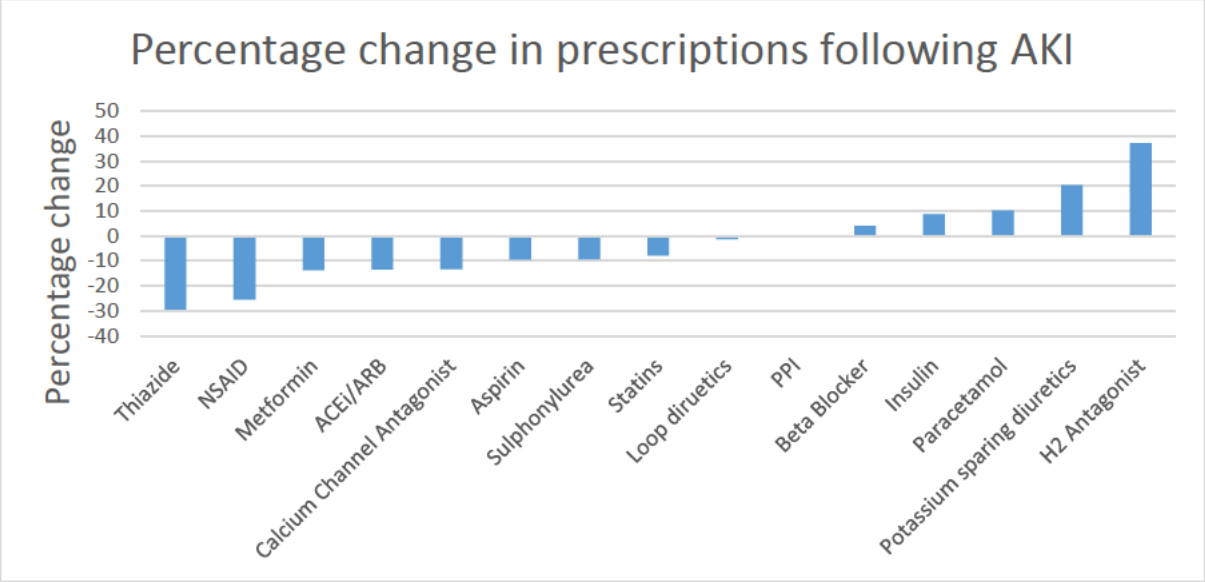
Percentage of patients with a prescription	90-days before AKI %	90-days after AKI and alive 30-days %	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	P Value (Chi Square)
PPI	44.5	44.3	0.99	0.96	1.02	0.57
ACEi/ARB	41.7	36	0.79	0.77	0.81	<0.01
Statin	41.5	38.2	0.87	0.85	0.90	<0.01
Loop Diuretic	30	29.6	0.98	0.95	1.01	0.22
Beta Blocker	29.8	31	1.06	1.03	1.09	<0.01
Paracetamol	26.6	29.3	1.14	1.11	1.18	<0.01
Aspirin	25.9	23.4	0.88	0.85	0.90	<0.01
CCB	21.9	18.9	0.84	0.81	0.86	<0.01
Metformin	12.4	10.7	0.85	0.81	0.88	<0.01
Thiazide	9.8	6.9	0.68	0.65	0.72	<0.01
K sparing diuretic	8.5	10.2	1.23	1.17	1.29	<0.01
NSAID	7.7	5.8	0.73	0.69	0.77	<0.01
Sulphonylurea	6.6	5.9	0.90	0.85	0.95	<0.01
H2 Antagonist	4.4	6	1.40	1.31	1.49	<0.01
Insulin	4.3	4.7	1.09	1.02	1.17	0.01

Table 98 - Prescriptions in the 90-days before and after AKI by our AKI identification. Comparison using Pearson chi square test

Key: PPI = Proton Pump Inhibitor, ACEi/ARB = Angiotensin Converting enzyme inhibitor/Angiotensin receptor blocker, CCB = Calcium Channel Antagonist, K sparing diuretic = Potassium sparing diuretic, NSAID = Non-steroidal anti-inflammatory, H2 Antagonist = Histamine receptor 2 Antagonist

This table shows that almost half (44.5%) of the patients in this cohort were prescribed proton pump inhibitors in the 90-days before their AKI (denominator 42,947) and the same after (44.3%) when examining all the patients with AKI alive at 30-days with SAIL primary care event data (34,876). The next most commonly used medications were statins and ACEi/ARB. The only drug in this group where there was clear guidance for the continued cessation following AKI was NSAID (231), which saw a reduction from 7.7% to 5.8% (p <0.01).

The graph below shows the percentage change in these groups;



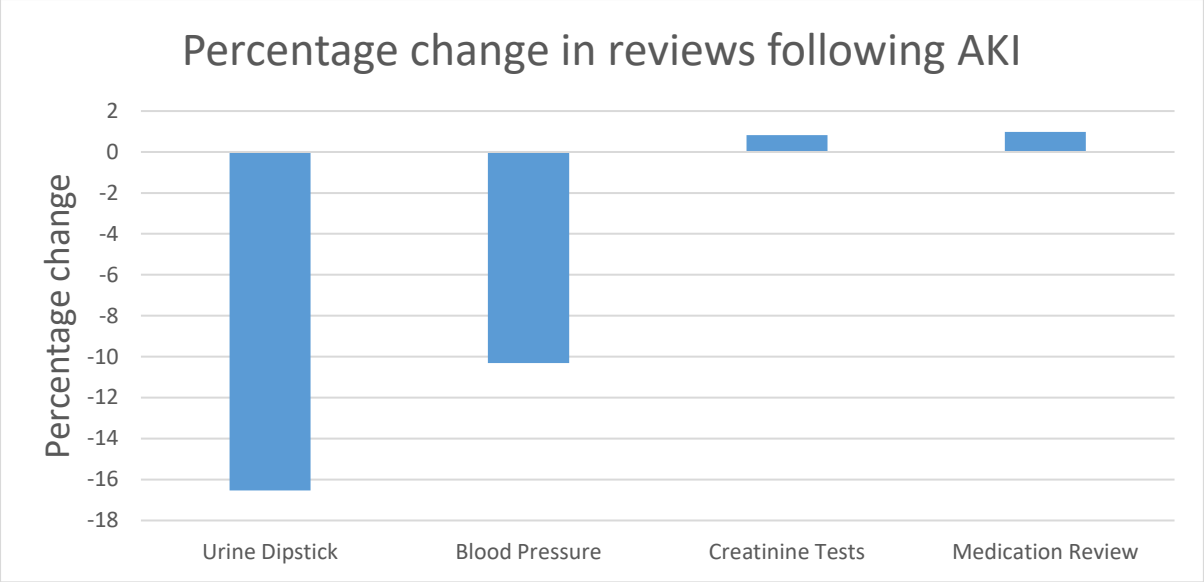
Graph 63 - Percentage change of prescriptions in the 90-days before and after AKI by our AKI identification.

From this we can see that many medications see a reduction in prescriptions such as thiazides, NSAIDS and metformin which was understandable as these medications can compound AKI or cause complications in AKI. ACEi/ARB also can compound AKI but have benefits for many patients upon recovery, nevertheless this sees a decrease in prescriptions in those alive after AKI. Some medications witnessed increased use such as Histamine receptor 2 antagonists, potassium sparing diuretics, paracetamol and insulin.

Percentage of patients with a prescription	90-days before AKI % (n = 42,947)	90-days after AKI and alive 30-days % (n = 34,876)	Odds Ratio	Lower 95% Confidence Interval	Upper 95% Confidence Interval	P value
Primary care serum creatinine	47.7	48.1	1.02	0.99	1.05	0.28
Blood pressure	47.1	42.2	0.82	0.8	0.85	<0.01
Medication review	15.9	16.1	1.01	0.97	1.05	0.55
Urine Dipstick	7.6	6.4	0.82	0.78	0.87	<0.01
AKI read code	1.5	3.2	2.2	2	2.43	<0.01

Table 99 - Primary care reviews in the 90-days before and after AKI by our AKI identification

Following AKI we see an increase in the number of patients having AKI Read code entries which was understandable. There was a decrease in the number of patients having blood pressure readings and urine dipsticks otherwise there were few changes. The graph below visualises the percentage change;



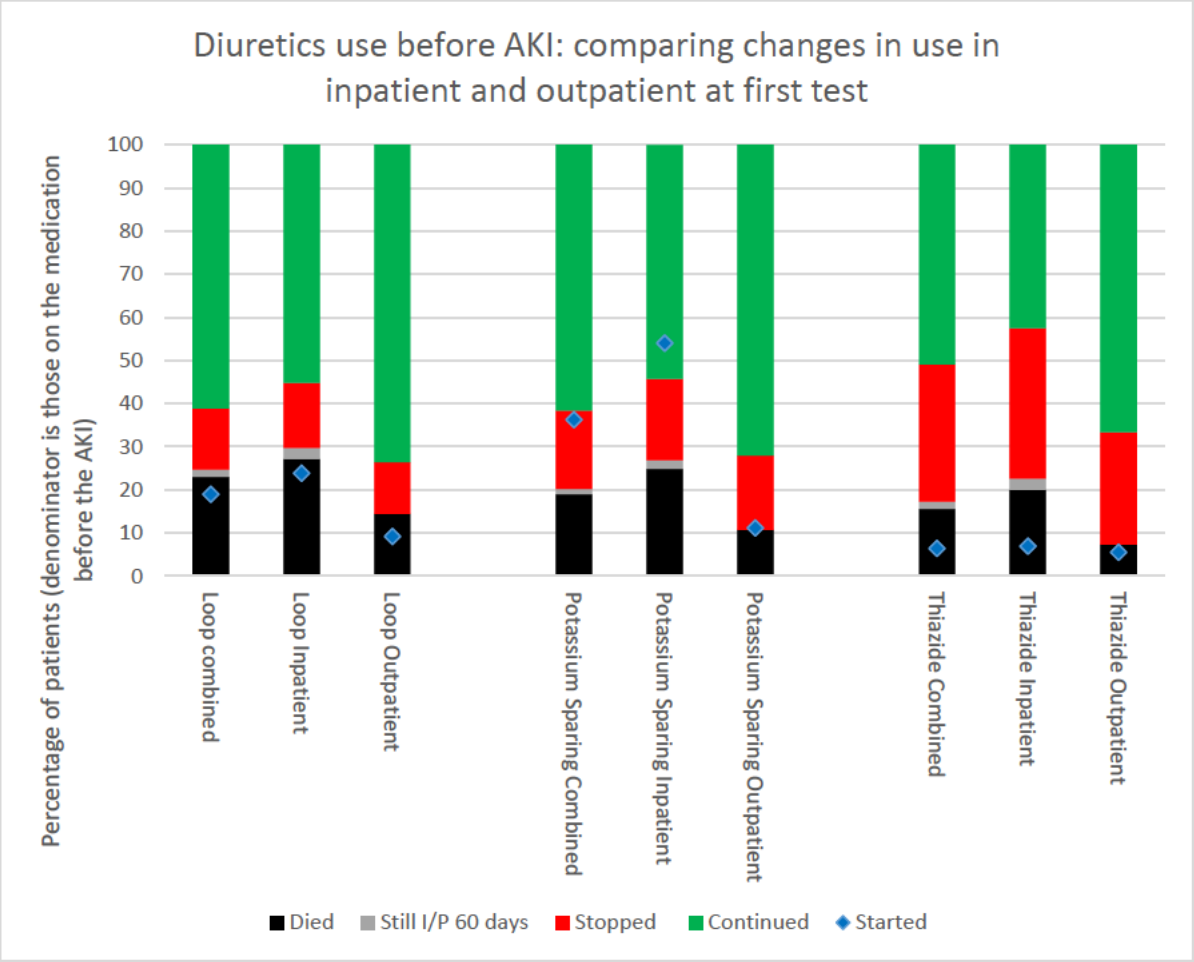
Graph 64 Percentage change of primary care reviews in the 90-days before and after AKI by our AKI identification.

This helps to understand the overall numbers of patients with different primary care entries, but not whether they were stopped or started, or the patients are dead. The next sections look to answer the question, what happens to the individuals on a certain medication following their AKI.

Prescribed before

In this section, I looked at what happens to patients on certain medications (as defined by a prescription for that medication in the 90-days before the AKI) and what happens to them following the AKI. I use two methods to look at the effect of AKI on prescription, one was to compare those on the medication with the cohort of patients on that medication beforehand, including using this as the denominator for those started on it afterwards, this allows us to see what happens to individuals on those medications and gives us an idea of the proportion started on the medications after (although the number of patients who are alive and can be started on the medications are lower). The second method was to look at the overall prescription of these medications. This group gives us a perspective of the scale of the medication use in the whole AKI cohort. For these comparisons the denominator for before and after differs appropriately to reflect those able to have a prescription, i.e. before it was those with primary care event data (42,947) and for the new starters it was those alive at 30-days and with primary care event data in SAIL (34,876). Using this data, I have also looked at those who are inpatient and outpatient at the time of their first AKI test. Some of those who are 'inpatient' may be outpatients at the time of the test but then admitted that day.

In the appendix (Graphs of medication changes on page 330) I have created graphs which show the studied medications, comparing the changes. In the graph below I have looked at the patients prescribed these diuretic medications in the 90-days before their AKI and observed what happened to these individuals after their AKI. The blue diamond part of the graph looks at those started on medications afterwards as a 'started' prescriptions using the number of patients on the medications before as the common denominator;

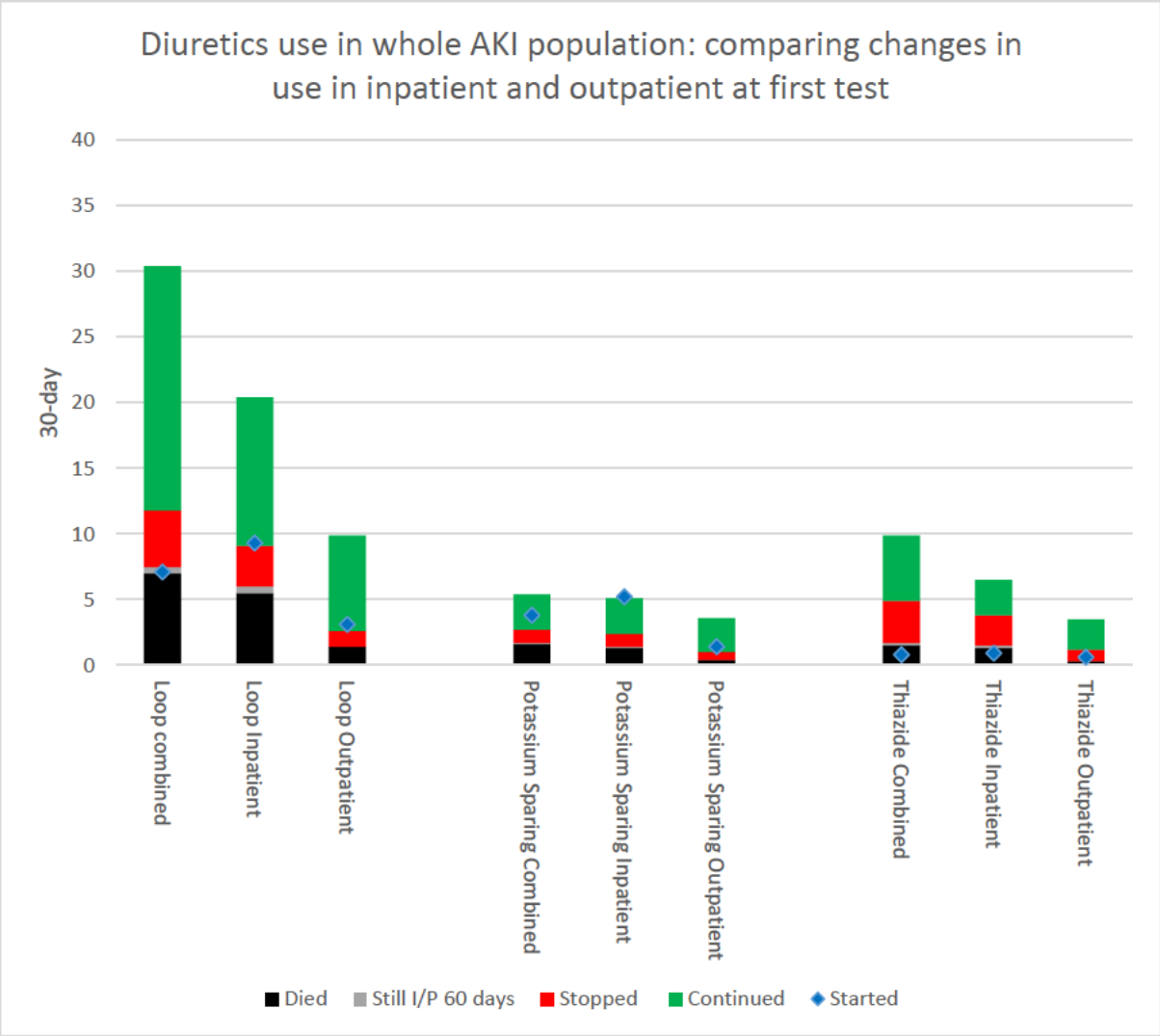


Graph 65 - Diuretics use before AKI: comparing changes in use in inpatient and outpatient at first test.

I/P = Inpatient

As can be seen here, when comparing to the patients on these medications before, potassium sparing diuretics had the greatest proportion of new starters after the AKI. The patients with the highest observed mortality proportion were those on loop diuretics at 23% compared to 19% and 15.6% in those on potassium sparing diuretics and thiazides (the overall 30-day mortality was 18.5%). When reviewing the proportion of those having medications stopped, thiazides were the highest at 31.8%, followed by potassium sparing diuretics and loop diuretics, 18.2% and 14.1% respectively. When looking at the breakdown of whether or not

the first test was during an admission or on the day of admission vs an outpatient test, then we see that the 30-day mortality was much higher in the inpatients group. Outpatient group was more likely to have a prescription for the medication to be continued again after the AKI. The inpatient group are more likely to receive a new prescription for these diuretics. This comparison gives us an idea of what happens to individuals on these medications, but to gain a better idea of the use of these medications in the whole population, I have looked at these medications comparing them to all the patients with primary care events before;



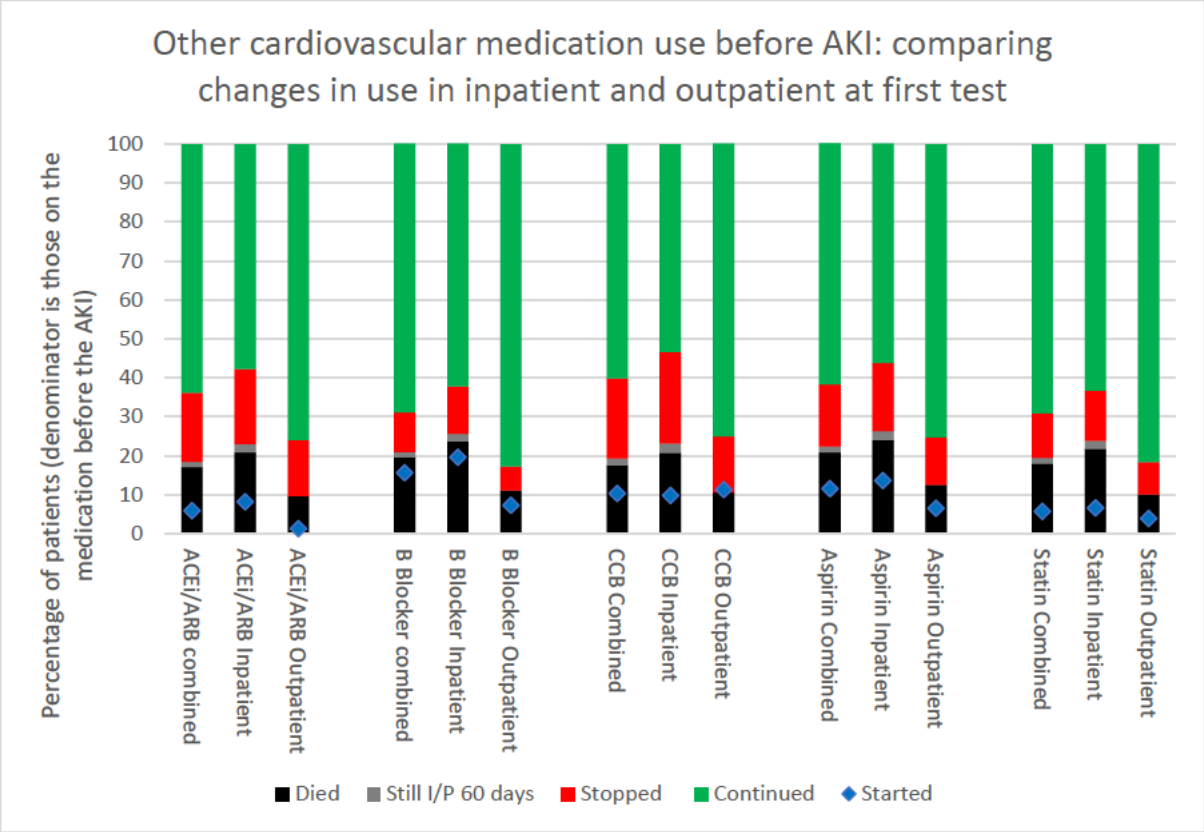
Graph 66 - Diuretics use in whole AKI population: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient, Loop means Diuretics working on the loop of henle

For the combined (all locations) 'started' group used here, the denominator was those alive at 30-days post first AKI result with primary care event data (34,876). From this analysis we can see that a quarter of all the patients are on loop diuretics following AKI (18.6% continuing and 7.1% started) and the majority of these patients come from the inpatient group. This

works out as 30% of those alive 30-days after their AKI. In the inpatient group, the denominator was those admitted and alive at 30-days (22,395) and in this group, almost 1 in 10 of the inpatients alive at 30-days after their AKI get started on loop diuretics which means that in the 90-days after AKI 1 in 5 are given a loop diuretic (started and continued). More than a third of all the patients with AKI see a loop diuretic prescription and this rises to 56% of the inpatient group. Although potassium sparing diuretics was the group with the most new starters in the previous graph (Graph 65) it represents fewer patients than those started on loops diuretics 3.8% vs 7.1%.

The next graph looks at the other used cardiovascular medications, again initially reviewing those on the medications before the AKI as the denominator;

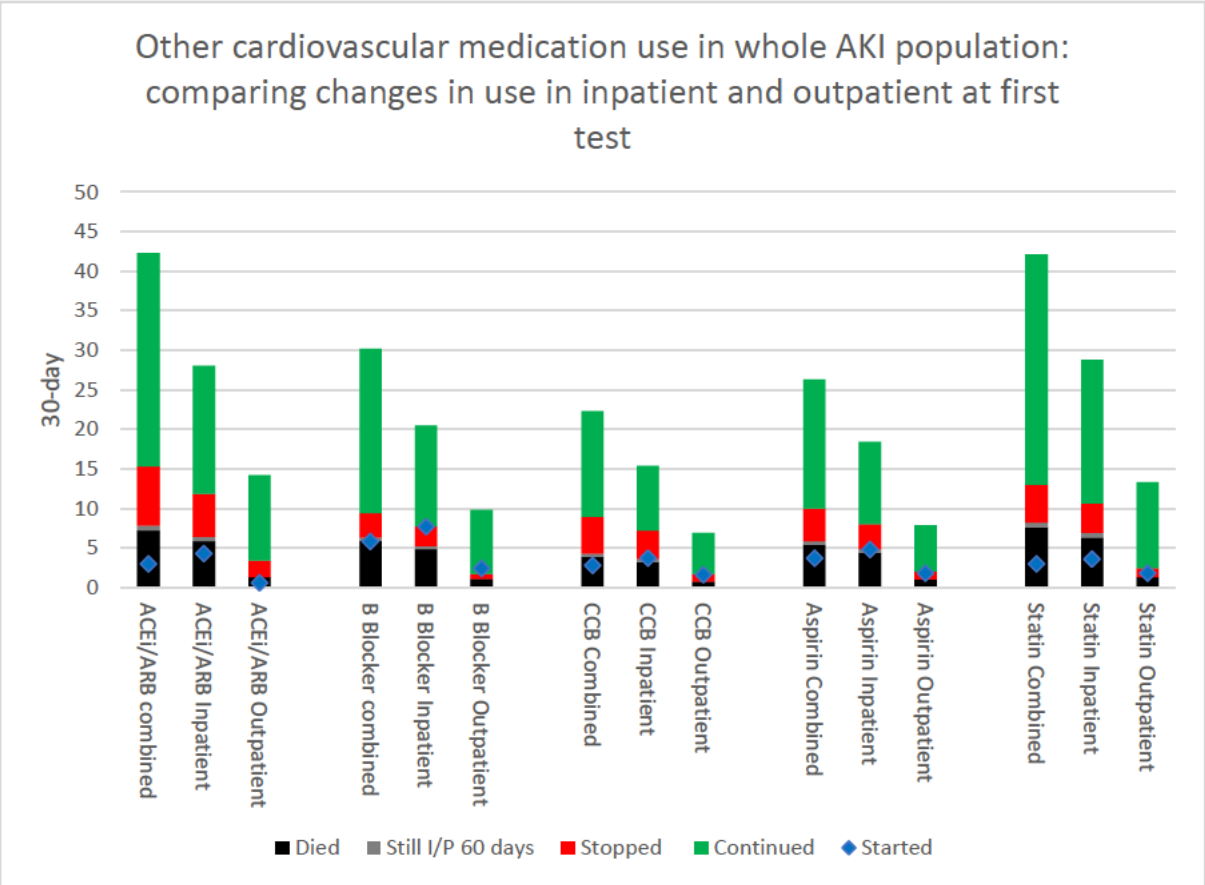


Graph 67 - Other cardiovascular medication use before AKI: comparing changes in use in inpatient and outpatient at first test.

ACEi = Angiotensin converting enzyme inhibitor, ARB = Angiotensin Receptor Blocker, CCB = Calcium channel Blocker, I/P = Inpatient

In these medications, calcium channel blockers had the highest proportion of medications stopped (20.2%), followed by ACEi/ARBs (17.7%), only 10.2% of those on beta blockers had them stopped. The highest 30-day mortality was seen in aspirin with 20.2% of those given an aspirin prescription in the 90-days before their AKI, dying within 30-days. Again, when we look

at the inpatient group we observe a higher mortality and the patients appear more likely to have medication stopped. B blockers had the highest proportion of started medications compared to those on it in the 90-days before, but again it was worth seeing this in comparison to the overall population.



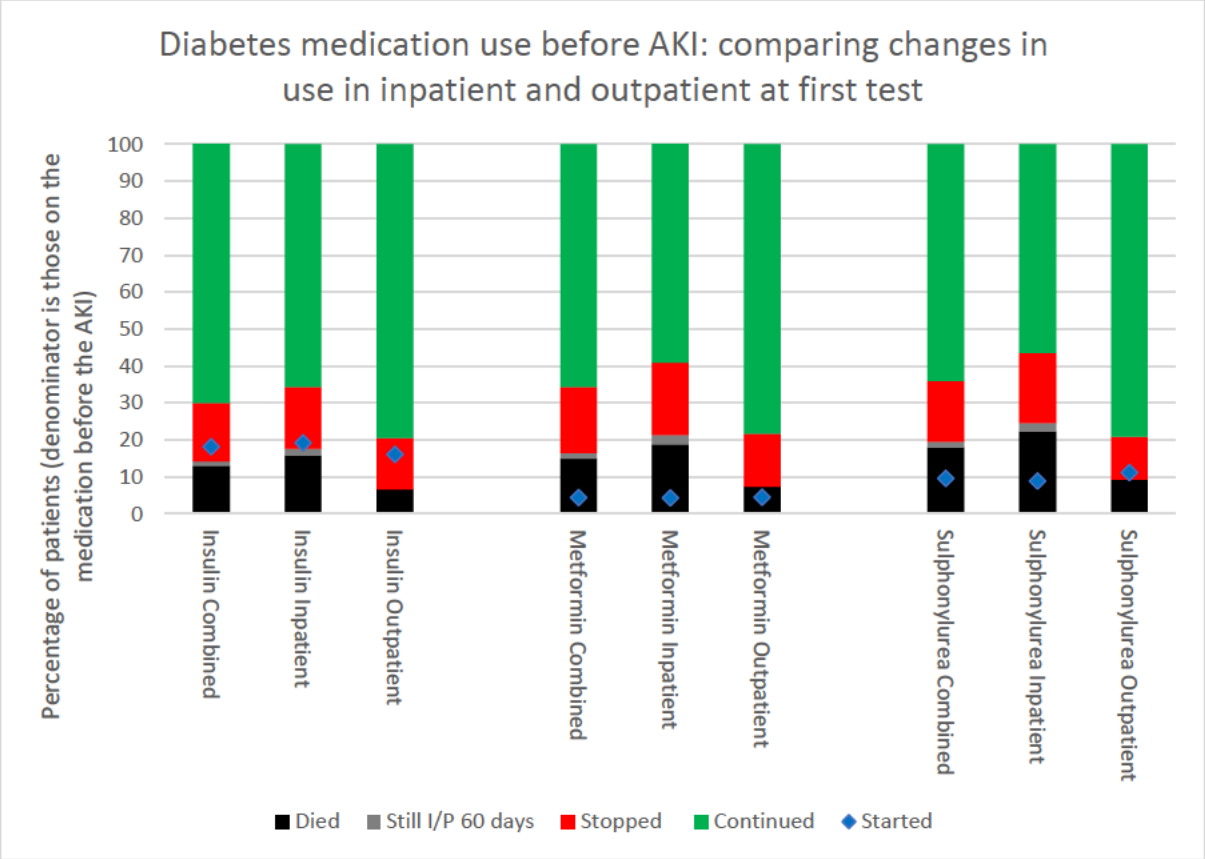
Graph 68 - Other cardiovascular medication use in whole AKI population: comparing changes in use in inpatient and outpatient at first test

ACEi = Angiotensin converting enzyme inhibitor, ARB = Angiotensin Receptor Blocker, CCB = Calcium channel Blocker, I/P = Inpatient

In this graph we can see that both statins and ACEi/ARBs are used in similar numbers of these AKI patients (45%), with a similar mortality figure, but with ACEi/ARBs more people have their medications stopped (7.5% of the overall population vs 4.8% in those on statins). This graph again shows that the majority of these patients on these cardiovascular medications were inpatients on the day of their first AKI test and beta blockers were the most likely to be started after AKI in this group (5.8%).

The next graph explores the changes in some diabetes medications. From this we can see the medications are stopped in similar proportions across the 3 medication but unsurprisingly

metformin was the medication with the highest stoppages, particularly in inpatients where it was 19.6%.

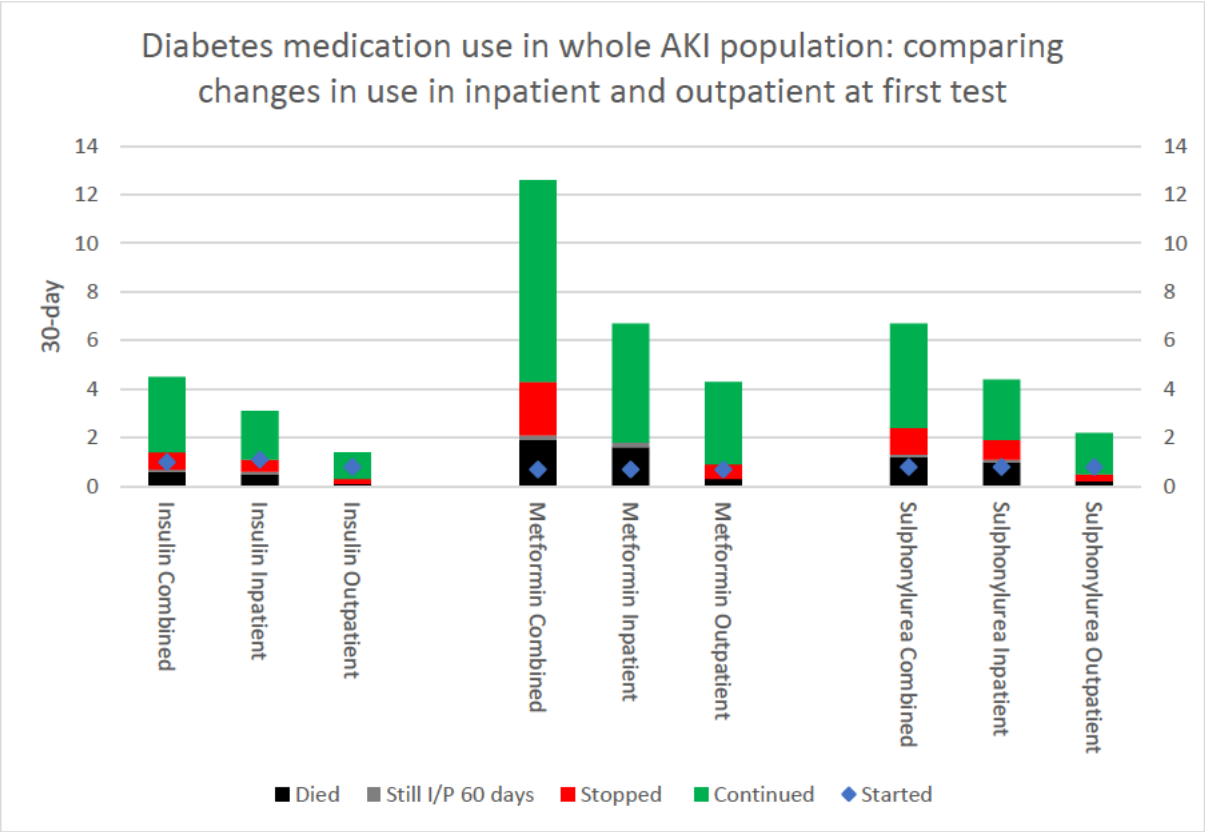


Graph 69 - Diabetes medication use before AKI: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient

The highest 30-day mortality was seen in the sulphonylurea group where it was as high as 22.3% in the inpatient group, compared to 18.8% and 15.9% in metformin and insulin respectively. Insulin had the highest proportion of new prescriptions which was similar in both the inpatient and outpatient groups.

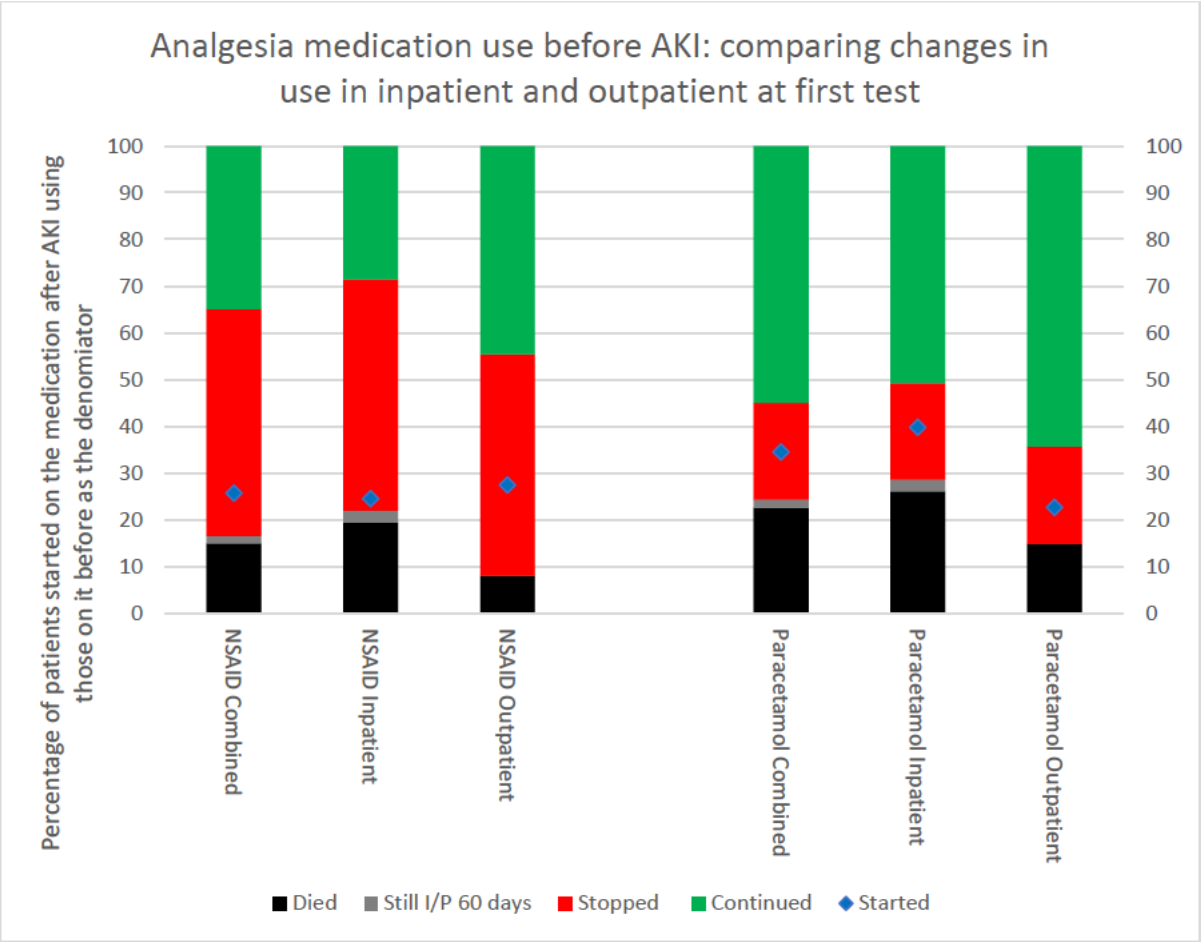
The next graph looks at these diabetes medications in this whole AKI cohort, where 13% of the AKI cohort have a metformin prescription during this study period. Although insulin by proportion sees the largest percentage of people starting it for the first time following AKI (Graph 69), when reviewing it across the whole AKI population it was 1.2%, and it does not show a vast difference compared with metformin (0.8%) and sulphonylureas (0.9%) overall.



Graph 70 - Diabetes medication use in whole AKI population: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient

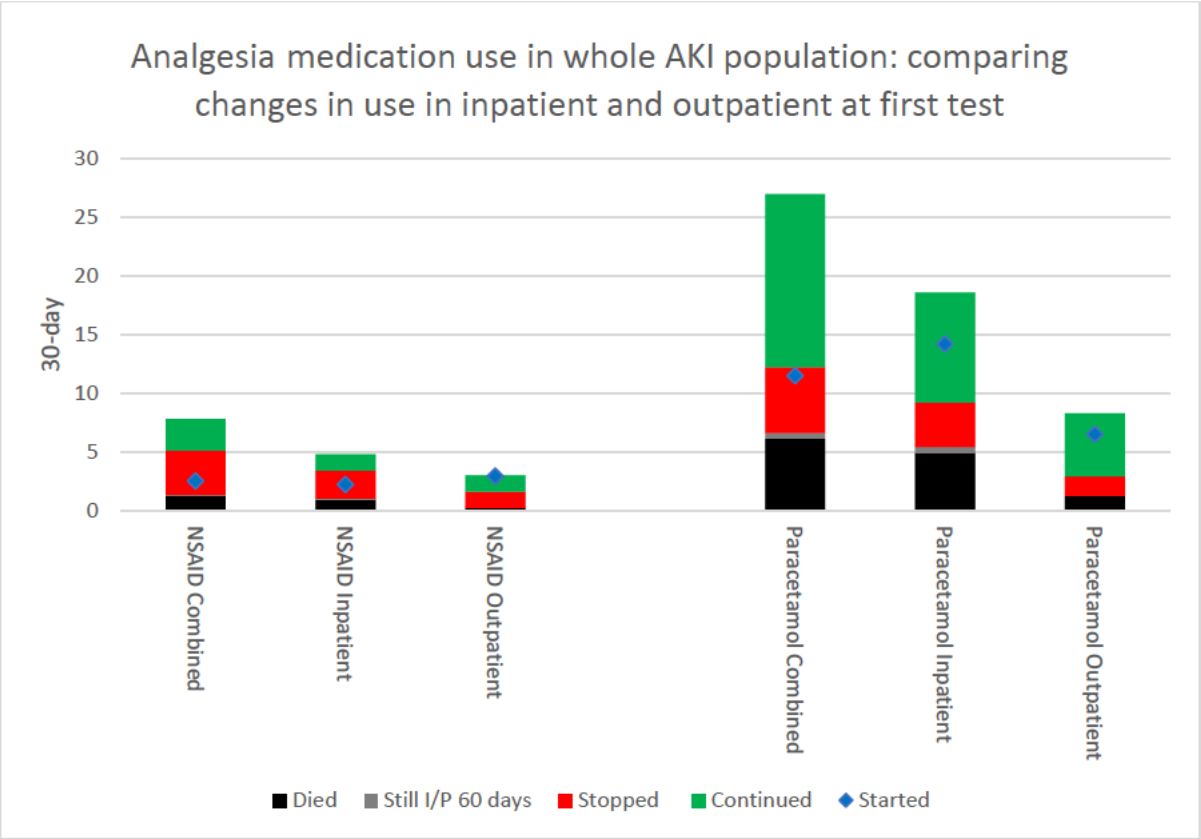
The next group of medications I have looked at are analgesics in the form of NSAIDs and paracetamol. The NSAIDs medication class is important as it can cause AKI via a number of mechanisms and therefore you would expect that in many cases it was stopped (199). Following the previously used pattern, first we will look at what happens to those on the medication using the prescriptions before 90-days as the denominator;



Graph 71 - Analgesia medication use before AKI: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient, NSAID = Non-steroidal anti-inflammatory medications

As can be seen, a large proportion of patients have their NSAIDs stopped 48.6% which was similar across the inpatient and outpatient group and was much higher than with paracetamol (20.7%). It was interesting, however that the mortality was lower in the NSAID group 14.9% vs 22.3% than in the paracetamol group which has the second highest mortality in the medications studied. This outcome was an incidental finding when trying to understand why certain medications were stopped, and the results were not corrected for frailty and comorbidities, therefore no firm conclusions can be drawn. The outpatient NSAID AKI group has the lowest 30-day mortality of the study. In the 90-days following AKI, an equivalent of 60% of those on NSAIDs before AKI are on them after (continued along with the newly started). This makes up 5.2% of the overall AKI population. It is important to recognise that both these medications can be easily purchases over the counter in the UK.

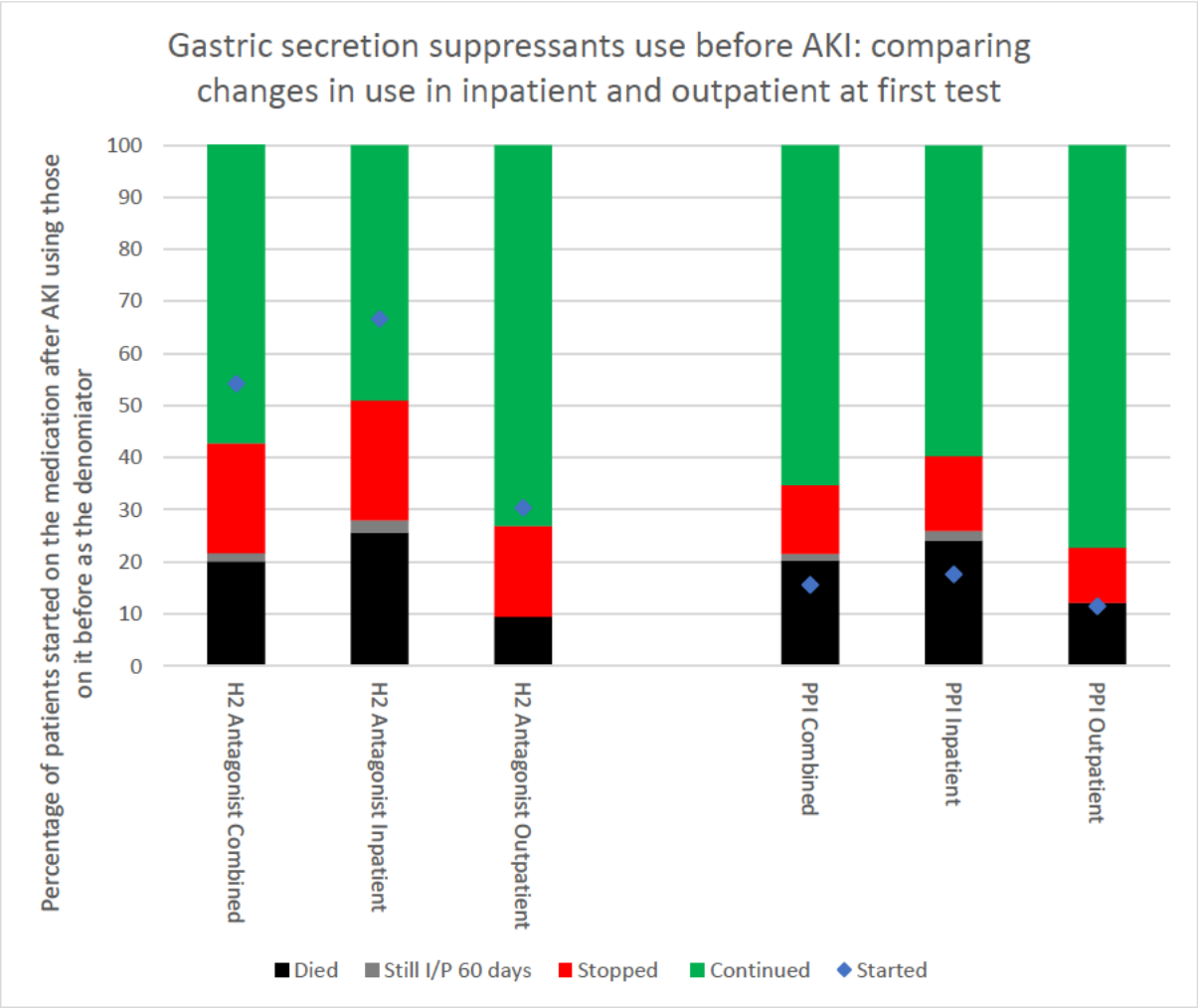


Graph 72 - Analgesia medication use in whole AKI population: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient, NSAID = Non-steroidal anti-inflammatory medications

Paracetamol was started in 11.5% of the whole AKI population alive at 30-days after AKI.

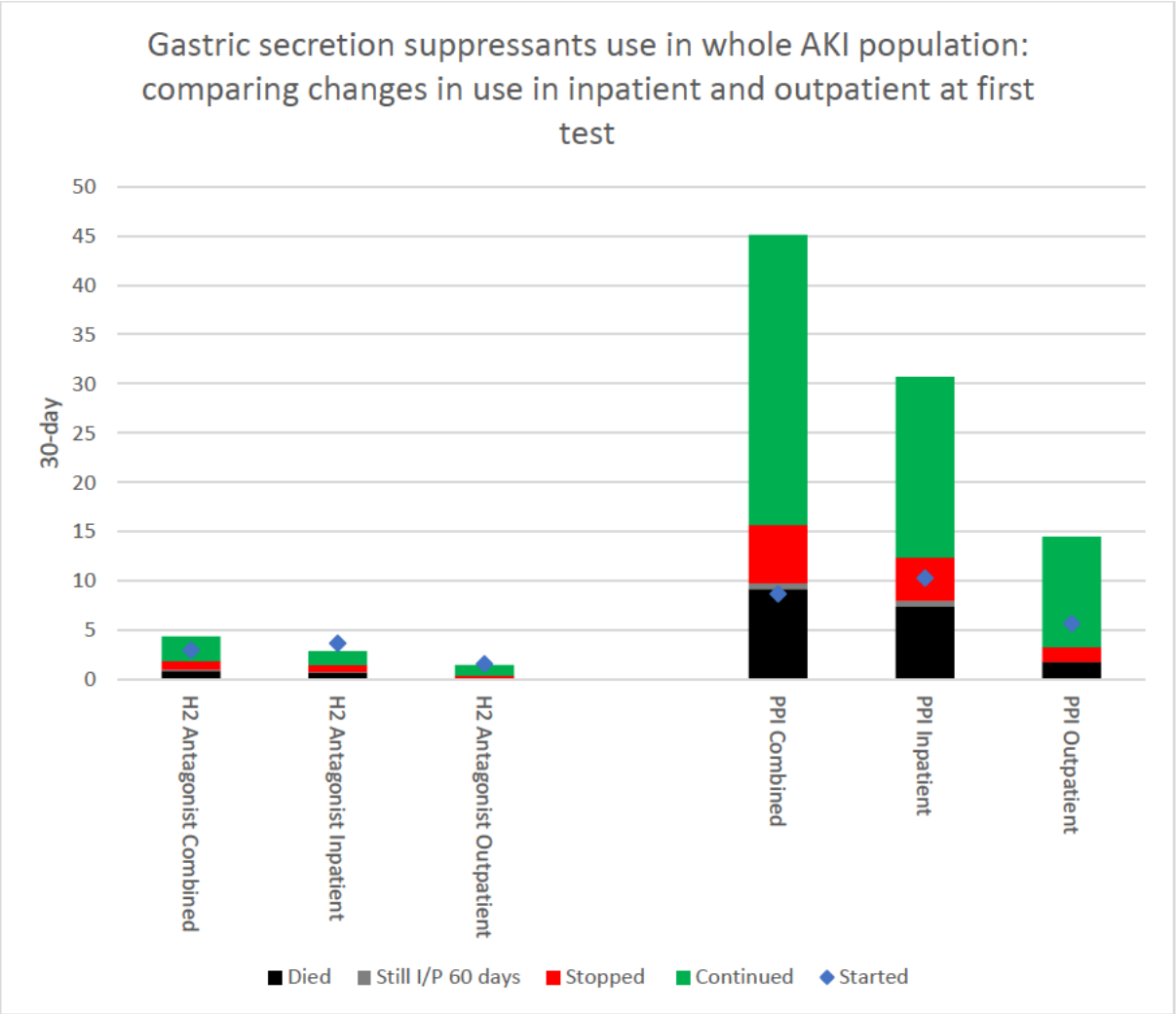
The final group reviewed are those on gastric secretion suppressants. Proton pump inhibitors are widely used medications that have been linked with kidney disease by some researchers (270). They are known to cause a form of AKI called acute interstitial nephritis in a small number of patients taking them.



Graph 73 - Gastric secretion suppressants use before AKI: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient, PPI = Proton Pump Inhibitor

As can be seen here H2 Antagonists are proportionally the most started medication, although this was most striking in inpatients. As a result of this, histamine receptor 2 antagonists are the only medication with a net gain in use following AKI (111.5% either continued the medication or are new starters). The mortality in the 2 groups were very similar but a greater proportion remained on PPIs.



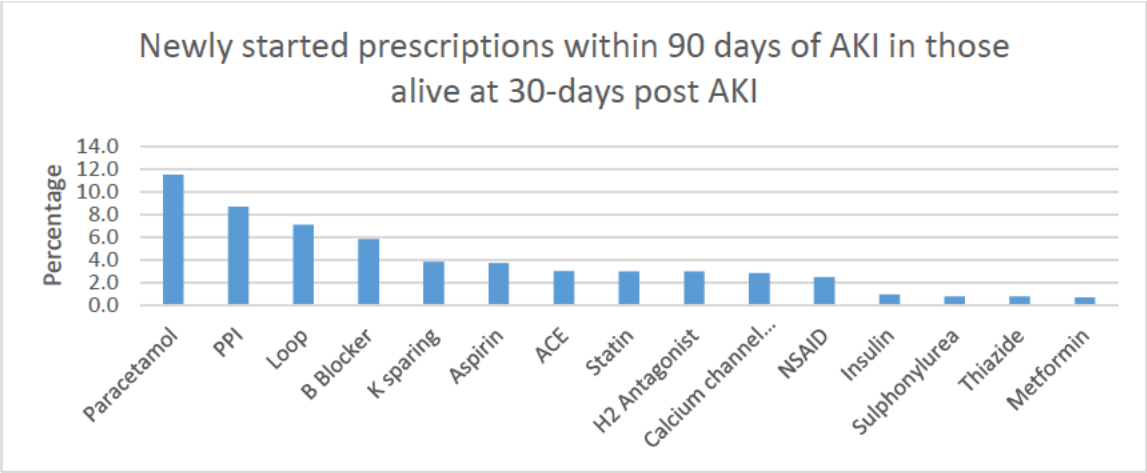
Graph 74 - Gastric secretion suppressants use in whole AKI population: comparing changes in use in inpatient and outpatient at first test

I/P = Inpatient, PPI = Proton Pump Inhibitor

When we use the whole population of the study, we can see that more than half the patients with AKI are prescribed a proton pump inhibitor in the 180 days around their AKI.

Started medications

This next graph shows the new prescriptions following AKI over the whole alive population with data, highlighting the 3 most commonly new started medications following AKI (in the drugs studied) are paracetamol, proton pump inhibitors and loop diuretics.



Graph 75 - Newly started prescriptions within 90-days of AKI in those alive at 30-days post AKI

As previously alluded to, non-steroidal anti-inflammatory medications can cause AKI by a number of mechanisms, and it was interesting that given this 2.5% of the AKI population that were alive at 30-days after the AKI had it started as a new medication following the AKI and over 5 percent of the AKI population are likely to be prescribed the medication following their AKI (continued and started).

Alert introduction

The next section explores if electronic AKI alerts seen in practice (WRRS alerts) has an effect on the primary care prescriptions. As discussed in the previous chapter, there are some problems when comparing our identified AKI with the WRRS alerts in that our AKI after do not completely match the WRRS alerts when they should as the method of creating them was intended to be the same (76% matching when looking at those with primary care data). In view of this, I compare our AKI before ('Before AKI alerts'), our AKI after ('After AKI alert') and WRRS alerts. Again, like the previous section, these are split into all patients (combined inpatient and outpatients) and inpatients to see if hospital admission changes the picture. In this section, I have performed Pearson chi-squared analysis to compare the 3 groups.

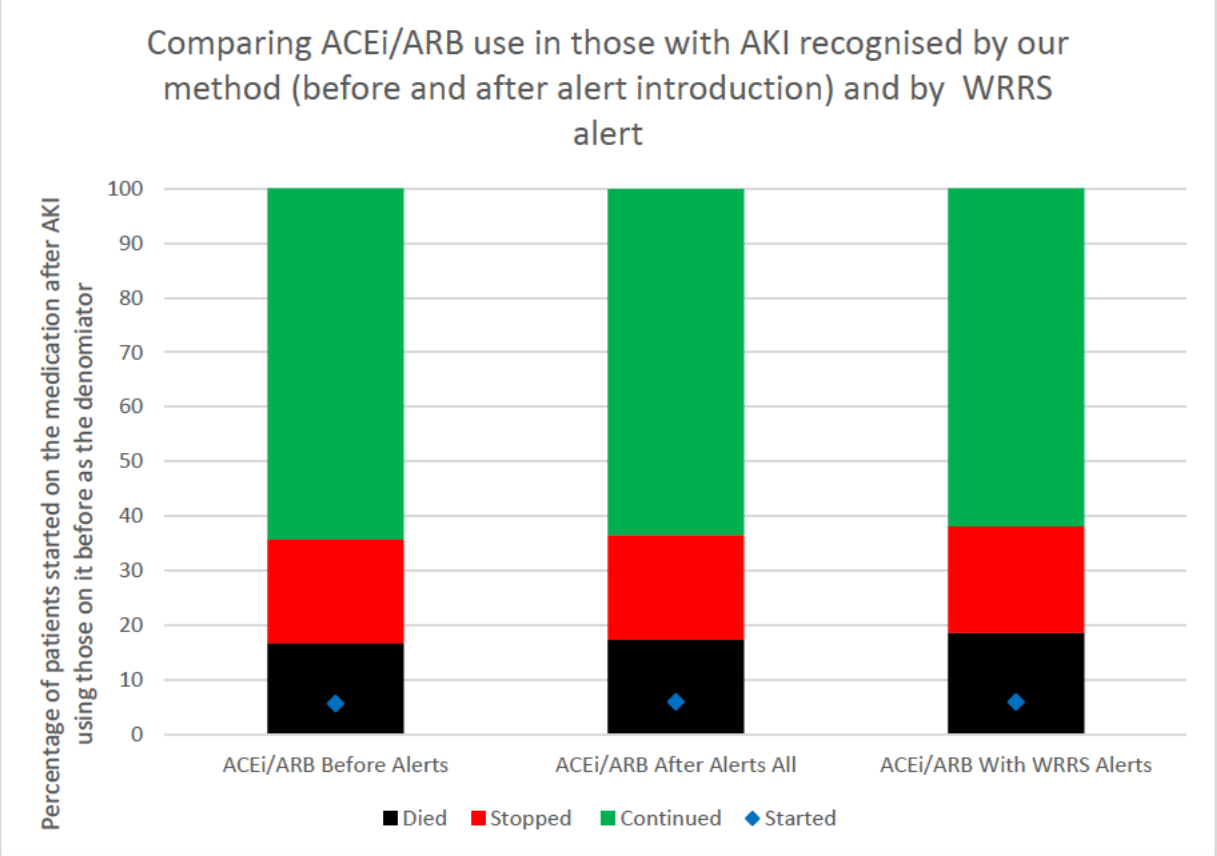
Following the introduction of alerts, there was no statistically significant difference in any of the aspects (continued, died, stopped and new) for NSAIDs.

All locations	Before AKI Alerts	After AKI Alerts		WRRS Alerts	
NSAIDs	Percentage	Percentage	P value	Percentage	P value
Continued	35.5	34.1	0.39	32.9	0.13
Stopped	49.9	50.5	0.75	50.2	0.89
Died	14.5	15.4	0.48	16.9	0.07
Started	26.0	25.3	0.63	23.2	0.08

Table 100 - Comparing NSAID use in AKI recognised by our algorithm and WRRS

There was also no statistically significant difference in any of the aspects in thiazides and potassium sparing diuretics, therefore they are not shown here.

The graph below (Graph 76) looks at patients prescribed an ACEi/ARB in the 90-days before their AKI comparing our AKI before ('before alerts') with our AKI after ('After alerts') and also comparing our AKI before with WRRS after. In this analysis, there was an increased 30-day mortality when comparing our group before alerts 'before alerts' (16.7%) and WRRS alerts (18.6%) with a p value of <0.01 (Table 101). There was also a difference when comparing these two groups and those continuing ACEi/ARBs where we saw a reduction in those continuing the medication in the WRRS group (61.9%) compared to our AKI before (64%), in part this was due to the mortality difference (p = <0.01). There was no difference however observed when comparing our identified AKIs before ('before alerts') and our identified AKIs after ('after alerts'). There were no statistically significant differences observed in the number of patients stopping the medications or starting the medication as a new medication. Also, analysis of the inpatient cohort of patients prescribed ACEi/ARBs did not find any significant differences between the groups.

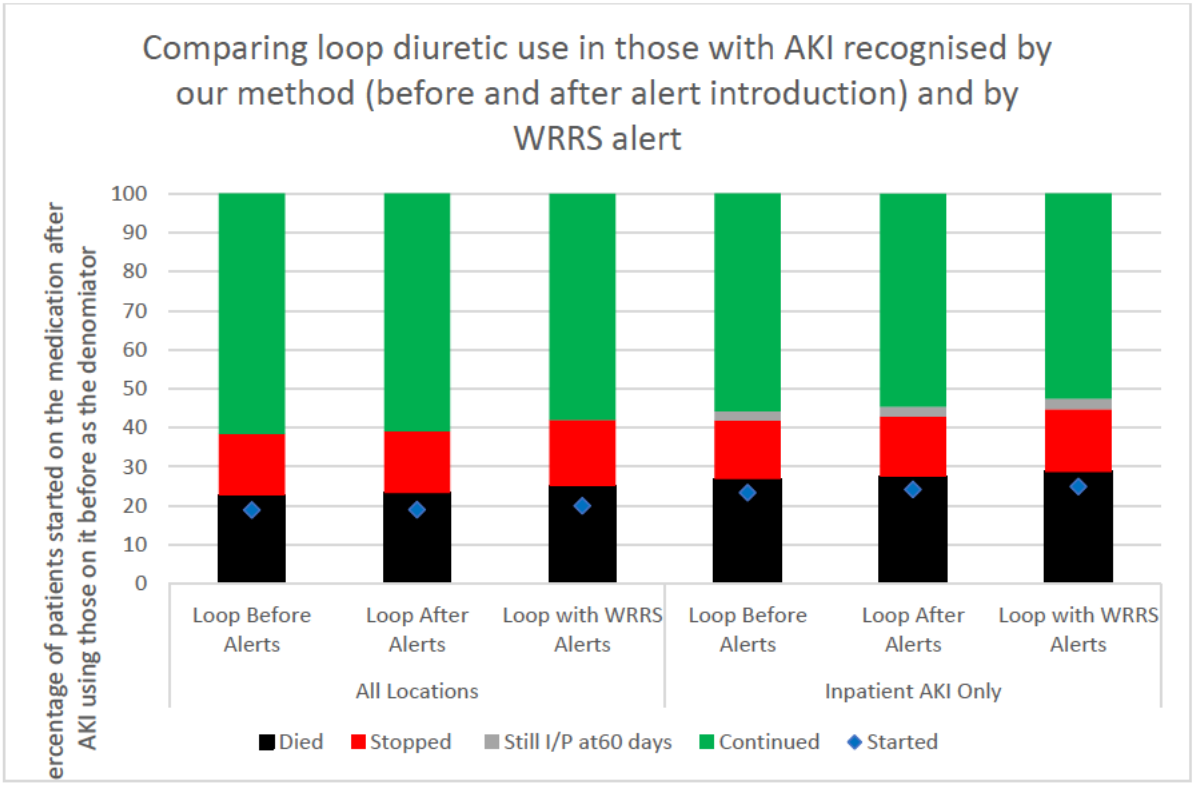


Graph 76 - Comparing ACEi/ARB use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

All locations	Before Alerts	After Alerts		WRRS	
ACEi/ARB	Percentage	Percentage	P value	Percentage	P value
Continued	64.4	63.4	0.18	61.9	<0.01
Stopped	18.9	19.2	0.69	19.5	0.36
Died	16.7	17.4	0.19	18.6	<0.01
Started	5.6	5.9	0.48	5.9	0.41

Table 101 - Comparing ACEi/ARB use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In those on loop diuretics before their AKI, we again saw an increased 30-day mortality in those that had an AKI alert (WRRS 25.1%) sent compared to those with AKI identified by our method before alerts were introduced (22.7%) with p<0.01.



Graph 77 - Comparing loop diuretic use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

I/P = Inpatient, PPI = Proton Pump Inhibitor

We also saw a fall in those continuing loop diuretics in those with a WRRS alert 57.9% vs 61.6% with a (p value <0.01).

All locations	Before Alerts	After Alerts		WRRS	
Loop	Percentage	Percentage	P value	Percentage	P value
Continued	61.6	60.8	0.35	57.9	<0.01
Stopped	15.7	15.8	0.86	16.9	0.08
Died	22.7	23.3	0.36	25.1	<0.01
Started	18.9	19.0	0.85	20.0	0.12

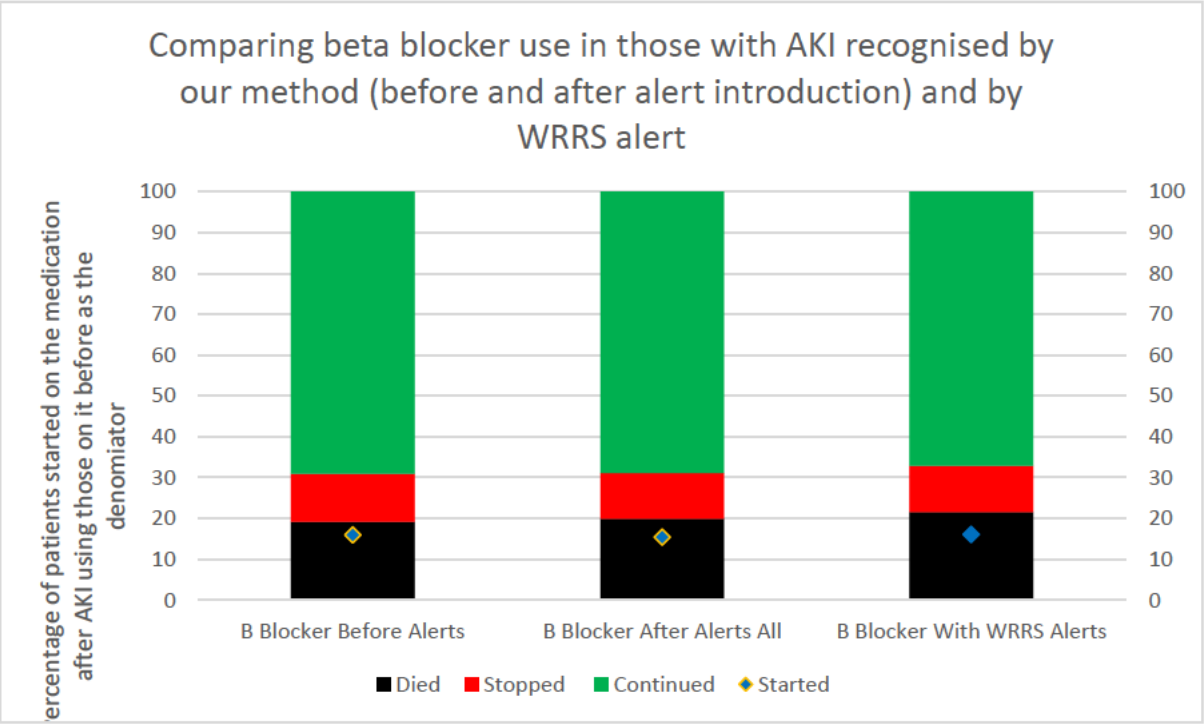
Table 102 - Comparing loop diuretic use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

The difference between those with diuretics stopped was not statistically significant in this study (15.7% before vs 16.9 WRRS, p value 0.08). When comparing the inpatient cohort, the only statistically significant difference was in those continuing the loop diuretic, with 55.8% before alerts and 52.5% after alerts (p value <0.01). There were no significant differences when comparing our identified AKI patients before and after the alert introduction.

Inpatient only	Before Alerts	After Alerts		WRRS	
Loop	Percentage	Percentage	P value	Percentage	P value
Continued	55.8	54.5	0.23	52.5	<0.01
Stopped	14.9	15.4	0.45	16.0	0.16
Died	26.9	27.5	0.51	28.7	0.07
Started	23.4	24.2	0.38	24.9	0.13

*Table 103 - Comparing loop diuretic use in **inpatients** with AKI recognised by our method (before and after alert introduction) and by WRRS alert*

In those on beta blockers, we saw the same trend, where there was an overall increased 30-day mortality and decreased continuation in the WRRS alert group (21.6% and 67%) compared to before alerts (19.2%, 69%) with p values of <0.01, but only in the combined 'all' group. There were no significant differences in the inpatient analysis.



Graph 78 - Comparing beta blocker use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

I/P = Inpatient, PPI = Proton Pump Inhibitor

All locations	Before Alerts	After Alerts		WRRS	
B Blocker	Percentage	Percentage	P value	Percentage	P value
Continued	69.0	68.9	0.92	67.1	0.03
Stopped	11.8	11.2	0.30	11.3	0.47
Died	19.2	19.9	0.35	21.6	<0.01
Started	15.9	15.4	0.45	16.0	0.79

Table 104 - Comparing beta blocker use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In the diabetes medications, there appears to be a higher 30-day mortality in the metformin and sulphonylureas patients with WRRS alerts (see Table 105) which was also observed when

they are inpatients. We also see fewer patients continuing on sulphonylureas in this WRRS group both as inpatients and outpatients, this was not observed however when comparing with all the patients we identify as AKI after the introduction of alerts ('after alerts'). In the insulin patients however, when we look at inpatients at the time of their first alert, we see a reduction in those patients continuing on the medication after the AKI in both the WRRS group and the 'after alert' AKI identified using our algorithm.

All locations	Insulin					Metformin					Sulphonylureas				
	Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS	
	%	%	P value	%	P value	%	%	P value	%	P value	%	%	P value	%	P value
Continued	71.8	68.4	0.11	67.7	0.08	65.7	65.7	0.98	64.2	0.28	65.1	62.8	0.19	60.3	0.01
Stopped	15.6	18.3	0.16	17.4	0.34	20.2	18.6	0.16	18.5	0.15	17.4	18.7	0.36	18.5	0.30
Died	12.6	13.3	0.66	14.9	0.18	14.1	15.6	0.12	17.3	<0.01	17.5	18.5	0.47	21.2	0.02
Started	18.7	17.9	0.65	18.7	1.00	4.4	4.3	0.91	4.3	0.82	9.9	9.3	0.61	8.5	0.23

Table 105 - Comparing diabetes medication use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

Inpatients	Insulin					Metformin					Sulphonylureas				
	Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS	
	%	%	P value	%	P value	%	%	P value	%	P value	%	%	P value	%	P value
Continued	68.4	63.1	0.04	61.8	0.02	58.9	59.5	0.74	58.8	0.94	58.4	54.5	0.08	53.1	0.03
I/P @ 60 d	1.2	2.2		2.1		2.8	2.2		2.3		2.5	2.2		2.1	
Stopped	15.1	18.2	0.13	17.7	0.24	20.4	18.7	0.21	18.3	0.14	18.0	19.8	0.31	19.2	0.52
Died	15.2	16.5	0.52	18.4	0.17	17.9	19.6	0.19	20.7	0.05	21.1	23.6	0.20	25.6	0.03
Started	19.4	19.0	0.85	20.3	0.74	4.3	4.3	0.99	4.3	0.95	9.9	7.8	0.10	7.4	0.07

Table 106 - Comparing diabetes medication use in inpatients with AKI recognised by our method (before and after alert introduction) and by WRRS alert

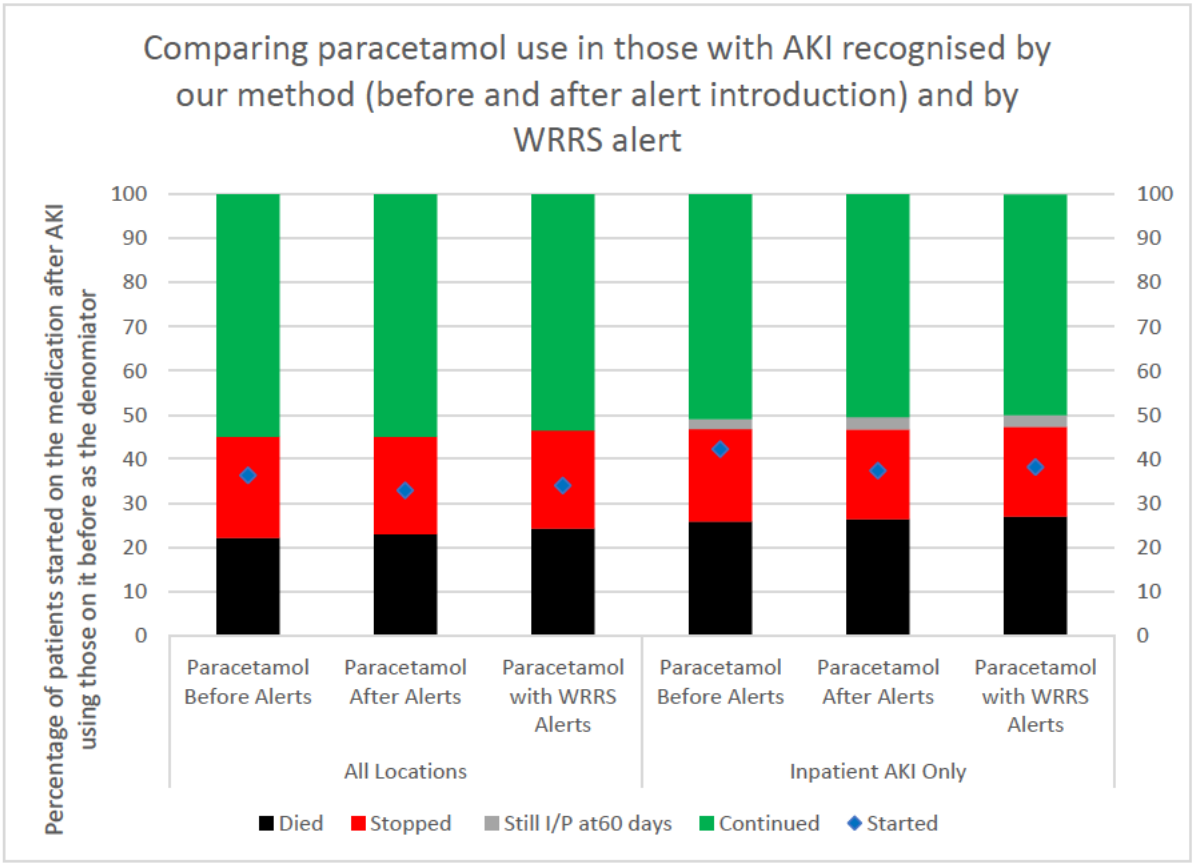
All locations	Proton pump inhibitors					Histamine receptor 2 antagonists				
	Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS	
	%	%	P value	%	P value	%	%	P value	%	P value
Continued	65.7	64.9	0.23	63.2	<0.01	56.1	58.3	0.33	53.9	0.38
Stopped	14.0	14.8	0.1	15.1	0.04	24.2	21.3	0.13	23.2	0.64
Died	20.3	20.3	1.00	21.6	<0.01	19.7	20.4	0.72	22.9	0.12
Started	16.6	14.7	0.00	14.7	<0.01	51.4	56.7	0.02	63.0	<0.01

Inpatient	Proton pump inhibitors					Histamine receptor 2 antagonists				
	Before Alerts	After Alerts		WRRS		Before Alerts	After Alerts		WRRS	
	%	%	P value	%	P value	%	%	P value	%	P value
Continued	60.2	59.0	0.17	58.3	0.04	48.0	50.0	0.48	46.9	0.72
Still I/P 60 days	1.8	2.1		2.1		3.2	1.7		1.6	
Stopped	13.7	15.1	0.02	15.1	0.03	23.0	23.0	0.99	24.9	0.47
Died	24.4	23.9	0.49	24.6	0.83	25.8	25.3	0.83	26.6	0.76
Started	18.4	16.7	0.01	16.6	0.01	62.8	70.0	0.01	75.5	<0.01

Table 107 - Gastric secretion suppressants use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert – all locations and inpatient only

Again, the gastric medications saw the greatest changes with decreased prescriptions (both continuations and new prescriptions) of PPIs following AKI in the WRRS group along with an increased 30-day mortality. The reduction in the new prescriptions was also seen when comparing AKI by our method before vs after. This was a similar pattern to that observed in the inpatients with previous proton pump inhibitor prescription, the only difference was that we see an increased proportion of patients stopping it in both after groups (WRRS and after alerts). For the histamine receptor 2 antagonists the only change was an increase in prescription following AKI seen again in both groups after the alert introduction, possibly because of the reduced prescriptions of proton pump inhibitors.

With paracetamol, we see a reduction in new use following AKI in the both the combined (all locations) and inpatient group, when comparing both after groups with before.



Graph 79 - Comparing paracetamol use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

We also see an increased 30-day mortality in both groups following the alert introduction in the combined ('all') group, however this was not replicated in the inpatients.

All locations	Before Alerts	After Alerts		WRRS	
Paracetamol	Percentage	Percentage	P value	Percentage	P value
Continued	55.0	55.0	0.99	53.5	0.13
Stopped	22.8	22.0	0.29	22.2	0.49
Died	22.2	23.0	<0.01	24.3	0.01
Started	36.3	32.9	<0.01	34.0	0.02

Table 108 - Comparing paracetamol use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In both the 'all locations' and the inpatient sample we see a lower new prescription rate of paracetamol in the after and WRRS group.

Inpatient	Before Alerts	After Alerts		WRRS	
Paracetamol	Percentage	Percentage	P value	Percentage	P value
Continued	51.0	50.6	0.67	49.9	0.36
Stopped	20.9	20.3	0.54	20.3	0.60
Died	25.9	26.4	0.66	27.0	0.32
Started	42.3	37.4	<0.01	38.2	<0.01

Table 109 - Comparing paracetamol use in inpatients with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In the calcium channel antagonist, aspirin and statins we see and increased mortality in the WRRS group but not between the before alerts and after alerts group.

All locations	Before Alerts		After Alerts	WRRS	
Calcium Channel antagonist	Percentage	Percentage	P value	Percentage	P value
Continued	60.2	60.1	0.96	58.6	0.14
Stopped	22.9	21.7	0.17	22.0	0.32
Died	16.9	18.1	0.12	19.4	<0.01
Started	10.2	10.4	0.65	10.2	0.90

Table 110 - Comparing calcium channel antagonist use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In aspirin and statins we saw a reduced continuation in the WRRS group.

All locations	Before	After		WRRS	
Statin	Percentage	Percentage	P value	Percentage	P value
Continued	69.8	68.4	0.05	67.0	<0.01
Stopped	12.7	13.0	0.49	12.9	0.64
Died	17.5	18.5	0.07	20.0	<0.01
Started	5.8	5.6	0.62	5.8	0.94

Table 111 - Comparing statin use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

In the aspirin group we also see an increased in those stopping it when comparing both with our 'after alerts' and WRRS, with fewer patients starting aspirin in the 'after alert' group but it does not reach statistical significance the WRRS group.

All locations	Before Alerts	After Alerts		WRRS	
Aspirin	Percentage	Percentage	P value	Percentage	P value
Continued	62.8	61.2	0.09	59.2	0.00
Stopped	16.8	18.2	0.05	18.6	0.02
Died	20.5	20.6	0.85	22.2	0.04
Started	12.3	10.6	0.01	11.1	0.07

Table 112 - Comparing aspirin use in those with AKI recognised by our method (before and after alert introduction) and by WRRS alert

Primary care reviews

I previously described the changes in reviews following AKI in Table 99, but we can further break this down into the time period before and after electronic alerts were introduced. It was important to highlight that the '90-days before AKI' includes all the patients as the denominator but the '90-days after AKI' only included those alive at 30 days as the denominator. The table below shows a comparison of those identified by our algorithm within SAIL;

	Before alerts introduced			After alerts introduced		
	90-days before AKI	90-days after AKI	p value	90-days before AKI	90-days after AKI	p value
Medication(s) Review	16.4%	16.1%	0.37	15.4%	16.0%	<0.01
AKI GP Coding	1.0%	2.4%	<0.01	2.0%	4.1%	<0.01
Blood Pressure	48.1%	43.1%	<0.01	46.0%	41.4%	<0.01
Primary Care SCr Test	48.2%	48.8%	0.25	47.2%	47.4%	0.70

Table 113 - Comparison of primary care reviews 90-days before and after AKI, split into 1-year period before and after eAlert introduction.

Here we observe a reduction in our identified blood pressure readings following AKI, understandably more AKI coding and in the time after alerts we saw an increase in medication review. However, it is important to note that this level of 16% is lower than both the 90-days before and 90-days after findings in the before alert introduced group. It is interesting that between 1 and 2% of those with AKI, have a code for AKI in the 90-day before AKI, especially when we consider that for this study we are using the first AKI for the patient in the time period studied (variable depending on health board, see Figure 41). When we look at those after the alerts introduction who received the alert (WRRS group) the findings are similar.

	After alerts introduced WRRS (alert)		
	90-days before AKI	90-days after AKI	p value
Medication(s) Review	15.5%	15.9%	0.08
AKI GP Coding	2.2%	4.5%	<0.01
Blood Pressure	45.8%	40.4%	<0.01
Primary Care SCr Test	46.5%	44.9%	<0.01

Table 114 - Comparison of primary care reviews 90-days before and after AKI, in those with an eAlert (WRRS alert)

Like the other groups, we see a reduction in the number blood pressure reading after, which may be in part because some of the patients had the blood pressure reading at the point of identifying AKI, and this may also be the reason for a fall in primary care requested SCr tests in this group.

I then looked at the Read codes for these reviews after AKI, comparing the 3 different group (before eAlerts, After eAlerts and those that actually received the eAlerts (WRRS alerts));

Reviews following AKI	Before eAlerts	After eAlerts	P value	Before eAlerts	WRRS Alerts	P value
Medication(s) Review	16.1%	16%	0.86	16.1%	15.9%	0.72
AKI GP Coding	2.4%	4.1%	<0.01	2.4%	4.5%	<0.01
Blood Pressure	43.1%	41.4%	<0.01	43.1%	40.4%	<0.01
Primary Care SCr Test	48.8%	47.4%	<0.01	48.8%	44.9%	<0.01

Table 115 - Comparison of primary care reviews in the 90-days after AKI, in those with before and after the introduction eAlert and with those that have eAlerts (WRRS alert)

From these we can see that following the introduction of eAlerts, there appears to be an increase in primary care AKI coding, but a decrease in blood pressure reviews and primary care requested SCr with no change in medication reviews. This suggests that the primary care team have an increased (albeit still very low recognition) of the AKI, but without discernible changes in the medication reviews and a fall in blood pressure and blood tests reviews. With only ~4% of patients having an AKI code in the primary care record, this raises 266question of whether they are informed of the AKI. I explored this from an audit in 2017 which I will discuss.

Discharge Summary Study

To understand help understand who makes the medication changes following AKI observed by primary care Read code entries for medications, it is important to look at what medications' patients are sent home from hospital on. This dataset was not available within SAIL, however discharge letters have standards (272) that should be met and as such I set out to audit some of these aspects examining AKI in particular. This allows for comparison with Reschen et al (223) and their evaluation of the effect of the CQUIN AKI standards(222).

Methods

A sample of patients with inpatient AKI in Morriston hospital were selected across 4 months between April 2017 and July 2017 by selecting all alerts from an inpatient or emergency department location on the 3rd, 11th, 19th and the 27th of these months. Only one alert per hospital admission was studied, even if there were alerts at separate times or months. The biochemistry data was gathered by the pathology department team where an electronic AKI alert was triggered from an inpatient location. By manually reviewing the temporal blood results of these patients, I was able to exclude those that I did not feel had AKI and those who were not admitted were excluded. Patients who were transferred to a hospital outside the trust were also excluded, but patients who were originally from outside the trust but who were discharged home from Morriston hospital were included. Using this cohort of patients with AKI, electronic discharge summaries were manually reviewed following the admissions looking for the mention of AKI, dialysis and advice around any medication changes.

Approval

The study was carried out as an audit through the health board's (Abertawe Bro Morgannwg University Health Board) audit process. It was carried out with approval from the audit department.

Results

There were 318 alerts in total. Duplicate alerts in patients were excluded from the study, as were those who were transferred to another hospital. Some patients were not admitted, some patients were chronic haemodialysis patients, and 22 patients were not AKI in my opinion upon review, usually because they had one falsely low test that was out of keeping with their baseline.

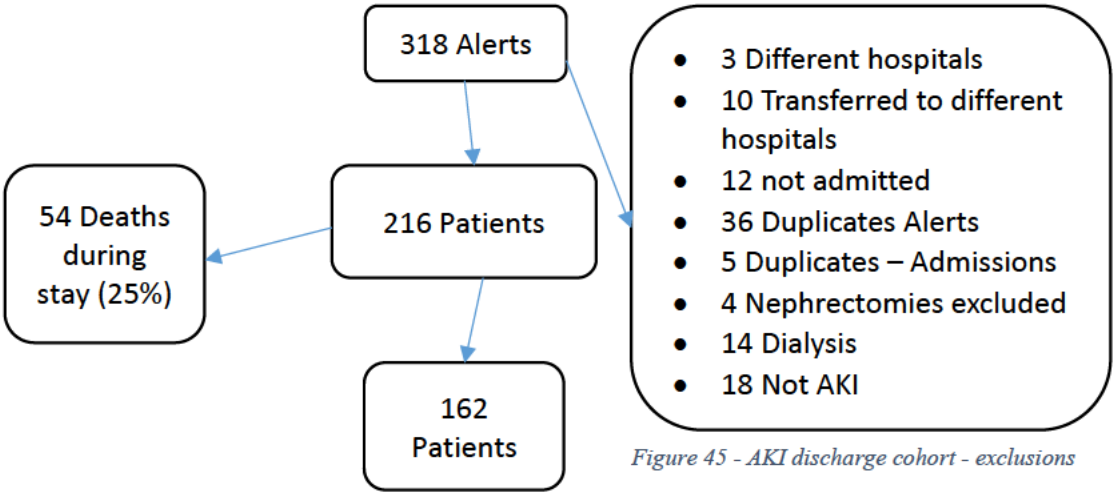


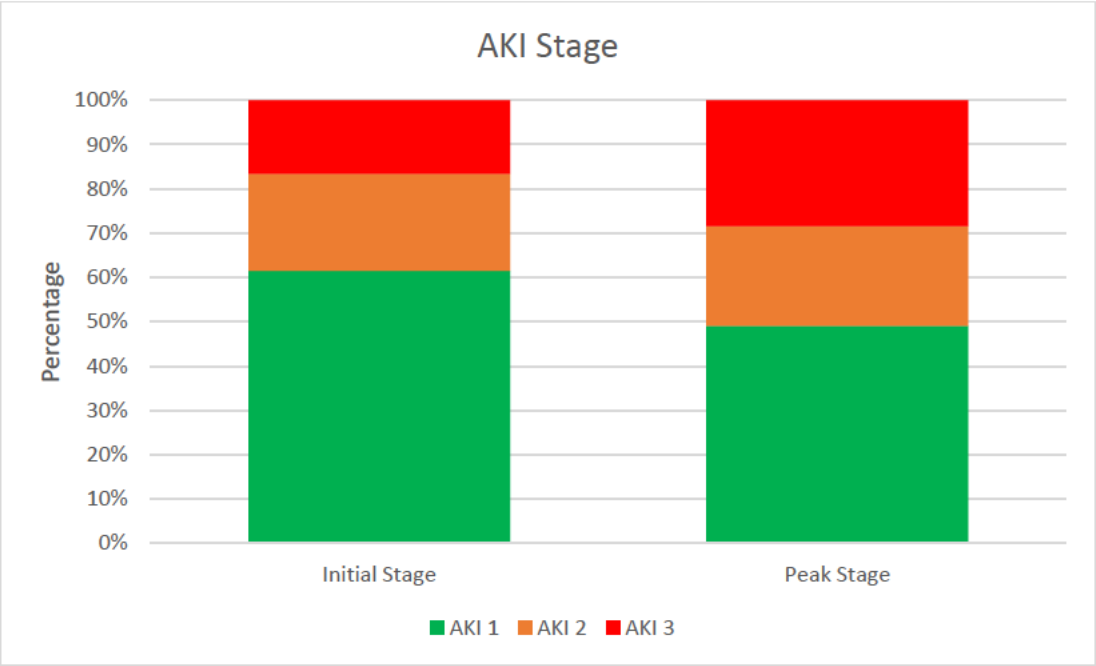
Figure 45 - AKI discharge cohort - exclusions

After the removal of these patients there were 218 patients that had inpatient AKI, 25% of whom died during their stay so were not included in the final analysis.

	Alive and discharged	**Died**
Mean Age (Median)	71.9 (74)	75.3 (74)
Female	53%	41.1%
Creatinine	176.3 (161)	229 (161.5)
Baseline	100 (88)	271 (184)
LOS	36 (17)	33 (16.5)
	First Test Location	
A&E	23.9%	9%
Inpatient Ward	57.3%	62.5%
Intensive Care	18.8%	28.6%

Table 116 - AKI discharge summary cohort

This population was very similar to that in the main part of this chapter, albeit it was a more unwell cohort with a slightly higher creatinine, longer length of stay. The initial stage of AKI was also more likely to be higher in this audit.



Graph 80 - AKI stage - initial test and peak in discharge summary cohort

Of those with AKI 92% (n= 149) had a medication discharge summary and 71% (n=115) had a clinical discharge summary. Of the patients with clinical summaries only 24.3% (n=28) had a mention of AKI and that was 17.3% (n=28) of all the AKI admissions alive at discharge. Of these patients that survive to discharge following hospital AKI, 25% (n=41) went on to die within a year. In those that had a peak of AKI stage 3, the number of patients with discharge summaries that mention AKI increases to 52% (n =13), nevertheless this remains at 35.1% (n=13) of all of the stage 3 AKI patients alive at discharge (i.e. when including those without a discharge summary). This group had an extremely high mortality, with 40.3% (n=28) of patients with AKI stage 3 (n =65 with 37 alive at discharge) as peak stage dying during admission and 64.5% (n = 15 further deaths, 43 in total) dying by 1-year. In those that survived to hospital discharge, 40.5% died within a year. In those with AKI treated with dialysis (n=27 with 17 alive at discharge), 50% of those with discharge summaries mentioned AKI (n=5), however this was only 29.4% of all the patients with AKI requiring dialysis alive at discharge (again, when including those with AKI requiring dialysis survived to discharge but did not have a summary). In this group the hospital mortality was 37% (n=10) and of those that survived to discharge 29.4% (n =5, total of 15 deaths) then went on to die within the year.

Of the patients with AKI alive at discharge, 64.4% (n=96) of the patients had a medication stopped. 4.9% (n=9) of the patients were on an NSAID and 22.2% (n = 2) of these patients

continued the medication on discharge. 44% of the patients were on an ACEi/ARB prior to their admission (n= 72) and 31.4% were on a diuretic (n =51), of which 35% (n = 25) and 23.5% (n=12) had their medications stopped. Of the 35% of patients who had their ACEi/ARB stopped, only 40% (n=10) had advice for the general practitioners (GPs) about withholding or restarting the medications and only 52% (n=13) mentioned that the patient had an AKI. This was similar in the 23.5% who had their diuretics stopped where only 33.3% (n=4) had advice for the GPs and only 50% mentioned AKI (n=6).

Of those that survived to discharge, 23.5% (n =37) were readmitted within 30-days and a further 10% (n =16) were unknown as they were discharged to a location outside the health board. Of those that had a discharge summary for their next admission, 21.6% (n=8) were due to fluid overload/ Dehydration/Further AKI. 48.6% (n= 18) of those readmitted did not have a discharge summary.

Discharge summary discussion

This single centre audit shows that information regarding an inpatient episode of AKI was not relayed to the primary care team in a significant number of patients. This condition was associated with a low 1-year survival and therefore communication and planning is crucial so that correct care can be delivered. AKI is associated with readmission for fluid overload (210) and therefore any cessation of medications that may effect this and should have a strategy for review if required. In this audit we saw that a third of ACEi/ARBs were stopped and a fifth of diuretics were stopped, but fewer than half these stoppages gave advice to the primary care team and only half even told the team of the AKI. This lack of communication means that the primary care professionals do not know when to restart or whether to continue to withhold medications. This may affect the readmission rate which was almost a quarter of the patients that were discharged from hospital.

Discussion

This study investigated 42,947 patients with AKI and primary care prescription data, finds a change in the primary care prescribing practice following AKI. Some medications see an overall increase in prescription such as histamine receptor 2 antagonists, potassium sparing

diuretics and paracetamol whereas others see a reduction in prescriptions such as thiazide diuretics, non-steroidal anti-inflammatories and metformin. There was also an increase in entries for AKI coding, but there was a decrease in blood pressure reading and urine dipstick following AKI. There was also a lack of change in medication reviews, which was a surprising finding, as you may expect this to avoid the well documented complications of AKI such as readmission and pulmonary oedema (197, 210, 233, 273).

In those individuals on medication beforehand, we saw the highest percentages of stopping medications in those on NSAIDs and thiazide diuretics which was not a surprise since these can lead to kidney impairment in some circumstances. ACEi/ARBs were proportionally the 6th most frequently stopped drugs of those studied. It may be expected that this would be higher up the table as it was commonly linked with AKI, particularly in some of the literature around the time of the alerts introduction (199, 200, 231), however it may represent the method in which the data are collected, in that it looks for any prescription for the medication in the 90-days following AKI. This means that some patients may stop the medications during the AKI and then restart it at a later date. This was potentially reassuring to see and these medications play a very important role in a number of conditions, but arguably most importantly in heart failure, therefore restarting after AKI episode was resolved was possibly as important as temporarily holding in pre-renal AKI (274).

The variation in mortality in patients on different medication was another interesting finding, albeit this was with an unadjusted analysis with many factors potentially influencing these findings and no conclusions of causation can be made based on this study. Nevertheless, there are some medications associated with a higher 30-day mortality. The highest was associated with loop diuretics which was understandable, in that this is a medication used in fluid overload and heart failure, a notoriously difficult to manage group with a high associated mortality (210, 213, 275). The next highest mortality was observed was in those on paracetamol prior to admission. This was an interesting finding, as this is a commonly prescribed medication most commonly used to treat pain caused by many different conditions. Perhaps this associated mortality, represents a marker of a frailty syndrome, in that the medication is one that can be purchased in a supermarket or pharmacy without prescriptions at a very low price, therefore those patients that the general practitioners

prescribe this to, possibly on a repeat prescription, represent those unable to easily get to a supermarket to pick it up themselves. In Wales primary care prescriptions are free, and paracetamol prescriptions are more expensive from pharmacies compared to supermarkets, therefore it has been a target for reducing prescriptions (276, 277). Another surprising feature was that the two medications with the lowest 30-day mortality are the diabetes medications insulin and metformin. The finding with insulin may be related to the size of the data as it was the least commonly used medications of those prescribed (4.3%), however over a tenth of the population are on metformin, so the changes are less likely to be due to chance in this group. Perhaps those patients on metformin, represent patient in an earlier stage of diabetes and less likely to have other significant comorbidities such as significant chronic kidney disease or heart failure due to the risk of developing lactic acidosis on metformin. This was however, beyond the scope of this study. The third lowest mortality was in NSAIDs. I suspect this was again due to patient selection over any potential benefit of the drug, which was not something this retrospective cohort study was able to delineate. There is correctly a reluctance to use NSAIDs in the elderly due to risk of peptic ulcers, fluid retention and renal failure therefore this NSAID AKI cohort may be younger with fewer comorbidities.

When it came to starting medications the most commonly started medication overall was paracetamol which was started in 1 in 10. This was followed by a proton pump inhibitor in 1 in 12 and then a loop diuretic which was started in 1 in 14. Surprisingly an NSAID was started in 1 in 40 of all the patient with AKI surviving beyond 30-days and proportionally it was the 4th most commonly started medication. I can think of very few indications that this would be done in the context of recent AKI, and I suspect it was because of the lack of recognition of AKI by the prescriber. This may well be because of the poor levels of communication between secondary and primary care as shown in the discharge summary study, where only 17.3% of patients alive at discharge had AKI mentioned in their discharge letter.

This lack of recognition of AKI was the reason that electronic alerts were introduced. Sadly, this study does not identify a significant improvement following the introduction of these WRRS AKI eAlerts. In fact, we see a higher mortality in those on loop diuretics, ACEi/ARB, beta blockers, metformin and sulphonylureas in the WRRS group compared to our AKI group prior to the eAlert introduction. As mentioned in the previous chapter, unfortunately these two

groups are not a perfect comparison, as the WRRS alerts only identify 72.6% of our AKI, nevertheless if there were any large changes as the result of the alert introduction, you would expect a difference in our AKI after and not one medication had a statistically significant change in stopping medications before or after the alert introduction using our identification of AKI. There was an increased cessation of aspirin and proton pump inhibitor in the WRRS group which was the only significant stoppage changes. When it comes to starting medication, we saw a significant decrease in prescriptions compared to before the alert's introduction with the medications, proton pump inhibitors and paracetamol in both after groups (after AKI alerts and WRRS). This may represent a change related to the alerts, but it could also represent changes in practices (this was the most recent group) as both of the medications, prescriptions have been discouraged – for paracetamol due to cost and availability (276, 277) and for proton pump inhibitors, due to the risk of side effects such as clostridium difficile infection and electrolyte abnormalities (278, 279). In both these medications, there are no major reasons that they should be avoided due to a recent unconnected AKI. Both can cause AKI in rare circumstances, but recent unrelated AKI is not a reason to avoid. Likely as a result of the reduced prescription of the PPIs, there was an increase in prescription of the histamine receptor 2 blockers in both groups after. As mentioned, there seems to be little by way of obvious effect from the introduction of the alerts. The effect on mortality may well be due to patient selection as observed in the previous chapter.

In the inpatient and outpatient comparisons there was very little difference, other than there appears to be a lower mortality in those outside hospital at the start of their AKI. In the outside group NSAIDs were the second most proportionally started medication, they also however had the highest proportion of stopping too. This group was confounded however by some patients getting admitted subsequently following their outpatient AKI test, therefore are not truly outpatient.

Limitations

It is important to recognise the imperfection of this method of identifying those on a medication. It relies on a number of assumptions. The first assumption was that because a medication was prescribed, the patient was still on it. Some patients may be prescribed a medication but no longer need it and therefore no longer taking it. For example, using an

NSAID for pain and the pain was no longer present. Although we may know what was prescribed, we do not know what was subsequently dispensed and even more difficult to ascertain was what was then taken. We also do not know what was still being take at the time of admission, as the method looks at 90-days before the admission, therefore in this time someone may have already stopped the medications, well in advance of the AKI. Some of the medications, particularly analgesia such as paracetamol and NSAIDs may be prescribed as acute and therefore limited prescription in this period. These confounders may mean that some of the patients that we believe have stopped the medication following the AKI, actually stopped it before the AKI. The reason I chose 90-days over 30-days was to try and capture those with prescription for 3 months. I previously looked at AKI identified by ICD-10 coding using the same methods, and when examining those patients, there were very little differences between 30 and 90-days (ICD-10 coded AKI pilot study on page 334).When the medications are stopped, we do not know who has stopped them, i.e. we do not know it was the primary care team or the hospital. In identifying those with prescriptions before their first AKI, we don't know if they are inpatient in the 90-days prior to the AKI, therefore some prescriptions would not be known. Some may also have had recent AKI, however the numbers of patients this includes is likely to be small as we are selecting the first AKI of the studied period (1-year before and after electronic AKI alert introduction as in Chapter 6 - Impact of electronic AKI Alerts). In some cases prescriptions may be provided by secondary care, including initial outpatient prescriptions, however the numbers and effects of this was likely to be small as the majority of prescriptions are from primary care (277). With the review section there was the potential to over and underestimate the situations, for example blood pressure or primary care creatinine values may be entered as Read codes, but they may have been done in secondary care which will overestimate the response to AKI. Conversely, medication reviews may be carried out but not entered as a Read code, underestimating the involvement.

Some of the patients that died before 30-days will have had a further prescription, and some will have stopped, nevertheless 30-days was chosen to avoid falsely suggesting medications were stopped in patients who died before a chance to have a further prescription. Some patients will have remained inpatients for the 90-day period after the AKI, however when I looked at this by examining the 60 days still inpatient, it was only around 2% of the population

so was unlikely to have a major effect on the findings. This does not however include readmission to hospital, again this may mean that the patients do not get a primary care repeat prescription but remains on the medications. The prescriptions are known using the primary care data, but due to the methods of documentation and technical limitations of Read codes, we do not know the doses. This has an effect on the outcomes and finding as some doses have 10-fold or more variation. Along with not knowing who made the changes, we do not know why any changes were made.

Overall, the size of this study means that the effects of minor biases and anomalies should be minimised. The manual review of inpatient AKI described in this chapter can help promote this confidence. In that study I reviewed the discharge data for all patients with an inpatient AKI alert on the selected days. 9 out of 10 of these summaries had the prescribing details of what was stopped, what was continued and what was started. In this inpatient group, the findings were very similar to this main SAIL based study in that 4.9% of patient were on an NSAID in the audit and 4.8% in the SAIL study. Similarly, 44% on an ACEi/ARB in the audit vs 45% in the SAIL study. The diuretic use was also similar in that 31.4% were on a diuretic in the audit and 30.2% on a loop diuretic in the SAIL study, this isn't a direct comparison, as in the audit I counted anyone on a diuretic as being on one, in the SAIL study I have broken down the types of diuretics, but you can't simply add them together as patients may be on multiple diuretics. What the audit also did, was it helps validate the data and finding in our study, but this works both ways. The main study findings help us validate the audit and give us an idea of the communication between secondary and primary care. Although this was a single centre audit, if it reflects wider practices, it gives potential avenues of exploration of improvements in AKI care.

The quality of the data used in this study was very good, it has been widely explored in this thesis, allowing for confidence in the algorithm. On top of that we have good coverage from the primary care data, with >80% of the patients having good quality primary care Read code events data. This means that we can trust that the prescriptions are accurate, with the caveats described in the pitfalls.

Future

We have a decent idea of what patients are on before their admission, but using retrospective data there are a few potential holes in our understanding that can be bridged. Using dispensing data we would know what was actually given to the patient along with further prescription and dose information. Also, the availability of electronic prescribing and medication administration data can plug the gaps of what goes on in hospitals. This can also be tied in with discharge prescriptions. This would allow for further depth and understanding of what patients with AKI are taking, who prescribed it and who stopped it. The 'why' will remain speculation, but this level of depth is achievable in the near future.

The study also found an interesting variation in mortality. It was beyond the scope of this to look at mortality but raises the question if certain medications are implicated in worsening outcomes after adjustment for comorbidities in AKI.

Implications

In England there was a period when Commissioning for Quality and Innovation (CQUIN) made the mentioning of inpatient AKI on discharge letters a financial incentive (222). The results of this and a quality improvement project coinciding with it in the Royal Berkshire Hospital lead to over 80% of inpatient AKI being mentioned on the discharge letter (223). There is the potential that an incentive like this in Wales, using automatic notification on a letter could be applied, possibly to then coincide with a primary or secondary care medication or clinical review. This can be tied in with the discharge medication review (DMR) service set up by the Welsh government with Community Pharmacy Wales (CPW) which allows community pharmacy teams access to hospital medication and discharge advice letters (DAL) (280).

Conclusion

There was a noticeable change in primary care prescribing practice following AKI with a reduction in thiazide diuretics, NSAIDs, ACEi/ARBs and calcium channel antagonists prescriptions. There was an increase in other medications such as histamine receptor 2 antagonists, potassium sparing diuretics and paracetamol. The AKI did not result in an increase in the number of medications reviews within 90-days. There was no noticeable

change following the introduction of AKI alerts in the stopping of most medication. In patients that have a hospital AKI alert that survive to discharge, under a fifth of them will have a discharge letter mentioning the AKI and in this group a quarter of these patients will die within the next year. There is room for better communications and reviews following AKI, whether this improves outcomes or not, it is not clear. There needs to be improvements in this condition which has a grave associated morbidity and mortality.

Chapter 8 – Concluding chapter

Acute Kidney injury (AKI) is a common problem in Wales and using serum creatinine (SCr) definitions alone it is found in 4% of all SCr tests. AKI is associated with a significant health burden and mortality (2) and the recognition and management of AKI is poor in the UK (156). Electronic AKI alerts were introduced with the aim of improving the recognition of this condition (117). Following the introduction of different types of electronic alerts across the globe there is growing interest in their impact (281). The first randomised controlled trial of electronic AKI alerts showed no improvement in mortality (183) and this was the same when the same team studied the effects of interruptive alerts 278cross 5 centres (262). The national implementation of this system comes with an expense, and it is important to know whether it is effective and, if not, what changes could be made to improve it.

Summary of main finding

In chapter one I established that there were gaps in the knowledge of understanding the implementation of the electronic alerts, understanding whether these made a difference to mortality and what happens to the patients after AKI in primary care. This led to the creation of an AKI algorithm with a renal dataset allowing for the accurate identification of patients undergoing renal replacement therapy. Using this dataset, I was able to compare with the alerts set in practice to clinicians. This revealed that only two thirds of AKI recognised by our methodology had electronic AKI alerts sent. This was because alerts sent in Welsh hospitals had a modification applied to the NHS England AKI algorithm used elsewhere in the UK, which was not previously described in literature. In fact, many publications believed that it was the same as the NHS England algorithm(153, 169, 190, 195, 252, 253). In the alerts sent to clinicians, 1 in 12 of these were false positives in dialysis patients. Hospital coding for AKI only identifies 34.8% of patients with AKI but the proportion was increasing over time. AKI alerts improve recovery from AKI but do not improve the need for dialysis, primary care medication reviews and, in all bar one health board, they do not reduce mortality at 30-days or at 1-year. We did not observe an increase in primary care medication reviews after AKI, but in a small secondary care sub-study, the communication to primary care from was very poor, with less than a fifth of inpatient AKIs recorded in the discharge summary. This raises the question of whether primary care knew about the episode of AKI. Nevertheless there were significant

changes in many medications, but who made these changes and whether they were the correct thing to do was beyond the scope of this study. I did not see changes in many important medication prescriptions following the introduction of AKI alerts.

Comparison with the literature

To understand if our AKI eAlerts in Wales have an effect, we must first validate and compare against other methods of identifying AKI. The eAlerts identify AKI using changes in SCr, which have been validated in the recognition of AKI (116) using retrospective data but how they perform in clinical practice has been less well studied. When comparing with our version of the NHS England electronic alert algorithm ('Our AKI') created in SAIL, there were fewer AKI alerts sent out in practice in Wales (WRRS alerts). These WRRS alerts had a sensitivity of 61.6% compared to 'Our AKI'. I found that there was a variation in the implementation of electronic AKI alerts in Wales. It was only at the end of this study that I discovered that the main reason for the variation was due to an additional rule that the Welsh system had created compared to the validated NHS England model. The additional rule was introduced to try to minimise the effects of alert fatigue, which is increasingly recognised (282-284). It is startling that the Welsh AKI steering group that published multiple articles using Welsh eAlerts did not know of this rule variation. They stated in their articles that it was the same as the NHS England algorithm (153, 190, 195, 248, 252, 253). What remains unclear, is who and when a decision was made to introduce this creeping creatinine code if the AKI steering group were unaware, particularly as their first peer reviewed paper on the matter stated;

> *''Although alert fatigue may be avoided by suppression of some alerts to reduce the number of alerts issued, the data also suggest that this would lead to the exclusion of a number of high-risk patients.'' (169)*

This was what I found, as there remained a high mortality in those identified by our AKI method (a recreation of the NHS England alerts) but not by the Welsh system and this group had the highest need for dialysis following AKI. Even within Wales there appears to have been some variation in the implementation, despite using the same LIMS and algorithm. This appears to be due to the methods of authorising the creatinine results and identifying those

on dialysis. This meant that 1 in 12 of the alerts sent (WRRS alerts) were false positives in dialysis patients, ranging from 1 in 6 to 1 in 28 across the health boards. Recognising this problem, the Welsh AKI steering group excluded tests from a renal or dialysis location (153, 190, 195, 252, 253). This method was adopted in some setting clinically and can lead to false negatives, which varied significantly between the health boards from 0 to 2.6%. This was based on a widely observed suppressed alert with a result comment 'No AKI alert generated as Patient Type is Dialysis'. There appeared to be further variation due to differences in the handling, storage, and authorisation of SCr test results in the different laboratories. In the last few years this issue was recognised and now the alerts no longer require authorised creatinine tests for an alert to be issued. This is likely to explain why there was an improvement in correlation of alerts from 54.7% and 72.6% (varied by health board from 2013-2015) to 68.4% and 93% first alerts in 2017. The finding of a third of alerts not being issued may influence the overall impact of the electronic alerts in Wales and these alerts are not accounted for and therefore are unknown for studies that use these alerts (153, 169, 190, 195, 252, 253). It is not only in Wales that there appears to be great variation in the implementation of a nationally standardised algorithm, the English AKI results show great variation in reporting to the renal registry (285) (see disclaim regarding RR publication in Renal Registry AKI report 2022). Even with the agreed acceptance of the KDIGO AKI criteria, there seems to be multiple ways it can be implemented, given the lack of definitive baseline definition. There have been many different baseline creatinine definitions applied, such as the lowest creatinine of 1 week used by large American RCTs studies (183, 262), the lowest in 2 weeks in a Korea study by Park et al (266), a large American retrospective study used the lowest creatinine in 1-year (256), then there are the multiple rules applied for the NHS England algorithm used by the English RCT (264), with similar rules used in Wales (153, 190, 195, 252, 253) and in Scotland (118, 172, 210). The Welsh AKI steering group found that when the AKIN and KDIGO criteria of lowest creatinine within a week was used, it missed important cases of AKI, particularly from the community (169).

We collaborated with other centres to show that careful introduction of AKI diagnostic criteria can lead to reproducible results (250). Some epidemiological studies looking to understand AKI use ICD-9 or 10 codes for AKI (116, 120, 124, 125, 129, 138, 142, 144) and it was clear from our data that there has been a great change in hospital episodes over the last 20 years.

It also shows that in the past, coding for AKI mostly picked up the most severe AKI, and with improvement in coding, it was now identifying less severe AKI. This means that the use of hospital coding to study temporal trends of AKI will identify changes in coding practice more than a change in incidence and inference of changes in outcomes such as mortality will not be accurate. Therefore, temporal studies require the use of SCr based criteria to understand the changing incidence and potentially in the future they can use alerts themselves. This study, however, highlights that alerts, although in theory should be the same, in practice there are variations in how they are implemented. This means that caution should be applied when they are used to examine temporal trends or in comparing different regions as there may be discrepancies unrelated to the condition.

Using the AKI cohort I created within SAIL, I looked to see if there had been an impact from the introduction of the alerts in the four health boards with data. This involved over 4 million tests, and due to the aforementioned differences between our code and the code used by the Welsh LIMS the comparison I made was in 3 parts comparing our AKI before the alerts to those identified by my method after and by the Welsh LIMS method after (WRRS alerts). Using this method, I found that mortality was higher in those with WRRS alerts, i.e. those after the introduction of the alerts. Given that they are not completely comparable, if I look at our AKI identified before and after, I found that they were equivalent with no significant difference in 30-day mortality (18.6% vs 19.3%, p0.08). This rules out large mortality improvements following the introduction of alerts and raises the question of potential harm. This is not the only research to have found this peculiarity, Wilson et al found similar findings in their RCT where they found no improvement in mortality overall and an excess mortality in non-teaching hospitals following eAlert introduction, albeit their methods were different, using only strict KDIGO criteria and they looked at 14-day mortality (262). It was not clear that there was a truly increased mortality from my study, given that the WRRS alerts may just identify a more unwell cohort and since I do not have access to the code used and so cannot directly compare. Nevertheless one possible reason I am potentially seeing harm is the withholding of life-saving medications such as diuretics and ACEi or ARBs. The over use of fluids and withholding of medications may explain high rates of readmission and readmission with pulmonary oedema (210) which I also observed in the hospital discharge summary audit (page 267). In one health board I observed an increase in mortality following AKI in patients with

heart failure which could support this. This was contradicted in the other health boards where there were no changes or improvement in mortality. Interestingly, the health board with an increased mortality in the heart failure population was the only health board that witnessed an improved mortality as a whole following the introduction of the eAlerts. Why this was the case was unclear, as this health board did not adopt any additional interventions beyond the alerts other than access to local guidelines. This health board did have a lower overall AKI mortality, which may be explained by the services it provides. If a health board offers tertiary services for other health boards, such as nephrology, it may select patients with AKI into it that are more likely to survive, i.e. a younger patient requiring dialysis for AKI and not a patient dying of other causes, such as cancer that also has AKI. This form of selection bias (in this case, appropriate clinical decision making) will affect the survival in that health board.

This AKI cohort helped me better understand the interactions with primary care following an episode of AKI, such as finding changes in prescribing practice with reduction in use of thiazide diuretics, NSAIDs, ACEi/ARBs and calcium channel antagonists and increases in histamine receptor 2 antagonists, potassium-sparing diuretics and paracetamol use within 90-days of the AKI. There were no significant changes in medication reviews within 90-days following AKI. This was hardly a surprise when we know that only a fifth of inpatient AKIs in one of the studied health boards have AKI mentioned in the discharge summary. There are challenges with these post AKI primary care reviews;

"Unclear and inconsistent information on discharge summaries contributed to concerns about additional work in primary care" (286)

These unclear and inconsistent messages are likely to be contributing to the lack of mortality benefit we have observed.

Understanding of the heterogenous condition of AKI is improving, with the number of publications in this undergoing incredible growth (Table 1 - Literature Search). It is good point to take stock and review what we understand and can learn from areas where improvements can be made. Electronic AKI alerts should not be a bad thing and it is understandable why there was great hope that they would improve patient care, nevertheless this study along

with others fails to find an improvement in survival following their introduction (183, 262-264, 287). It may be that the finding of creatinine changes are too late to avert the course of AKI (24) and other biomarkers require utilisation (95, 103, 255). Another deficit of the current system could be the communication of AKI, we know that the communication between primary and secondary care is poor from my audit which is backed up by the finding of Reschen et al study which found that before the introduction of a commissioning incentive the communication to primary care was poor (22%) but improved following the incentivisation (>90%) (223). If we can make small gains over several aspects of AKI care I suspect we can make the improvements we desire, with real time, interruptive (176, 257) and escalating alerts (288), with clinical decision support tools (256, 289) including medications reviews for interactions (163, 290), electronic prescribing and Medicines Administration systems (173) and utilising learning healthcare systems to identify those that would benefit most and helping tailor intervention. As shown, simple care bundles effectively applied can lead to improved outcomes (265, 291, 292), and these approaches can be applied now. Communication with primary care can improve with interruptive reminders like those used by Nye et al (268) and using commissioning (222, 223). Any intervention should be introduced with a sustainable and multidisciplinary education programme (155, 265, 291). With studies utilising these interventions and other therapeutic studies, we need to standardise our approach to aid comparison and understanding, standardising baseline creatinine values, AKI definitions, recovery definition and outcomes of interest (3). In Wales and across the United Kingdom, the design and implementation of our AKI alerts should be standardised, and based on this study, I see no reason to favour the Welsh adjusted version over the more widely adapted NHS England version.

Implications for practice

Following this research, electronic alerts in Wales are being standardised in line with NHS England removing the additional rule. This will mean an increase in the number of alerts, including in many patients with a high mortality as shown in the validation chapter. It also allows for direct comparisons across England, Wales and Scotland. I am now leading a Welsh AKI group which is looking to update the eAlerts with stage of AKI which will allow concordance with the NICE guidelines.

Implications for research

This research highlights the growing need for standardised approaches, both in the implementation of electronic warning systems such as eAlerts, but also in the application of these rules in scientific research. Slight variation in the implementation of these systems can result in variation in the results and therefore the reproducibility of the outcomes. This was particularly highlighted in the validation chapter (Chapter– 4 - Validation of electronic AKI Alerts). Through this research I have highlighted the methodological challenges faced with setting rules (i.e. eAlert algorithm and renal dataset timeline) to real world data from different sources. I have created a methodology for developing a renal dataset based on coded timeline entries and individual dialysis treatments that could accurately identify patient on dialysis and was comparable to the renal registry data. This methodology can now be replicated and used for further data linkage research within SAIL. The need for standardisation and replicable data was studied in the work linked with this research examining reproducing AKI cohorts across 3 sites(250) which allowed for exploration of our datasets. Additional research in these aspects remains key to developing a better understanding of AKI and allowing us to focus intervention, but this research and others highlight the need for clear definitions of baseline creatinine(111), defining an episode of AKI(190, 253) and diagnosing recovery from AKI(3, 217).

A wider understanding of the communications between secondary and primary care is needed, to build upon the findings of chapter 7(Chapter 7 - Prescriptions and reviews in primary care following AKI) exploring and painting greater depth of knowledge on the reviews prior to admission, the changes within the admission, the documentation on discharge and the follow up actions. At the moment, the recommendations for primary care providers on the follow up management of AKI remains relatively weak in its evidence (269, 293). Developing further on these aspects, using SAIL data or similar data seems a natural progression, particularly with the future availability of discharge medication data and dispensary data. This research also raises the question of why some medications are associated with higher mortality. It was beyond the scope of this project to delve deep within the data to understand and correct for comorbidities, however it does raise the question of whether some routinely used medications have unrecognised harm in AKI or can they be used as a further variable in risk stratifying patients with AKI.

Strength

This study used some large, widely used datasets, but it also used some large, previously unused datasets. The methodology chapters show the level of detail that was explored, and the efforts undertaken to make sure the data were as robust as possible. I gathered the data, tested it across time (WRRS pathology - Cross check with PAMO/PABR on page 93), looking for anomalies, finding some and correcting them (Validation on page 79), then reassess. I improved the depth of the data with the pathology data (Missing suppressed alert and eAlerts on page 97) and with the dialysis data across the North Wales sites. There were times that I was concerned, such as with validation chapter (page 160) and the discrepancies between our alerts and the clinical practice WRRS alerts, but by following the methodology (page 173), manually reviewing alerts and missed alerts, I was confident that our code was correct and that there was a problem with the WRRS alerts. This was eventually realised in the summer of 2022 when this additional rule came to light (page 183). This level of scrutiny and understanding of the data gives me confidence in the subsequent finding further results chapters. The resulting coding, impact and primary care chapters, provide large data results build up the evidence to questions like what is the sensitivity of coding? Do eAlerts improve mortality? And what medications are stopped following AKI? Nevertheless, it also creates many more, such as, why do some health boards see a fall in mortality following the introduction of the eAlerts? What is the longer-term impact of the alerts? And who is making the medication changes?

Another strength of this study was that when some datasets that were not complete, such as the all Wales renal dataset, I managed to improve the depth and coverage by extracting further data. This will be of benefit for researchers using SAIL for years to come.

Limitations

There are several limitations to this study. The first was that unfortunately we were not able to access good quality creatinine data for the entirety of the study in some of the Welsh health boards. This was not known at the beginning of the study as the all Wales data were not available (until the winter of 2019) and therefore much of the planning was based on all Wales

coverage. Once I found out that the data were incomplete, I embarked on trying to improve the depth, this did result in further uploads of data including AKI alerts and supressed alerts, but as the Cardiff and the Vale and Aneurin Bevan universities health board did not have the back data uploaded to the Welsh Results Reports Service, I could not access it. I did offer to help, but the main issue was server capacity at the National Health Service Wales Informatics Service. In view of this, the impact chapter and the primary care data do not include two large health boards and therefore the outcomes do not represent the whole of Wales. The other main limiting factor was that the alerts created do not match those sent in practice via WRRS. This was mostly due to the algorithm deviation created by Digital Health Care Wales, which I and other researchers were unaware of and there are no publications mentioning it, so it was unavoidable. There were some smaller variations to do with my interpretation of the algorithm, nevertheless, the finding of these described variations are important and will help other researchers understand some of the implementation challenges. It has also allowed me to remove this 6% increase in creatinine rule from the Welsh eAlert system aligning with England and Scotland. To mitigate the effect of these variations, bearing in mind that it was only in the late summer of 2022 that we found out exactly what they are and why they existed, we created an extra comparator group of our AKI after, which helped us to understand the effect of these alerts.

The findings of this study gives an idea of the impact of AKI alerts in Wales and how the eAlerts are implemented, but this cannot be generalised to places beyond Wales, however it should raise the question of whether the alerts are implicated in a truly standardised way elsewhere (England and Scotland).

Conclusion

The implementation of electronic alerts in Wales using an adaptation of the NHS England algorithm has not had the desired effect. The Welsh algorithm will report more than a third fewer electronic alerts than its English counterpart with 1 in 12 alerts being falsely sent in dialysis patients. These alerts have not resulted in an improved 30-day mortality, need for dialysis or primary care medication reviews. Alerts in their current format alone are not

enough to improve outcomes in Wales and standardising alerts in Wales with those sent throughout the rest of the United Kingdom should be considered. One health board that did show improvement in 30-day mortality which provides hope but the reason for the improvement was not clear. Methods of making alerts interruptive, escalating alerts linked with electronic prescriptions, targeted at those that would benefit the most with tailored interventions may have the desired effect and should be the focus of future research and this should be in conjunction with primary care to facilitate early intervention and post AKI care.

Glossary

Acute Kidney Injury – a deterioration in the kidneys ability to clear products of metabolism occurring over hours to weeks.

Chronic Kidney Disease – Impairment in the kidney function of a duration of greater than 3 months.

Our AKI – this is a cohort of patients identified as having AKI within SAIL by a recreation of the NHS England electronic AKI algorithm. This is based on serum creatinine tests.

Primary Care – This is a health care service that acts as the first point of contact within a health care system. This is most commonly applied to general practices but can also include community pharmacy, dental, and optometry (eye health) services.

Primary care services provide the first point of contact in the healthcare system, acting as the ‘front door' of the NHS. Primary care includes general practice,

Pseudo-anonymisation – The process of anonymising a record so that it is not easily identified but still maintaining the ability to cross link it to other records from the same source.

Secure anonymised information linkage data bank – This is a system set up with in Swansea university which allow for analysis of data that has undergone pseudo-anonymisation. It contains multiple datasets which can be linked.

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Appendix

Method (appendix)

Example of my SQL coding

```
select count (distinct alf_pe) from (
    select a.alf_pe, a.death_dt, b.dod, a.deathcause_1, a.deathcause_2, a.deathcause_3,
    a.deathcause_4, a.deathcause_5
            from sail0505v.ADDE_DEATHS_20–0712 a
    --left join -- To check DOD
      right join --To check  Death_Dt
            sail0505v.WDSD_AR_PERS_20170711 b
    on a.alf_pe=b.alf_pe
where b.dod is not null -- Need in Right Join only
)
where death_dt is null
```

This code compares the date of death in the office of national statistics death dataset (ADDE) to the Welsh demographics service dataset (WDSD).

Columns of interests

Within different SAIL tables, there are many columns with different roles, some of the key tables are outline below with brief descriptions;

PABR – Bridgend Pathology

The diagram above shows the column headings within the dataset and the linkage. Their meanings are explained in the table below;

Columns	Comment
PAT_NUM_PE	Unique patient number used in this dataset
ALF_PE	Unique patient number, used across all datasets
LSOA_CD	Lower layer super output area
WOB	Week of birth
GNDR_CD	Gender
REQUEST_CD	Unique test request code
COLLECTION_DT	Date sample was taken
COLLECTION_TM	Time sample was taken
RECEIVED_DT	Date received
RECEIVED_TM	Time received
SPCM_NUM_PE	Unique specimen number
MED_SPECIALTY	Consultant speciality by code
TEST_CD	Test name – i.e. Creatinine = ‘CREAT’
RESULT	Value

Table 117 Bridgend pathology - first upload columns

The second upload was presented in an easier to use format. There are two tables with this dataset. The usual demographic file and a results table. The result table column headings are shown below;

Columns	Comment
HOSP_NUM_PE	Linkage Field
SAMPLE_NUM_PE	Sample Number
DATE_COLLECTED	Date of sample
TIME_COLLECTED	Time of sample
DATE_RECEIVED	Date the sample is received in the lab.
TIME_RECEIVED	Time the sample is received in the lab.
SPECIMEN_TYPE	Type of specimen – i.e. 'S' for Serum
REPORT_COMMENT	Laboratory Comment
DRUG_THERAPY	Medication (for drug levels)
LOCATION	Request location
PATIENT_CATEGORY	'NH' for NHS or Private
SPECIALTY	Speciality that requested the test
SET	Tests Set – e.g. 'Full Blood Count'
TEST	Test type – 'CREAT' or 'ECRE'
TEST_RESULT	Result

Table 118 – Bridgend pathology - second upload columns

The next table below shows the different tables from these two uploads. The older tables (from 2008) are not intuitive and therefore take some effort to understand, however the 2017 update is;

Table Name	Comment	Date From
PABR_BLOODSCI	Test details	27/08/2008
PABR_BLOODSCI_PATIENT	Demographics	27/08/2008
PABR_BLOODSCI_REPORT	Result comments	16/10/2009
PABR_BLOODSCI_–ET_CD	Look up table - Set code names	23/10/2009
PABR_BLOODSCI_SE–_TEST	Look up table - Test codes	23/10/2009
PABR_BLOODSCI_T–ST_CD	Look up table - Test code names	16/10/2009
PABR_BLOODSCI_TEST_DETAIL	Results	23/10/2009
PABR_MICROBIO	Test details	17/11/2008
PABR_MICROBIO_OTHER	Test details	14/11/2008
PABR_MICROBIO_PATIENT	Demographics	14/11/2008
PABR_RESULT_2017ETC	Test–details and results - update	29/03/2017
PABR_RESULT_2017–TC_ALF	Demographics - update	29/03/2017

Table 119 Bridgend tables

PAMO – Morriston Pathology

Columns	Comment
SYSTEM_REQST_NUM_PE	Unique patient number used in this dataset
ALF_PE	Unique patient number, used across all datasets
LSOA_CD	Lower layer super output area
WOB	Week of birth
GNDR_CD	Gender
PAT_SEQ_NUMB_PE	Unique patient number used in this dataset
DEPT_CD	Department running test – i.e. Chem pathology
SOURCE_CD	Test location
SPCM_DT	Date sample was taken
SPCM_TM	Time sample was taken
RECEIPT_DT	Date received
RECEIPT_TM	Time received
TEST_CD	Test name – i.e. Creatinine = 'CREA'
TEST_TYPE	Type of test
RESULT	Value

Table 120 – Swansea pathology columns

PATH – All Wales Pathology

Column	Comment
MASTER_REPORT_ID_PE	Unique patient number used in this dataset
ALF_PE	Unique patient number, used across all datasets
LSOA2001_CD	Lower layer super output area
LSOA2011_CD	Lower layer super output area
WOB	Week of birth
GNDR_CD	Gender
REPORT_ID_PE	Encrypted test number
SPCM_COLLECTED_DTTM	Date and time that the sample was taken
SPCM_RECEIVED_DTTM	Date and time that the sample was received
TESTSETID_PE	Encrypted code
TESTSET_CD	Test set code
TESTSETNAME	Test set description
VALUETYPE	CE or SN
CODE	Test code
VALUE	Result
UNITOFMEASUREMENT	Unit of measurement
REFERENCERANGE	Reference range
PROV_DEPT_SITE_CD	Provider site code
PROV_DEPT_SITE_DESC	Provider site description
SUBJECTSITE_CD	Subject site code
SUBJECTSITE_DESC	Subject site description
SUBJECT_LOC_CD	Subject location code
SUBJECT_LOC_DESC	Subject location description
REQUESTOR_SPEC_CD	Requestor specialty code
REQUESTOR_SPEC_DESC	Requestor specialty description
PAT_CAT_CD	Patient treatment category
PAT_TYPE_CD	Patient type category
AUTHORISED_DTTM	Time and date of result authorisation
AVAIL_FROM_DT	2018-08-31

Table 121 - All Wales pathology table columns

PEDW – Patient episode dataset

In PEDW there are 3 main tables that I have used for our creatinine and AKI cohort

Diagnosis – PEDW_DIAG_20191213

Column	Description
SPELL_NUM_PE	Unique spell ID (Linkage)
PROV_UNIT_CD	Health care provider (Linkage)
EPI_NUM	Episode number
DIAG_NUM	Diagnosis number
DIAG_CD_123	ICD-10 diagnosis by coding
DIAG_CD_1234	ICD-10 diagnosis by coding

Table 122 - PEDW diagnosis coding table columns

Episode - PEDW_EPISODE_20191213

Column	Description
SPELL_NUM_PE	Spell ID (Linkage)
PROV_UNIT_CD	Health care provider (Linkage)
EPI_NUM	Episode number
EPI_STR_DT	Episode start date
EPI_END_DT	Episode end date
AGE_EPI_STR_YR	Age at start of episode
DIAG_CD_123	Main ICD-10 diagnosis

Table 123 - Hospital Episodes table

Spell – PEDW_SPELL_20191213

Column	Description
SPELL_NUM_PE	Spell ID (Linkage)
PROV_UNIT_CD	Health care provider (Linkage)
ALF_PE	Unique identifier (Cross dataset linkage)
LSOA_CD	LSOA at time of admission
EPI_NUM	Episode number (Linkage with episodes table)
GNDR_CD	Gender
ADMIS_DT	Admission date
ADMIS_MTHD_CD	Admission – planned/emergency/elective etc…
ADMIS_SOURCE_CD	Where the patient is admitted from
DISCH_DT	Discharge date
DISCH_MTHD_CD	Discharge method i.e. Death/Discharged
DISCH_DESTINATION_CD	Discharge destination i.e. Home/Nursing home
ADMIS_DUR	Days in hospital
ADMIS_SPEC_CD	Admitting speciality
DISCH_SPEC_CD	Discharging speciality
CURR_LOCAL_HEALTH_GRP_CD	Local health authority where patients is admitted
PAT_CLASS_CD	Spell Admission Detail – i.e. Ordinary Admission, Day Case, Regular Attender (Day/Night) and Maternity.

Table 124 - Hospital spell table

WLGP – Primary care

The primary care dataset has some important tables which have been used, the columns and their meaning are shown below;

WLGP_PATIENT_ALF_CLEANSED

Columns	Description
PRAC_CD_PE	Unique practice number
LOCAL_NUM_PE	Patient number – unique to patient at a practice.
ALF_PE	Unique identifier (Cross dataset linkage)
LSOA_CD	LSOA for patient
WOB	Week of birth
GNDR_CD	Gender
REG_CAT_CD	Registration category
OPT_OUT_FLG	Whether the person h–s opted out of SAIL - 747

Table 125 - WLGP ALF columns of interest

WLGP_GP_EVENT_CLEANSED

Columns	Descriptions
PRAC_CD_PE	Unique practice number
LOCAL_NUM_PE	Patient number – unique to patient at a practice.
EVENT_CD_VRS	
EVENT_CD	Read Code
EVENT_VAL	Entry value
EVENT_DT	Date of entry

Table 126 – WLGP Event columns of interest

WLGP_CLEAN_GP_REG_BY_PRAC_INCLNONSAIL_MEDIAN_20180820

Columns	Descriptions
ALF_PE	Unique identifier (Cross dataset linkage)
START_DATE	GP practice registration start date
END_DATE	GP practice registration end date
GP_DATA_FLAG	Practice data in SAIL
PRAC_CD_PE	Unique practice number

Table 127 - WLGP GP Registrations columns of interest

WDSD – Welsh Demographic Service

The WDSD tables are from the Welsh demographic service. There are 3 tables, they are shown below;

*WDSD_AR_PERS_*

Columns	Descriptions
PERS_ID_PE	WDSD unique ID
ALF_PE	Unique cross dataset ID
WOB	Week of birth
DOD	Date of death
GNDR_CD	Gender

Table 128 - WDSD Persons columns of interest

*PERS_ADD_*

Columns	Descriptions
LSOA_CD	Lower Super Output Area Code
PERS_ID_PE	WDSD unique ID
ROW_STS	‘a’ active, ‘d’ not active
FROM_DT	Address start date
TO_DT	Address end date

Table 129 - WDSD Addresses columns of interest

PERS_GP_20190408

Columns	Descriptions
PERS_ID_PE	WDSD unique ID
PRAC_CD_PE	GP practice code
ROW_STS	‘a’ active, ‘d’ not active
FROM_DT	Start Date of Data
TO_DT	End date / ongoing

Table 130 - WDSD GP columns of interest

CCDS_CRITICAL_CARE_EPISODE_20190315

The critical care table is one large table, the columns of interest are shown here;

Columns	Descriptions
ALF_PE	Unique cross dataset ID
DUR_ADMIS_DISCH_HOURS	Admission duration – Hours
DUR_DISCH_READY_DISCH_HOURS	Admission to Discharge Ready – Hours
DUR_LEVEL2_SUPPORT_DAYS	Days with level 2 of support needed
DUR_LEVEL3_SUPPORT_DAYS	Days with level 3 of support needed
DUR_ADVANCED_CARDIO_SUPPORT_DAYS	Days of advanced cardiac Support
DUR_BASIC_CARDIO_SUPPORT_DAYS	Days of basic cardiac support
DUR_ADVANCED_RESPIRATORY_SUPPORT_DAYS	Days of advanced Respiratory support
DUR_BASIC_RESPIRATORY_SUPPORT_DAYS	Days of basic respiratory support
DUR_DERMATOLOGICAL_SUPPORT_DAYS	Days of dermatological support
DUR_GASTROINTESTINAL_SUPPORT_DAYS	Days of gastrointestinal support
DUR_LIVER_SUPPORT_DAYS	Days of liver support
DUR_NEUROLOGICAL_SUPPORT_DAYS	Days of neurological support
DUR_RENAL_SUPPORT_DAYS	Days of renal support
DUR_DELAYED_TRANSFER_OF_CARE_HOURS	Duration of delayed discharge
PAT_STATS_CURR_CENSUS_LSOA_CD	LSOA
PAT_STATS_CURR_CENSUS_HEALTH_ORG_NAME	Health Board
PAT_SEX_CD	Sex 1=Male 2= Female
ADMIN_CAT_DESC	NHS or Private
ADMIS_DT	Admission date
ADMIS_TM	Admission time
PAT_ADMIS_AGE_YEARS	Age on admission
TREAT_SITE_ORG_NAME	Hospital
TREAT_SPEC_DESC	Speciality managing patient
ADMIS_SOURCE_DESC	Admission source – ‘Same Site’ etc…
ADMIS_TYPE_DESC	Admission type – i.e. ‘planned’, ‘unplanned’
SOURCE_LOC_DESC	Admission location – ‘Theatre’, A&E
ORGAN_SUPPORT_MAX	Maximum number of organs supported
DIS_READY_DT	Date patient is ready for discharge
DIS_DT	Date of discharge
DISCH_STS_DESC	Discharge status
DISCH_LOC_DESC	Discharge location – i.e. ‘Ward’
DISCH_DEST_DESC	Discharge destination – i.e. Hospital

Table 131 - Critical care columns of interest

Validation of the Outpatient dataset

The outpatient table contains details on the attendance type (new/follow up), the referral source and the outcome type;

Code	Number	FIRST_ATTEND_CD
1	17,328,587	New Attendance
2	43,271,139	Follow Up Attendance
Unknown	996,792	

Table 132 - First clinic attendances

28% of outpatient reviews are new appointments. The table below categorises the source of the referrals with 55.6% coming from primary care;

Code	Number	SOURCE_OF_REF_CD
1	1,600,532	Following Emergency Admission
2	2,4873	Following a domiciliary visit
3	36,069,061	Referral from General Medical Practitioner
4	1,535,497	Referral from an A&E department
5	10,241,207	Referral from a Consultant or Independent Nurse, other than in an A&E department
6	614,122	Self-referral
7	1,991	Referral from Prosthetist
8	5,743,987	Other source of referral
10	127,428	Following an A&E attendance
11	3,608,532	Other
92	968,709	General Dental Practitioner
93	4,806	Community Dental Service
Unknown	1,055,773	

Table 133 - Source of referral

The final table shows the outcomes data for the outpatient reviews, most of which is unknown (68.6%);

Code	Number	OUTCOME_CD
1	3,625,625	Discharged from Consultant care (last attendance) or Independent
2	10,139,061	Another appointment given
3	5,559,958	Appointment to be made at a later date
Unknown	42,271,874	

Table 134- Outcome of clinic review

Depth of ICD-10 Coding – Standard deviation

	Mean Depth of ICD-10 coding by year (Standard Deviation)						
Year	ABMUHB	ABMUHB	BCUHB	CTUHB	CVUHB	HDUHB	PTUHB
2000	2.67 (2.08)	2.12 (1.46)	2.30 (1.59)	1.69 (1.18)	2.19 (1.65)	2.20 (1.59)	2.52 (1.89)
2001	2.79 (2.2)	2.22 (1.63)	2.36 (1.58)	1.81 (1.27)	2.10 (1.65)	2.27 (1.66)	2.99 (2.02)
2002	2.80 (2.23)	2.48 (1.89)	2.49 (1.64)	2.17 (1.58)	1.97 (1.65)	2.50 (1.78)	3.35 (2.26)
2003	3.00 (2.47)	2.61 (1.94)	2.69 (1.75)	2.67 (1.94)	2.03 (1.86)	2.64 (1.82)	3.70 (2.52)
2004	3.16 (2.71)	2.69 (1.99)	2.88 (1.93)	2.71 (2.06)	2.49 (2.07)	2.84 (2.01)	3.71 (2.77)
2005	3.63 (2.92)	2.80 (2.04)	3.17 (2.06)	3.15 (2.35)	3.00 (2.48)	3.01 (2.15)	3.90 (2.98)
2006	3.62 (2.78)	2.82 (2.08)	3.35 (2.24)	3.13 (2.21)	3.38 (2.67)	3.02 (2.13)	4.57 (3.39)
2007	3.51(2.69)	2.82 (2.19)	3.44 (2.45)	3.09 (2.25)	3.55 (2.72)	2.84 (2.03)	5.00 (3.74)
2008	3.53 (2.72)	2.75 (2.20)	3.55 (2.55)	2.99 (2.22)	4.01 (2.99)	2.83 (2.04)	5.13 (3.76)
2009	3.53 (2.76)	3.10 (2.45)	3.49 (2.55)	3.06 (2.42)	4.14 (3.14)	2.74 (2.02)	5.07 (3.74)
2010	3.90 (3.05)	3.47 (2.61)	3.89 (2.94)	3.26 (2.58)	4.28 (3.25)	3.13 (2.39)	4.98 (3.78)
2011	4.07 (3.16)	3.70 (2.84)	3.94 (3.00)	3.50 (2.87)	3.85 (3.31)	3.13 (2.38)	4.97 (3.82)
2012	4.28 (3.31)	3.70 (2.77)	4.00 (3.05)	3.56 (2.85)	3.64 (3.32)	3.48 (2.67)	4.93 (3.86)
2013	4.39 (3.37)	3.85 (2.9)	4.17 (3.11)	4.00 (3.13)	4.08 (3.43)	3.99 (2.95)	4.64 (3.73)
2014	4.52 (3.45)	4.11 (3.28)	4.41 (3.30)	4.14 (3.12)	4.21 (3.57)	4.42 (3.11)	4.79 (3.88)
2015	4.47 (3.54)	4.27 (3.45)	4.30 (3.42)	4.36 (3.20)	4.33 (3.71)	4.36 (3.20)	4.56 (3.65)
2016	4.51 (3.63)	4.22 (3.47)	4.32 (3.47)	4.74 (3.51)	4.60 (3.82)	4.42 (3.24)	4.93 (3.82)
2017	4.55 (3.54)	3.97 (3.65)	4.32 (3.45)	5.23 (3.74)	4.89 (3.84)	4.47 (3.43)	5.22 (3.93)
2018	4.54 (3.60)	4.09 (3.78)	4.41 (3.43)	5.16 (4.02)	4.83 (3.73)	4.27 (3.55)	5.26 (3.89)

Table 13535 - Depth of coding - standard deviation

AWRD - Renal dataset

For this project, there are a few crucial tables, they are outlined below;

C_ DEMOGRAPHICS_ALF_20190829 and M_ DEMOGRAPHICS_ALF_20190829

Name	Comment
ALF_PE	Unique Identifier (cross dataset linkage)
ALF_STS_CD	Code for type of ALF match
FIELD_1	C or M depending on table
GNDR_CD	Gender Code
LSOA_CD	Lower Layer Super Output Area code
SYSTEM_ID_PE	Unique Patient code for dataset within area (C or M)
WOB	Week Of Birth

Table 136 - AWRD Demographics

C_TIMELINE_20190829 and M_TIMELINE_20190829

Name	Comment
SYSTEM_ID_PE	Unique Patient code for dataset within area (C or M)
T9DATE	Timeline Entry Date
T9MOD	Timeline Entry Code

Table 137 - AWRD Timeline

C_HDTREATMENT_20190829 and M_HDTREATMENT_20190829

Morriston	Cardiff	Comment
SYSTEM_ID_PE	SYSTEM_ID_PE	Unique Patient code for dataset within area (C or M)
HPDATE	DMDATE	Dialysis Date
HPWTPR	DMWGT1	Pre dialysis Weight
HPWTPO	DMWGT2	Post Dialysis Weight

Table 138 - AWRD Sessions

Swansea timeline codes

Timeline codes within the Swansea renal data set and what they are then coded as and what sort of trigger they cause;

Code	Code Definition	Treatment	Trigger
5106	Acute Haemodialysis	ACUTE	Start
5120	Satellite HD/HF	HD	Start
5124	First PD dialysis	PD	Start
5159	Initiation of dialysis	HD	Start
5280	Acute Dialysis ITU	ACUTE	Start
5281	Acute Dialysis CARDIAC	ACUTE	Start
5282	Acute Dialysis BURNS	ACUTE	Start
19301	Haemodialysis	HD	Start

19302	Haemofiltration	HD	Start
19303	Haemodiafiltration	HD	Start
19304	Haemodialysis > 4 days per week / daily	HD	Start
19305	Ultrafiltration	HD	Start
19309	Haemodialysis - type unknown	HD	Start
19310	CAPD standard	PD	Start
19311	CAPD	PD	Start
19312	Cycling PD >= 6 nights /wk dry	PD	Start
19313	Cycling PD < 6 nights/wk dry	PD	Start
19314	Cycling PD >= 6 nights/wk wet (day dwell)	PD	Start
19315	Cycling PD < 6 nights/wk wet (day dwell)	PD	Start
19319	Peritoneal dialysis - type unknown	PD	Start
19320	Transplant; Cadaver donor	TRANSPLANT	Start
19321	Transplant; Live related - sibling	TRANSPLANT	Start
19322	Transplant; Live related - parent or child	TRANSPLANT	Start
19323	Transplant; Live genetically unrelated	TRANSPLANT	Start
19324	Transplant; Cadaver donor + transp other organ	TRANSPLANT	Start
19325	Transplant; Live donor + transplant other organ	TRANSPLANT	Start
19326	Transplant; Live related - other	TRANSPLANT	Start
19328	Transplant; non heart beating donor NHB	TRANSPLANT	Start
19329	Transplant; type unknown	TRANSPLANT	Start
19341	Transfer in on : Haemodialysis	HD	Start
19342	Transfer in on : Haemofiltration	HD	Start
19343	Transfer in on : Haemodiafiltration	HD	Start
19344	Transfer in on: Haemodialysis > 4 days per week	HD	Start
19345	Transfer in on : Ultrafiltration	HD	Start
19349	Transfer in on : Haemodialysis - type unknown	HD	Start
19350	Transfer in on : CAPD standard	PD	Start
19351	Transfer in on : CAPD	PD	Start
19352	Transfer in on : Cycling PD >=6 nights/wk dry	PD	Start
19353	Transfer in on : Cycling PD < 6 nights/wk dry	PD	Start
19354	Transfer in on : Cycling PD >= 6 nights/wk wet (day dwell)	PD	Start
19355	Transfer in on : Cycling PD < 6 nights/wk wet (day dwell)	PD	Start
19359	Transfer in on : Peritoneal dialysis - type unknown	PD	Start
19360	Transfer in on : Transplant; Cadaver donor	TRANSPLANT	Start
19361	Transfer in on : Transplant; Live related - sibling	TRANSPLANT	Start
19362	Transfer in on : Transplant; Live related - parent or child	TRANSPLANT	Start
19363	Transfer in on : Transplant; Live genetically unrelated	TRANSPLANT	Start

19364	Transfer in on : Transplant; Cadaver + transp other organ	TRANSPLANT	Start
19365	Transfer in on : Transplant; Live donor + transp other organ	TRANSPLANT	Start
19366	Transfer in on : Transplant; Live related - other	TRANSPLANT	Start
19368	Transfer in on : Transplant; non heart beating donor	TRANSPLANT	Start
19369	Transfer in on : Transplant; type unknown	TRANSPLANT	Start
19371	Acute Dialysis	ACUTE	Start
140055	Haemodialysis + Plasma Exchange	HD	Start
140056	Plasma Exchange (Renal)	HD	Start
140066	Temporary Holiday Haemodialysis - Start	HD	Start
140067	Haemodialysis - Nocturnal	HD	Start
140140	Transfer out pre-emptive transplant	TRANSPLANT	Start
140741	Assisted APD	PD	Start
141199	Assisted CAPD	PD	Start
141200	Hybrid CAPD with HD	PD	Start
141201	Hybrid APD with HD	PD	Start
141202	Hybrid APD with CAPD	PD	Start
141203	Transplant ; Live related - father	TRANSPLANT	Start
141204	Transplant ; Live related - mother	TRANSPLANT	Start
141205	Transplant ; Live related - child	TRANSPLANT	Start
141206	Transplant ; Live donor non-UK transplant	TRANSPLANT	Start
141207	Transfer in on : Plasmapharesis / plasma exchange	HD	Start
141210	Transfer in on : Assisted APD	PD	Start
141211	Transfer in on : Hybrid CAPD with HD	PD	Start
141212	Transfer in on : Hybrid APD with HD	PD	Start
141213	Transfer in on : Hybrid APD with CAPD	PD	Start
141214	Transfer in on : APD	PD	Start
141216	Acute haemofiltration â€“ ARF	ACUTE	Start
141217	Acute peritoneal dialysis â€“ ARF	ACUTE	Start
141228	APD	PD	Start
19338	Patient transferred out (RRT)	TRANSFERRED OUT	END
19391	Patient choice- treatment stopped (without recovery of function)	STOPPED	END
19392	Clinician choice- treatment stopped (without recovery of function)	STOPPED	END
5208	Stopped Treatment without recovering renal function	STOPPED	END
-310	Transplant recovered function	TRANSPLANT	START
19395	Patient lost to follow up	TRANSFERRED OUT	END
19370	Died	DEATH	END

19390	Patient - renal function recovered	RECOVERED	END
140209	Temporary Holiday Haemodialysis - End	TRANSFERRED OUT	END
140210	Patient transferred out (Non-RRT)	TRANSFERRED OUT	END
141220	ARF â€“ transferred out	TRANSFERRED OUT	END

Table 139 - AWRD Swansea Timeline Codes

Cardiff timeline codes

Timeline codes within the Cardiff renal data set and what they are then coded as and what sort of trigger they cause;

Code	Code Definition	Treatment	Trigger
2301	Haemodialysis	HD	Start
2302	Haemofiltration	HD	Start
2303	Haemodiafiltration	HD	Start
2304	Haemodialysis > 4 days per week / daily	HD	Start
2305	Ultrafiltration	HD	Start
2309	Haemodialysis - type unknown	HD	Start
2310	CAPD standard	PD	Start
2311	CAPD	PD	Start
2312	APD	PD	Start
2313	Cycling PD < 6 nights/wk dry	PD	Start
2314	APD Old	PD	Start
2315	Cycling PD < 6 nights/wk wet (day dwell)	PD	Start
2319	Peritoneal dialysis - type unknown	PD	Start
2320	Transplant; Cadaver donor (After Brain Stem Death)	TRANSPLANT	Start
2321	Transplant; Live related - sibling	TRANSPLANT	Start
2322	Transplant; Live related - parent or child	TRANSPLANT	Start
2323	Transplant; Live genetically unrelated	TRANSPLANT	Start
2324	Transplant; Cadaver donor + transplant other organ	TRANSPLANT	Start
2325	Transplant; Live donor + transplant other organ	TRANSPLANT	Start
2326	Transplant; Live related - other	TRANSPLANT	Start
2328	Transplant; Cadaver donor (After Cardiac Death)	TRANSPLANT	Start
2329	Transplant; Type unknown	TRANSPLANT	Start
2341	Transfer in on : Haemodialysis	HD	Start
2342	Transfer in on : Haemofiltration	HD	Start
2343	Transfer in on : Haemodiafiltration	HD	Start
2344	Transfer in on : Haemodialysis > 4 days per week	HD	Start
2345	Transfer in on : Ultrafiltration	HD	Start
2349	Transfer in on : Haemodialysis - type unknown	HD	Start

2350	Transfer in on : CAPD standard	PD	Start
2351	Transfer in on : CAPD	PD	Start
2352	Transfer in on : APD	PD	Start
2353	Transfer in on : Cycling PD < 6 nights /wk	PD	Start
2354	Transfer in on : Cycling PD < 6 nights/wk dry	PD	Start
2355	Transfer in on : Cycling PD >= 6 nights/wk wet (day dwell)	PD	Start
2359	Transfer in on : Peritoneal dialysis - type unknown	PD	Start
2360	Transfer in on : Transplant; Cadaver donor	TRANSPLANT	Start
2361	Transfer in on : Transplant; Live related - sibling	TRANSPLANT	Start
2362	Transfer in on : Transplant; Live related - parent or child	TRANSPLANT	Start
2363	Transfer in on : Transplant; Live genetically unrelated	TRANSPLANT	Start
2364	Transfer in on : Transplant; Cadaver + transp other organ	TRANSPLANT	Start
2365	Transfer in on : Transplant; Live donor + transp other organ	TRANSPLANT	Start
2366	Transfer in on : Transplant; Live related - other	TRANSPLANT	Start
2368	Transfer in on : Transplant; Non heart beating donor	TRANSPLANT	Start
2369	Transfer in on : Transplant; Type unknown	TRANSPLANT	Start
2371	Acute dialysis	ACUTE	Start
3719	Swansea HD	HD	Start
3720	Swansea Home HD	HD	Start
3721	Swansea APD	PD	Start
3722	Swansea CAPD	PD	Start
14032	APD (assisted)	PD	Start
14033	CAPD (assisted)	PD	Start
14034	Hybrid dialysis (CAPD with HD)	PD	Start
14035	Hybrid dialysis (APD with HD)	PD	Start
14036	Hybrid dialysis (APD with CAPD)	PD	Start
14039	Transfer in for pre-emptive transplant	TRANSPLANT	Start
14040	Transfer out for pre-emptive transplant elsewhere	TRANSPLANT	Start
14043	Transfer in on : APD (assisted)	PD	Start
14044	Transfer in on : Hybrid CAPD with HD	PD	Start
14045	Transfer in on : Hybrid APD with HD	PD	Start
14046	Transfer in on : Hybrid APD with CAPD	PD	Start
14049	AKI - Acute haemodialysis	ACUTE	Start
14050	AKI - Acute haemofiltration	ACUTE	Start
14051	AKI - Acute PD	ACUTE	Start
14052	AKI - Acute haemofiltration	ACUTE	Start
2338	Patient transferred out	TRANSFERRED OUT	End

2370	Died	DEATH	End
2390	Renal function recovered	RECOVERED	End
2395	Patient lost to follow up	TRANSFERRED OUT	End
13086	Acute recovered function	RECOVERED	End
14053	AKI - recovered function	RECOVERED	End
14055	AKI - transferred out	TRANSFERRED OUT	End
2372	Graft functioning	TRANSPLANT	START
2391	Treatment stopped without recovery - patient driven	STOPPED	END
2392	Treatment stopped without recovery - clinical decision	STOPPED	END
2395	Patient lost to follow up	TRANSFERRED OUT	END
14054	AKI - stopped dialysis (without recovery of renal function)	STOPPED	END

Table 140 - AWRD Cardiff Timeline Codes

RRT data check code

Where I found anomalies, I checked the raw data using the below SQL code;

```
SELECT *
    FROM SAIL0505V.M/C_ALF_20170127 a
    LEFT JOIN
    SAIL0505V.M/C_TIMELINE_20161231 b
    ON a.SYSTEM_ID_PE=b.SYSTEM_ID_PE
    WHERE ALF_PE = ‘ ’
```

Bangor Timeline codes

Timeline codes within the Bangor renal data set and what they are then coded as and what sort of trigger they cause;

BANGORCODE	Treatment	Trigger
ACUTE	ACUTE	START
Conservative Care	-	-
Death	DEATH	END
Donor	-	-
HD	HD	START
PD	PD	START
Pre	-	-
Recovered Function	RECOVERED	END
Stopped	STOPPED	END
Transferred Out	TRASFERRED OUT	END
Transplant	TRANSPLANT	START
Withdrawn	STOPPED	END

Table 141 - AWRD Bangor Timeline Codes

Wrexham Timeline

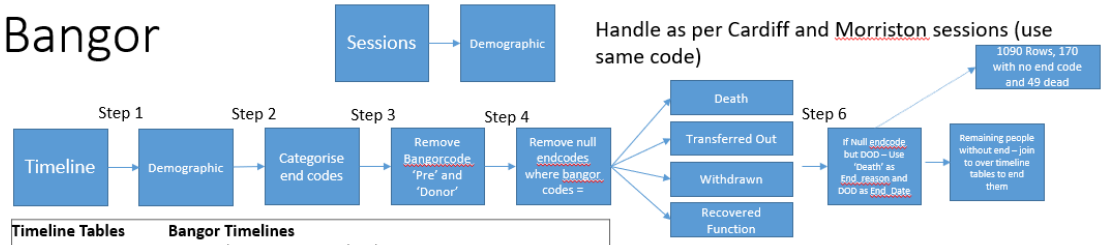
Timeline codes within the Wrexham renal data set and what they are then coded as and what sort of trigger they cause;

WREXHAM_TIMELINE_MODALITY	Treatment	Trigger
APD	PD	START
Acute	ACUTE	START
CAPD	PD	START
Elsewr HD	HD	START
Elsewr PD	PD	START
Elsewr TX	TRANSPLANT	START
HD	HD	START
HHD	HD	START
PlasmaX	PLASMA	-
T/P - cad	TRANSPLANT	START
T/P – live	TRANSPLANT	START
Trans Out	TRANSFERRED OUT	END

Table 142 - AWRD Wrexham Timeline Codes

Bangor Tables

How the Bangor table was created;



Timeline Tables	Bangor Timelines
ALF_PE	ALF_PE (From Demographics)
SYSTEM_ID_PE	SYSTEM_ID_PE
EVENT_SEQUENCE	Order
FIELD_1	"B"
TST_CODE	BangorModality
START_REASON	BangorCode
START_DT	STARTDATE
END_DT	ENDDATE
END_REASON	Derrived from end code - see table
TET_CODE	ENDCODE
ACUTE_TRIGGER	"1" if Bangorcode = 'ACUTE' / Startcode ='00 Acute' ELSE "2"
DS_SPELL_CT	Will need to count
DS_TOTAL_CT	Will need to count
TSC_DT	STARTDATE
TEC_DT	ENDDATE
RRT_TRIGGER	"1" (timeline)

Tables

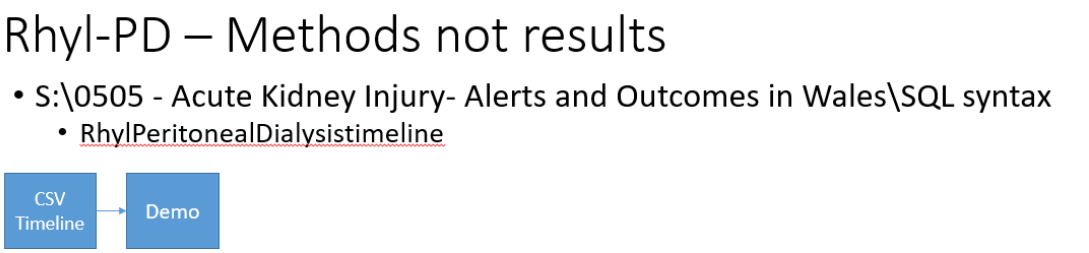
AWRD_B_DEMOGRAPHICS_ALF_20190829

AWRD_B_HDSESSIONS_20190708

AWRD_B_TIMELINE_20190708

Rhyl Tables

How the Rhyl table was created;



Timeline Tables	Rhyl Table
ALF_PE	ALF_PE (From Demographics)
SYSTEM_ID_PE	SYSTEM_ID_PE
EVENT_SEQUENCE	Order
FIELD_1	"R"
TST_CODE	Null
START_REASON	"PD"
START_DT	START_DATE
END_DT	END_DATE
END_REASON	End_Reason
TET_CODE	Null
ACUTE_TRIGGER	2
DS_SPELL_CT	Will need to count
DS_TOTAL_CT	Will need to count
TSC_DT	Null
TEC_DT	Null
RRT_TRIGGER	"1" (timeline)

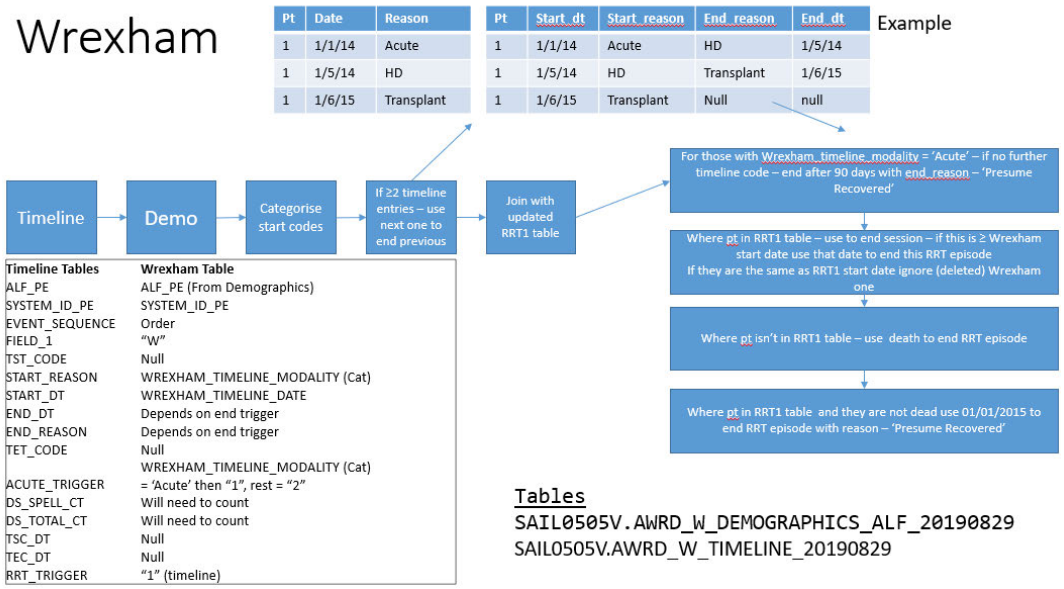
Tables

SAIL0505V.AWRD_R_PD_20190829 (original - now use CSV - import as table)

SAIL0505V.AWRD_R_DEMOGRAPHICS_ALF_20190829

Wrexham Tables

How the Wrexham table was created;



AKI test table from PAMO and PABR

Column	Derived from	Comment
ALF_PE		For ongoing linkage
GNDR_CD		Use WSDS
WOB		Use WSDS
LSOA_CD		Use pathology LSOA
REQST_NO	SYSTEM_REQST_NUM REQUEST_CD	For sample identification
COLLECTION_DT	COLLECTION_DT SPCM_DT	Top hierarchy
COLLECTION_TM	COLLECTION_TM SPCM_TM	Top hierarchy
PATH_DT	RECEIVED_DT RECEIPT_DT	Use for comparison with COLLECTION_DT
PATH_TM	RECEIVED_TM RECEIPT_TM	Use if COLLECTION_TM unavailable
SOURCE_CD		Bridgend – NA_BGN
MED_SPEC	MED_SPECIALTY	Swansea – No information – NA_SWA
TEST_CD		
RESULT		

Table 143 -AKI test table from PAMO and PABR

NHS England Algorithm text

E-alert algorithm documentation (https://www.england.nhs.uk/akiprogramme/aki-algorithm/) (157)
Definitions of terms used by the algorithm:

C1	Index Serum Creatinine (SCr) value (current result entered and authorised on the system)
RV1	Reference value 1 = lowest SCr value existing within the last 7 days
RV2	Reference value 2 = median of SCr values existing within 8-365 days
D	Difference between C1 and lowest previous SCr within 48hrs
RI	Population reference interval
RV	Reference SCr value with which C1 is compared

E-alert rules

The following set of rules trigger the Laboratory Information Management System (LIMS) to

send out an associated alert message to highlight the possibility of AKI to the requesting clinician:

Rule	Trigger	Associated alert
Rule 1	>26µmol/L increase in creatinine within 48hrs	*Acute Kidney Injury alert: rising creatinine within last 48 hrs.*
Rule 2	>50% increase in creatinine within 7 days	*Acute Kidney Injury alert: rising creatinine within last 7 days.*
Rule 3	>50% increase in creatinine against median result 8-365 days	*Acute Kidney Injury alert: creatinine has increased over median value from past year; consider also progressive CKD.*
Rule 4	No index value available from past year but creatinine above reference range	*Raised creatinine: if not known CKD suggest repeat to rule out Acute Kidney Injury.*

List of e-alert codes and corresponding trigger, rule, AKI stage, and comment:

E-alert code	Trigger	Rule	AKI stage	Comment
SAKI	C1 - RV1 > 26 µmol/L with no other rule triggered*	N/A	N/A	*Creatinine has increased > 26 µmol/L in < 7 days. Consider requesting repeat if CKD unlikely.*
DELTA1	D >26 µmol/L with no other rule triggered	1	1	*Acute Kidney Injury alert: rising creatinine within last 48 hrs.*
ABS1	C1/RV1 > C1/RV2 and C1/RV1 > 1.5 or C1 > 354µmol/L**	2	3	*Acute Kidney Injury alert: rising creatinine within last 7 days.*
ABS2	C1/RV2 > C1/RV1 and C1/RV2 > 1.5 or C1 > 354µmol/L**	3	3	*Acute Kidney Injury alert – creatinine increase over baseline value*
R1AKI1	C1/RV1 > C1/RV2 and C1/RV1 is in range 1.5–1.99	2	1	*Acute Kidney Injury alert: rising creatinine within last 7 days.*
R1AKI2	C1/RV1 > C1/RV2 and C1/RV1 is in range 2.0–2.99	2	2	*Acute Kidney Injury alert: rising creatinine within last 7 days.*
R1AKI3	C1/RV1 > C1/RV2 and C1/RV1 is ≥ 3.0	2	3	*Acute Kidney Injury alert: rising creatinine within last 7 days.*
R2AKI1	C1/RV2 > C1/RV1 and C1/RV2 is in range 1.5–1.99	3	1	*Acute Kidney Injury alert – creatinine increase over baseline value*
R2AKI2	C1/RV2 > C1/RV1 and C1/RV2 is in range 2.0–2.99	3	2	*Acute Kidney Injury alert – creatinine increase over baseline value*
R2AKI3	C1/RV2 > C1/RV1 and C1/RV2 is ≥ 3.0	3	3	*Acute Kidney Injury alert – creatinine increase over baseline value*

*SAKI is not an AKI alert based on current definitions

** Paediatric level is 3 x upper limit of age - related reference range

Notes:

- As requested by the renal physicians/AKI steering group different e-alerts frequently generate the same comment expansion.
- All e-alert codes except SAKI also have primary care counterparts. If a triggering C1 occurs in a GP surgery then the e-alert code issued by LIMS will be the same as a

regular e-alert code but with 'GP' appended. For instance if an individual's SCr tested in a GP surgery triggers AKI then the e-alert code generated by LIMS will be DELTA1GP or ABS1GP etc. The associated trigger, rule and AKI stage will be the same as in a regular e-alert code. The comment expansion attached to the e-alert will be different. The content of the comments is to be determined by work of the Community workstream.

- There is no e-alert code associated with rule 4 however when there is no index value available from the past year but SCr is above the reference range a comment - similar to that of the SAKI comment - warning of potential AKI is attached to the result.

Rule 4 refers to the population reference interval (RI). This is between 45 and 90µmol/L for females and 60 to 110µmol/L for males.

Creating AKI table

Creating the cohort table from AKI cohort

1. All tests – running our AKI alert code, gender, age, location of tests, dialysis at time of test, dialysis at time +1 day
2. Left join with the electronic AKI alerts – where the 'CODE' is AKIALERT, as well as the suppressed alerts.
3. Categorise the results into LHBs
4. Where the patients have an AKI episode – any method – left join with creatinine tests from the original table for Alert patients only.
5. Join with PEDW – Current test inpatient Spell – Admission date to discharge date. Getting length of stay, ICD-10 primary code, N17 ICD-10 code, Admission and discharge dates
6. Then use PEDW for 7 days– where test is not in PEDW, does the test + 7 days fall within a **spell**.
7. PEDW 30 days post discharge – For [5] – using discharge date – readmission within in 30 days for discharge date. Looking at LOS and coding for; AKI, CKD, Pulmonary Oedema, Dehydration, Heart Failure
8. Dialysis – where dialysis and dialysis +1 are blank, what is future dialysis date – 1st one only.
9. Death Date – ONS and WDS
10. Critical care admission – At time of test , within 7 days of test, length of stay, renal support days. Could be duplicates therefore take the one related to the critical care stay at the time of admission.
11. Creatine Values within 90 days – take the last

AKI table

This is the format of the AKI table that was created by the analyst (Gareth Davies)

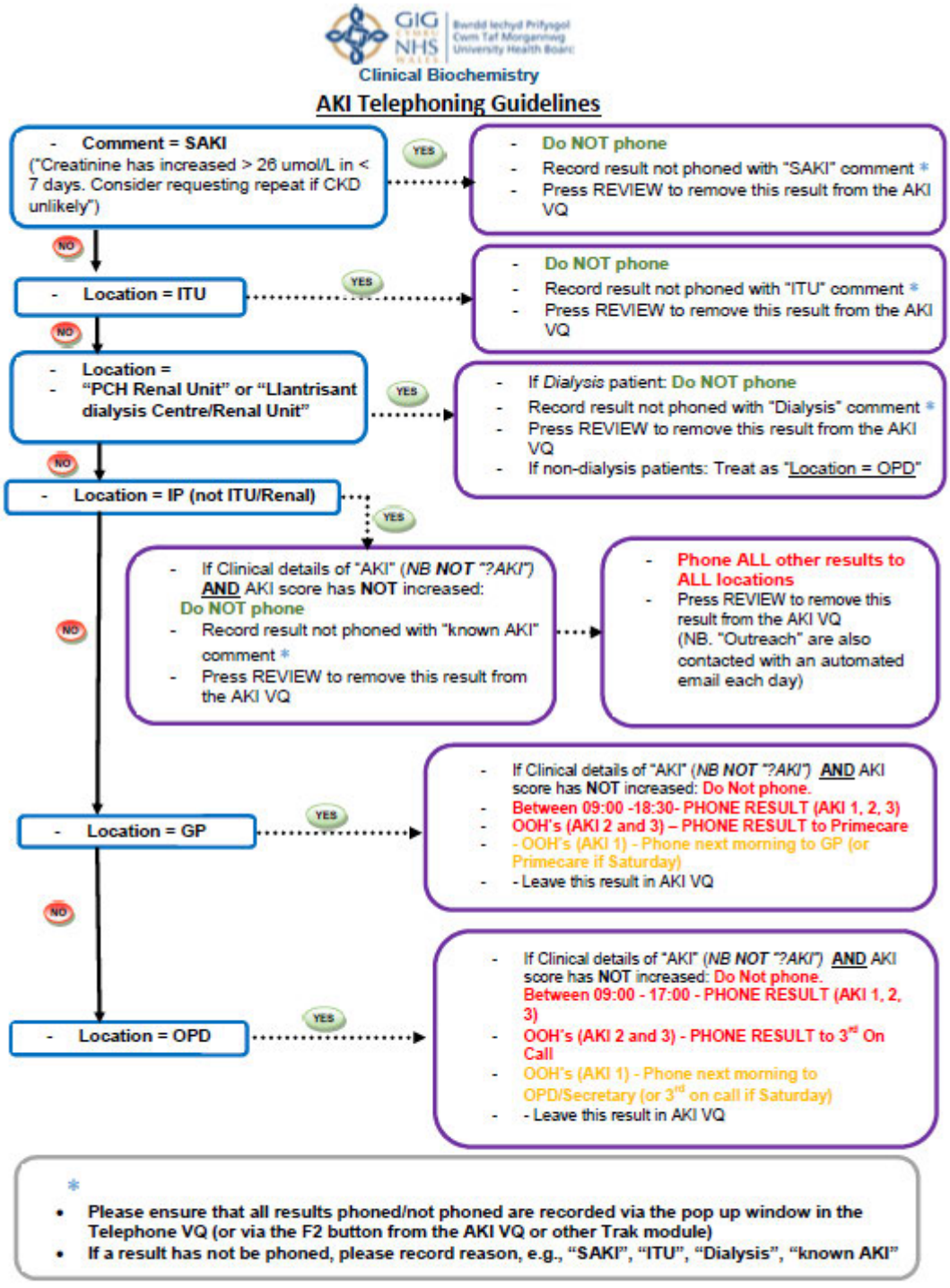
ROWS	DESCRIPTIONS
ALF_PE	Unique identifier
TEST_NUMBER	Unique test number
C1	Result
C1_DT	Date
EPISODE_15_NO	Episode by 15
EPISODE_12_NO	Episode by 12

EPISODE_90_NO	Episode by 90
EPISODE_ALT_NO	Episode by alert
RV1	Lowest creatinine 7 days
RV2	Median creatinine 8-365 days
RV3	Lowest creatinine 48 hours
RV1_BASELINE	Lowest creatinine with alert in 7 days
RV2_BASELINE	Median creatinine with alert 8-365 days
C1_OVER_BASE_RV1	Value over RV1 baseline ratio
C1_OVER_BASE_RV2	Value over RV2 baseline ratio
C1_MINUS_RV3	Value minus RV3 baseline
DATE_15_DIFF_DAYS	Day difference better test and fixed baseline
HIGHEST_ALERT	Alert stage
HIGHEST_ALERT_REASON	Alert reason
AGE_EP_START	Age at time of alert
GNDR_CD_WDS	Gender from WDS
DIAL_NO	Dialysis at time of test
DIAL_ST_DT	Dialysis start date
DIAL_END_DT	Dialysis end date
DIALYSIS	At time of test
DIALYSISMINUS1	Dialysis day before test
DIALYSIS_FUTURE	Future Dialysis date (closest)
TRANSPLANT	Transplant at time of test
TRANSPLANT_DT	Transplant date
LOCN_1ST_TEST	Location of first alert test – health board
SUBJECT_LOC_1ST_TEST	Categorised first test location
PROV_DEPT_SITE_DESC	Hospital running test
WRRSALERT	WRRS alerts
WRRSALERT7DAYCREATININE	WRRS alert within 7 days
WRRSALERTWITHNULLVALUE	WRRS alert is Null
WRRS_SUPPRESSED	To be updated
BEFORE_OR_AFTER_EALERT	Before or after alert introduction
LOCATION	Health Board
SUBJECT_LOCATION	Categorised test location
TEST_LOCATION	To add the actual test location, i.e. SUBJECT_LOC_DESC
REQUESTOR_ID	REQUESTOR_SPEC_DESC
HB_COMPARISON_STATUS	Categorised health board before / after
TEST_INPATIENT	In PEDW at time – binary
ADMIS_DT	Where patient inpatient at time, admission date
DISCH_DT	Where patient inpatient at time, discharge date
ADMIS_LOS	Where patient inpatient at time, length of stay (spell)
PRIMARY_DIAG_ICD10	Primary diagnosis code – i.e. DIAG_NUM=1

AKI_ICD10	Any position – like 'N17%'
PEDW7	Admitted within 7 days of the alert
PEDW7_AKI	Admitted within 7 days with AKI
PEDW7_LOS	Admitted within 7 days – length of stay
READMISSION_30DAYS	Readmitted 30 day post discharge
READMISSION_AKI	N17% Code
READMISSION_CKD	N18% Code
READMISSION_PULM_OEDEMA	J81 I50.1
READMISSION_HEART_FAILURE	I50%
READMISSION_DEHYDRATION	E86
READMISSION_LOS	Length of stay in readmission
DEATH_ONS	Death Date ONS
DEATH_WDS	Death Date WDS
CRITICAL_ADMISSION	Critical Care at time of index
CRITICAL_LOS	Critical length of stay if inpatient at time of index
CRITICAL_RRTDAYS	Number of days renal support if inpatient at time of index
CRITICAL_CARE30DAYS	Admission within 30 days
CRITICAL_CARE30LOS	Length of stay if admission within 30 days
CRITICAL_CARE30RRT	Length of renal support if admission within 30 days
CREATININE90DAYS	Last creatinine value 90 days
CREATININE90DAYS_DT	Last creatinine value 90 days date
RENALOPD_BEFORE	Renal Outpatient before date – CONS_SPEC_MAIN_CD = 361
RENALOPD_AFTER	Renal follow after date – CONS_SPEC_MAIN_CD = 361
RENALOPD_ONDAY	Renal follow on date – CONS_SPEC_MAIN_CD = 361
RENALOPD_AFTERNEW	Renal follow on date – CONS_SPEC_MAIN_CD = 361 with
RENALOPD_AFTERNEW_SOURCE	SOURCE_OF_REF_CD = FIRST_ATTEND_CD = 1

Table 144- AKI table columns

Cwm Taf Alerts rules



Appendix for Chapter 7

This appendix covers some of the code and results for the Chapter 7 - Prescriptions and reviews in primary care following AKI on page 235.

Read Codes

Medications Read codes used. The 'like' and the % part of the codes pulls any derivatives of this code;

1. Non-steroidal anti-inflammatories - Like 'j2%'
2. Angiotensin converting enzyme inhibitors and Angiotensin receptor blockers - like 'bi%' or like 'bk%'
3. Furosemide, Bumetanide or Torsemide (Loop diuretics) – Like 'b31%' or like 'b32%'or event_cd like 'b35%')
4. Beta Blockers - like 'bd%'
5. Thiazide Diuretics - like 'b2%'
6. Potassium Sparing Diuretics - like 'b4%'
7. HMG-CoA reductase inhibitor (Statin) - like 'bxi%' or like 'bxj%' or like 'bxg%' or like 'bxe%' or like 'bxk%' or like 'bxd%'
8. Aspirin - like 'bu2%'
9. Sulphonylureas - like 'f3%'
10. Insulin - like 'f1%' or like 'f2%'
11. Metformin – like 'f41%'
12. Calcium Channel Antagonist like 'bl5%' or like 'bl6%' or like 'bl7%' or like 'bl8%' or like 'blb%' or like 'blc%' or like 'ble%' or like 'blg%' or like 'blh%' or like 'blj%' or like 'bll%'
13. Proton Pump Inhibitors - like 'a6b%' or like 'a6c%' or like 'a6e%' or like 'a6f%' or like 'a6h%'
14. Paracetamol - like 'di2%'
15. Histamine receptor 2 Antagonists - like 'a61%' or like 'a62%' or like 'a63%' or like 'a68%' or like 'a69%'
16. Blood pressure - like '246%' or like '9OD%' or like 'ZV70B%'
17. AKI primary care record - like 'K04%' or like 'SK08%'or like 'L393%'
18. Medication review - like '8B3S%' (Post Hospital Medication Review)

    or like '8BT%' (Medication Review) or like '8B3x%' (Medication Review)

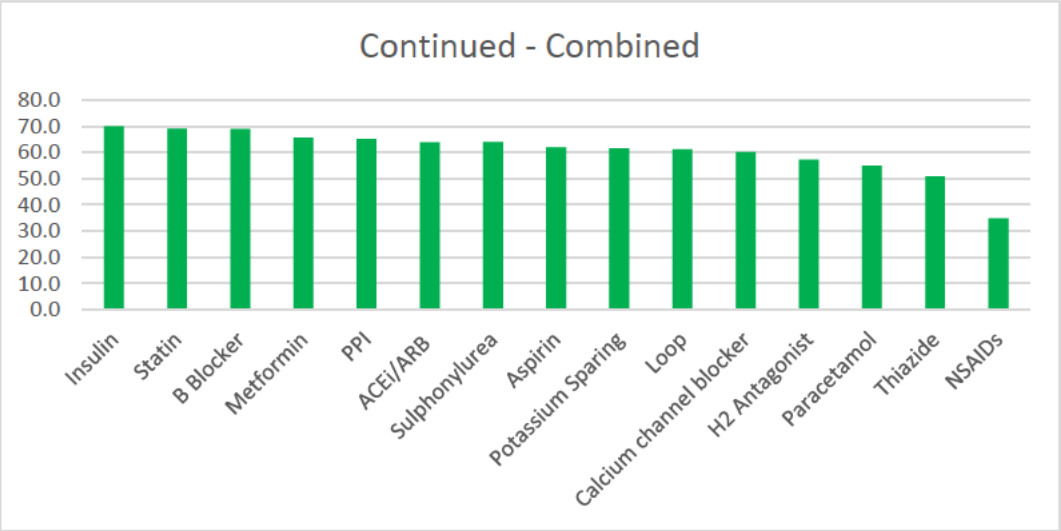
or like '8BMJ%' (Medication Review)

19. Urine dipstick - like '4618%' (Urine Dipstick)

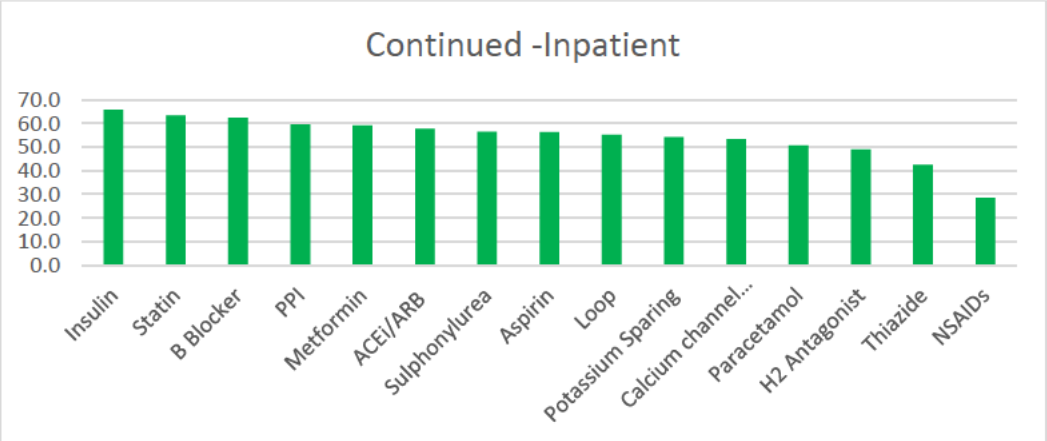
    or like '4612%' (Urinalysis requested)
    or like '4613%' (Urinalysis no abnormality)
    or like '4614%' (Urinalysis abnormality)
    or like '463%' (Urine SG)
    or like '4672%' (Urine Protein)
    or like '4673%' (Urine Protein)
    or like '4674%' (Urine Protein)
    or like '4675%' (Urine Protein)
    or like '4676%' (Urine Protein)
    or like '4677%' (Urine Protein)
    or like '4679%' (Urine Protein)
    or like '46A%' (Urine pH)
    or like '46X%' (Urine Nitrite)
    or like '46f%' (Urine Leucocyte)
20. Creatinine Test - like '44J3%'

Graphs of medication changes

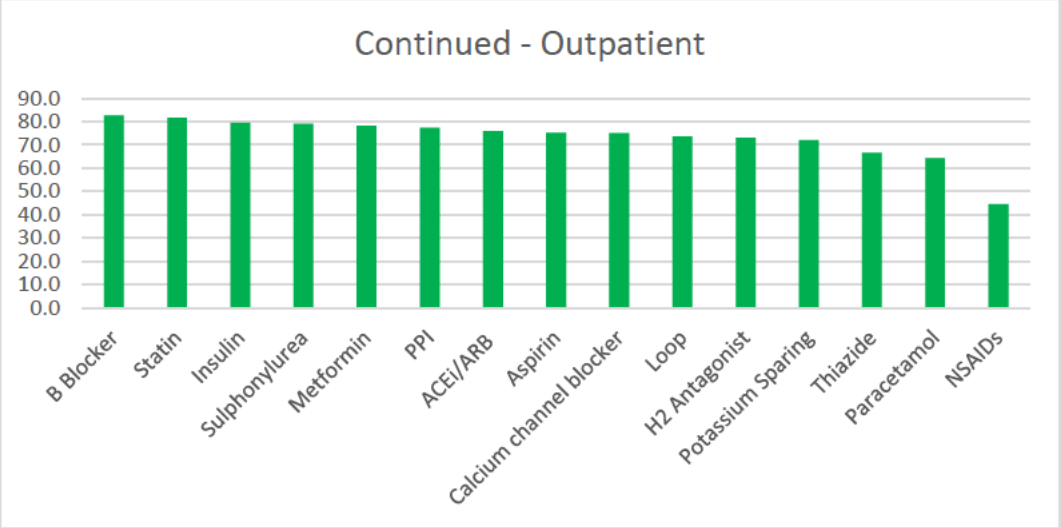
Percentage of medicines continued – inpatient and outpatients



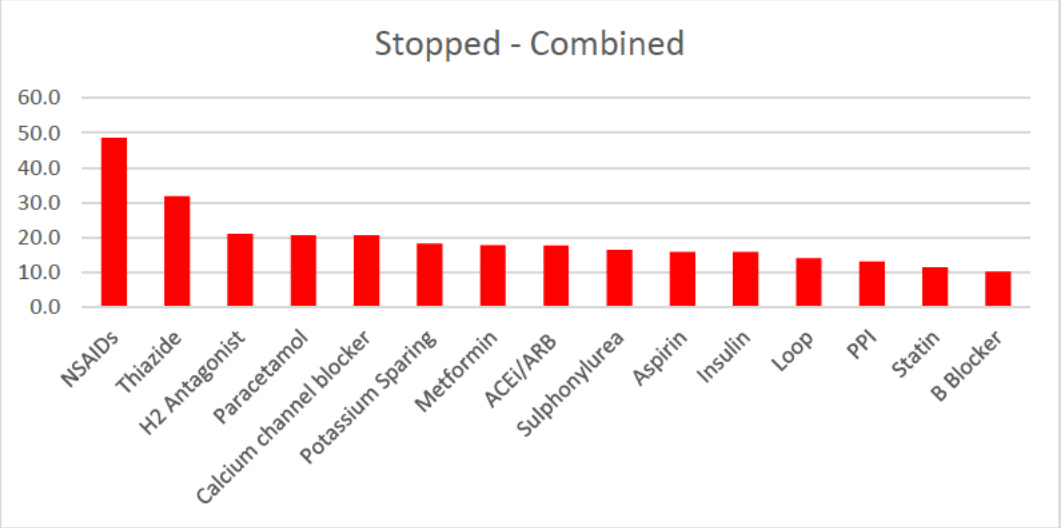
Percentage of medicines continued – inpatient;



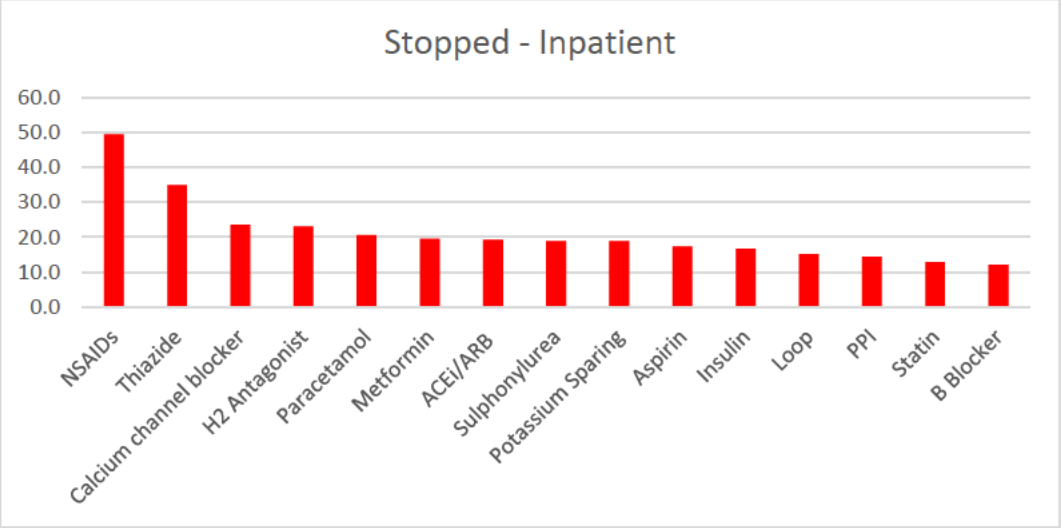
Percentage of medicines continued –outpatients;



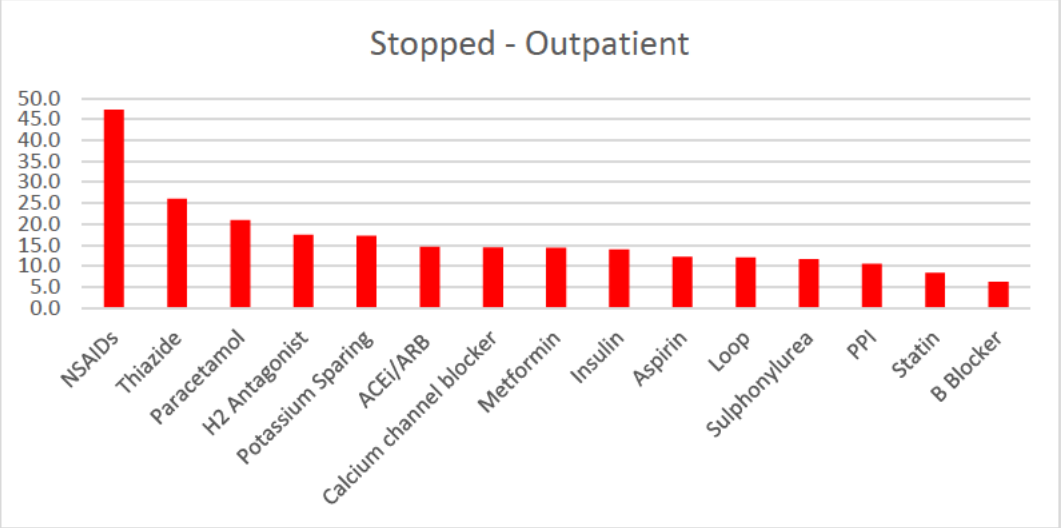
Percentage of medicines Stopped – inpatient and outpatients;



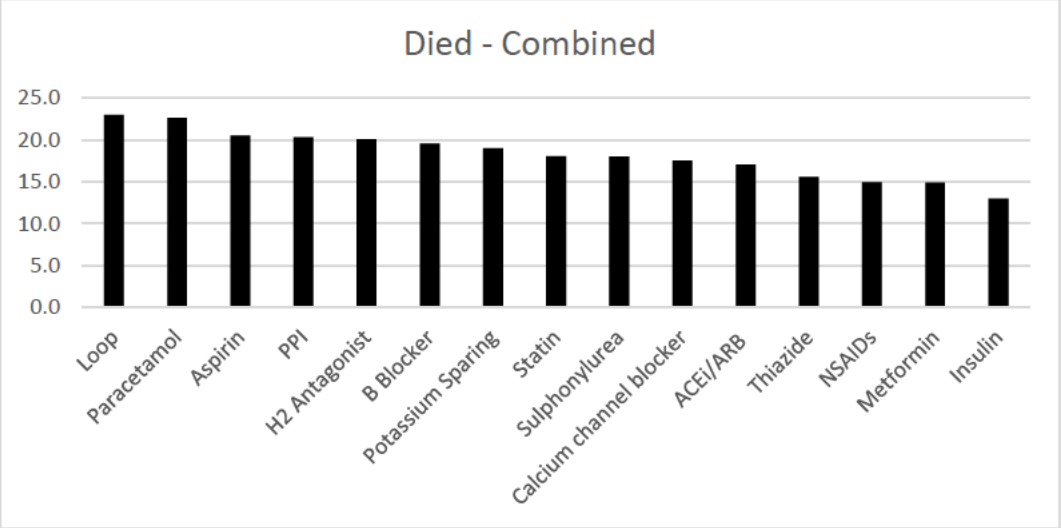
Percentage of medicines Stopped – inpatient;



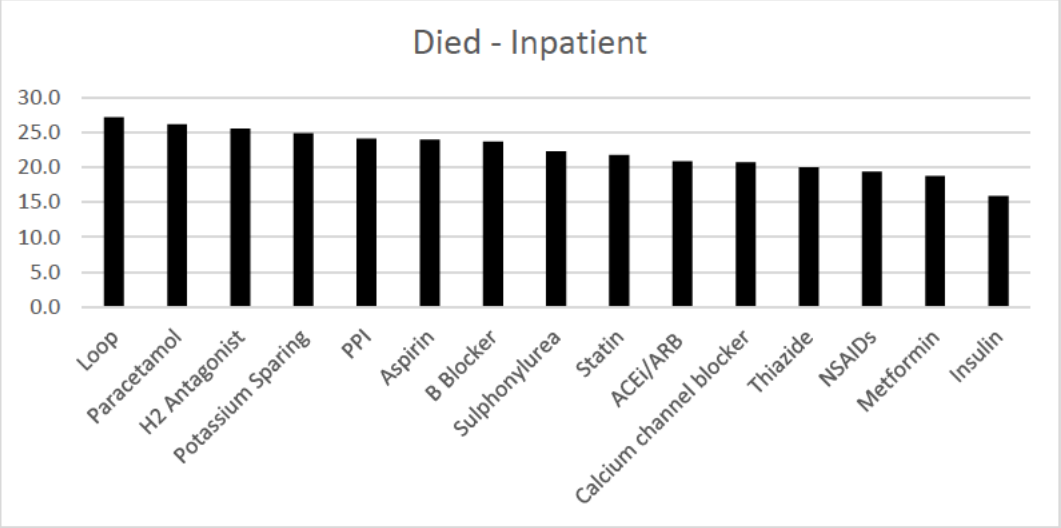
Percentage of medicines Stopped - outpatients;



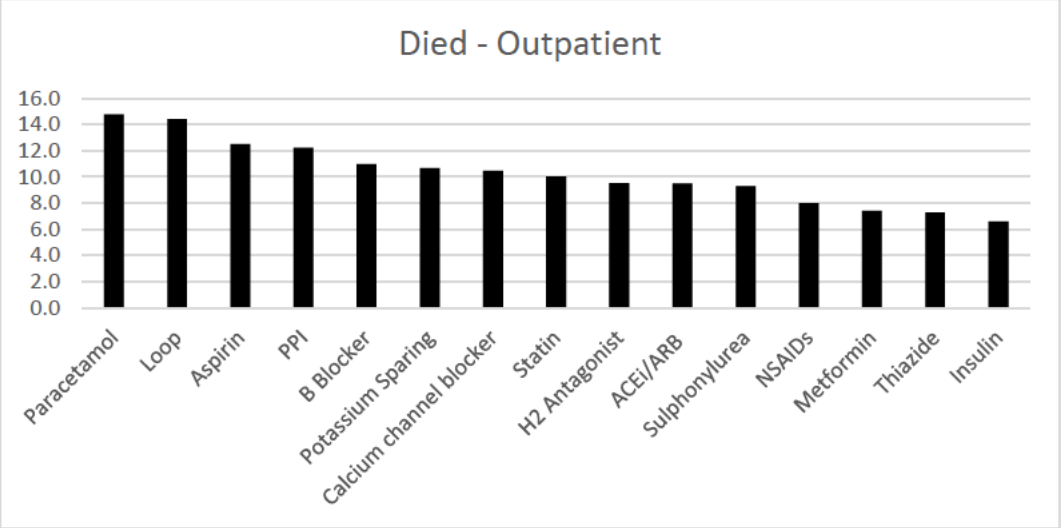
Percentage of medicines Died – inpatient and outpatients;



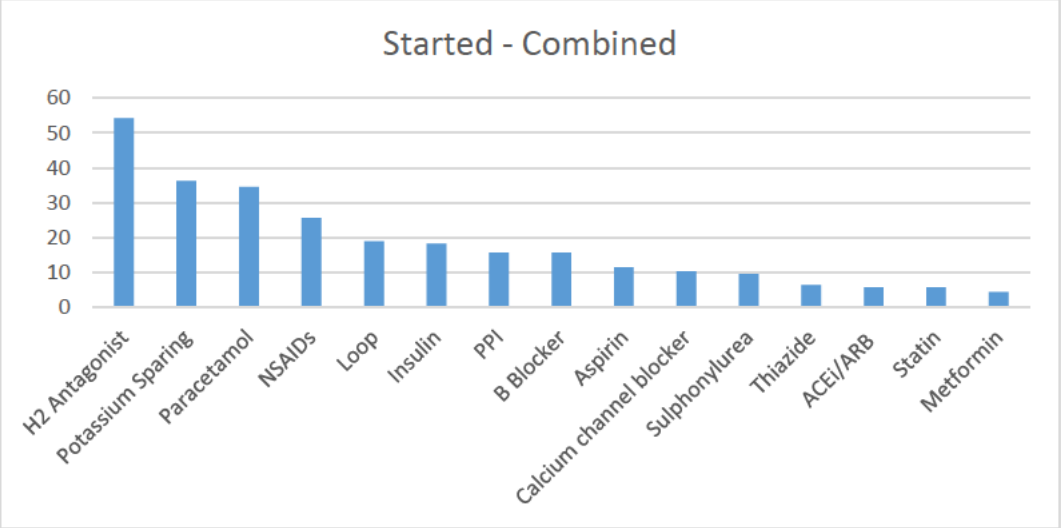
Percentage of medicines Died – inpatients;



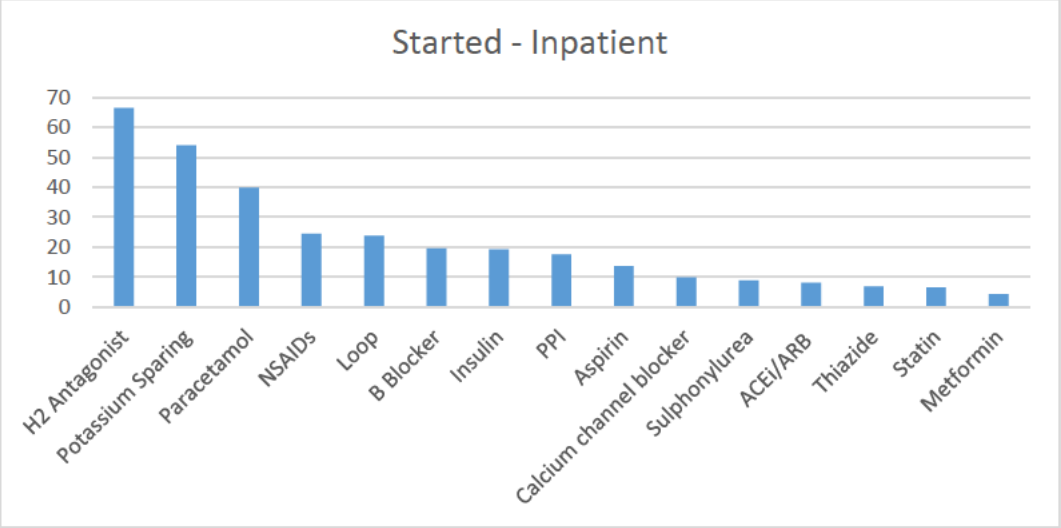
Percentage of medicines Died – outpatients;



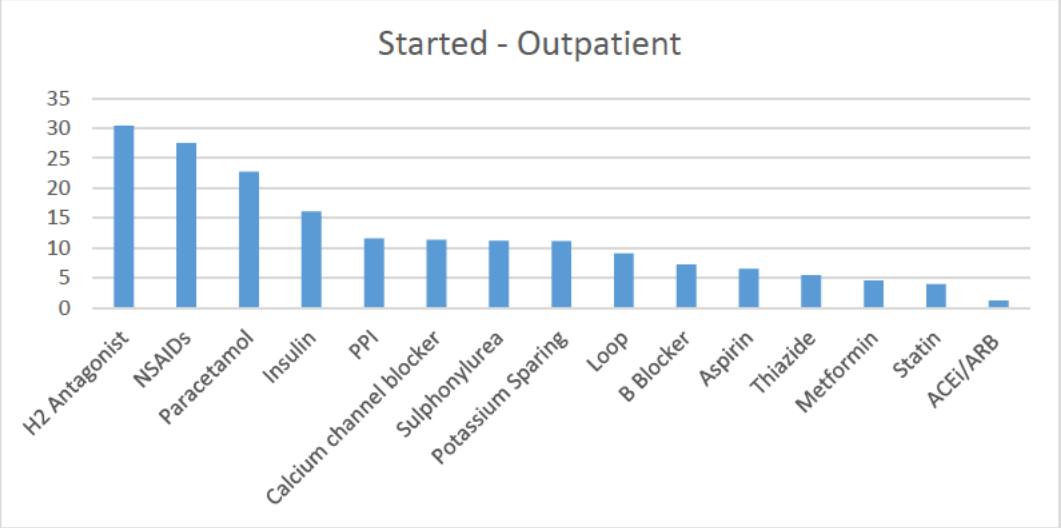
Percentage of medicines started – inpatient and outpatients;



Percentage of medicines started – inpatients;



Percentage of medicines started –outpatients;

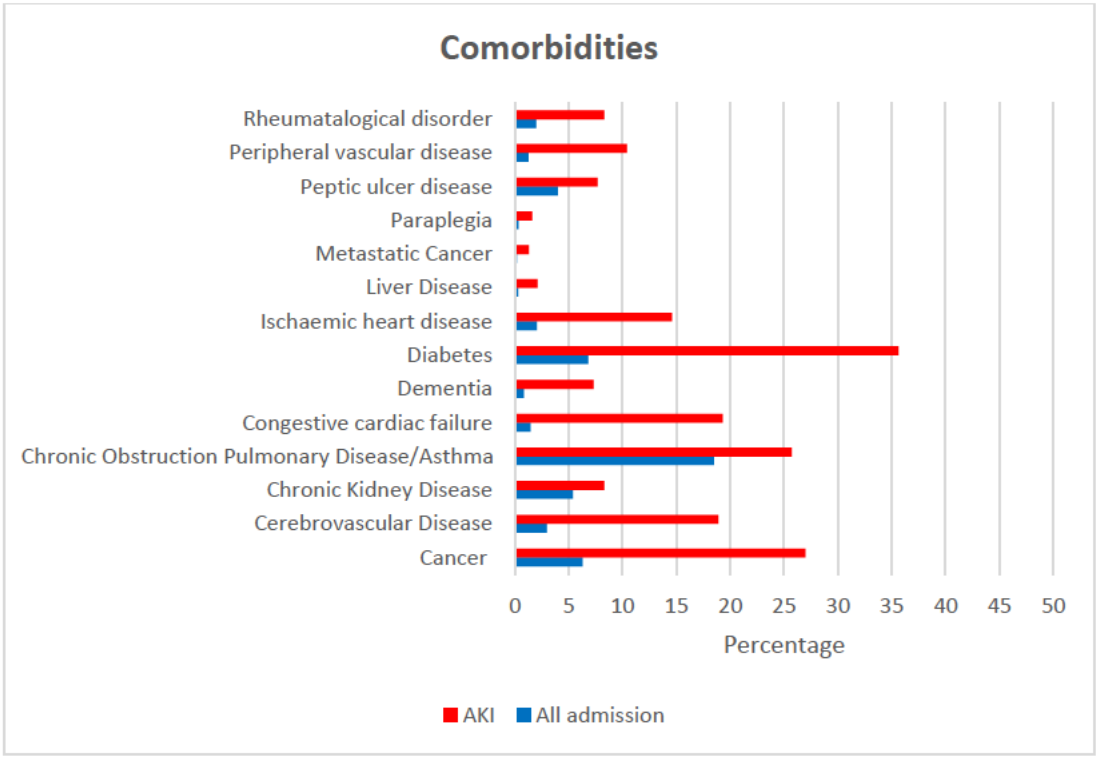


ICD-10 coded AKI pilot study

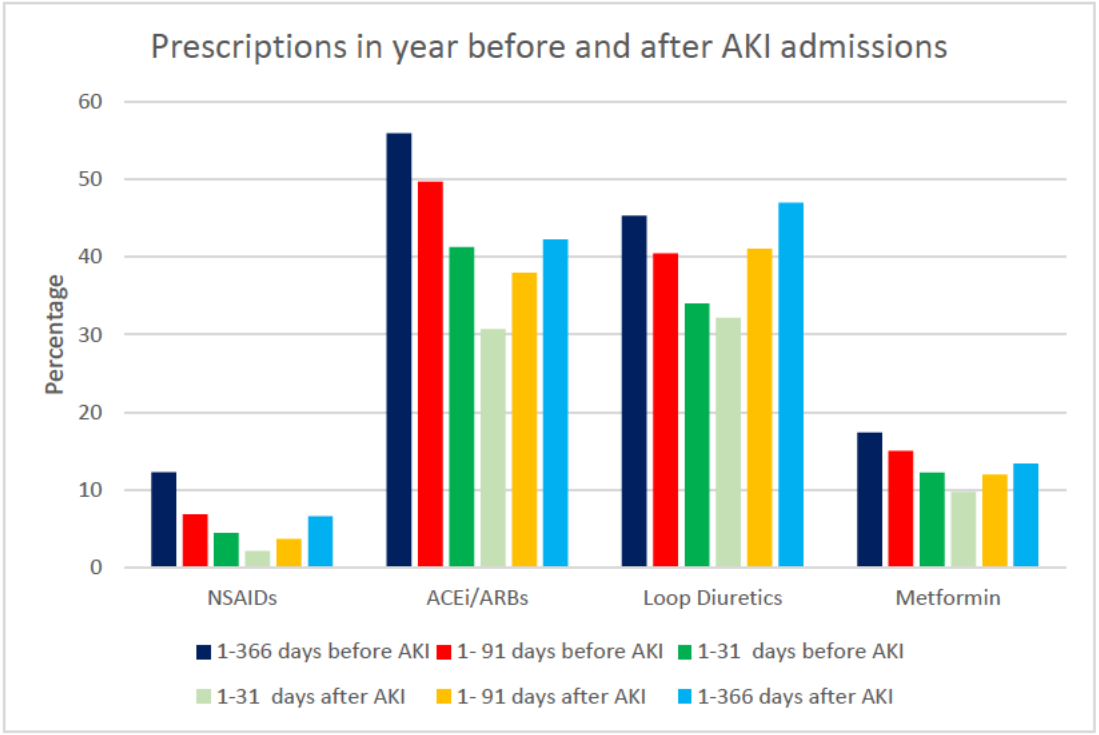
A pilot study was carried out examining the prescription and review changes in primary care following hospital coded AKI in Wales between 2010-2015. Like the main study chapter 7 (Chapter 7 - Prescriptions and reviews in primary care following AKI235), the study was caried out within SAIL but in this pilot study, ICD-10 coding for hospital admissions was used to identify a AKI cohort. I then used the primary care data within SAIL to compare the prescriptions and reviews before and after the AKI admissions. The prescriptions and reviews were identified using the Read codes previously described (Read Codes). All the code for this was written by myself using structure query language (SQL). Only emergency or elective admissions were used, and AKI coding was counted if it is in any diagnostic position.

Results

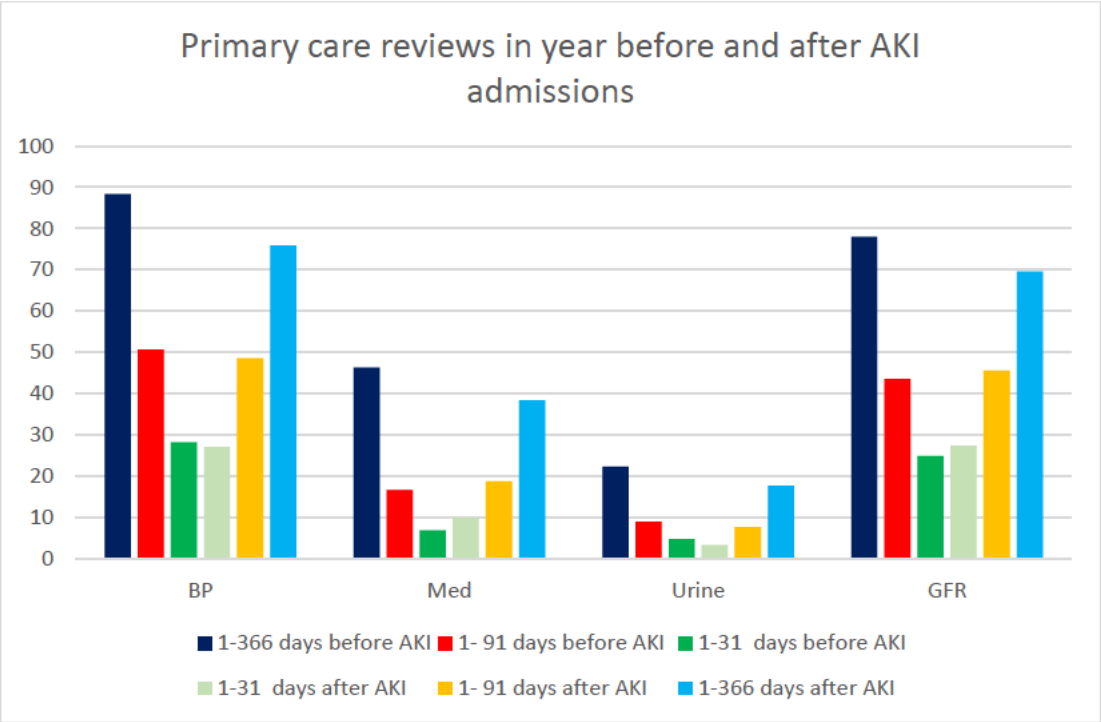
In the 6 years of this study there were 4,203,268 inpatients spells in 1,584,838 people. Of these admissions there were 80,009 admissions coded for AKI. I used the first admission of that year to avoid duplication, for which there were 65,574 AKI admission, 45,992 of which had primary care data prior to the admission. In this cohort the inpatient mortality was 27.4% and the 1-year mortality was 51%. The graph below shows a breakdown of the comorbidities comparing the overall inpatient population comorbidities to the AKI cohort;



To understand the relationship between time and prescriptions I look at a 1-year period, 90-days and 30 days before and after the AKI.

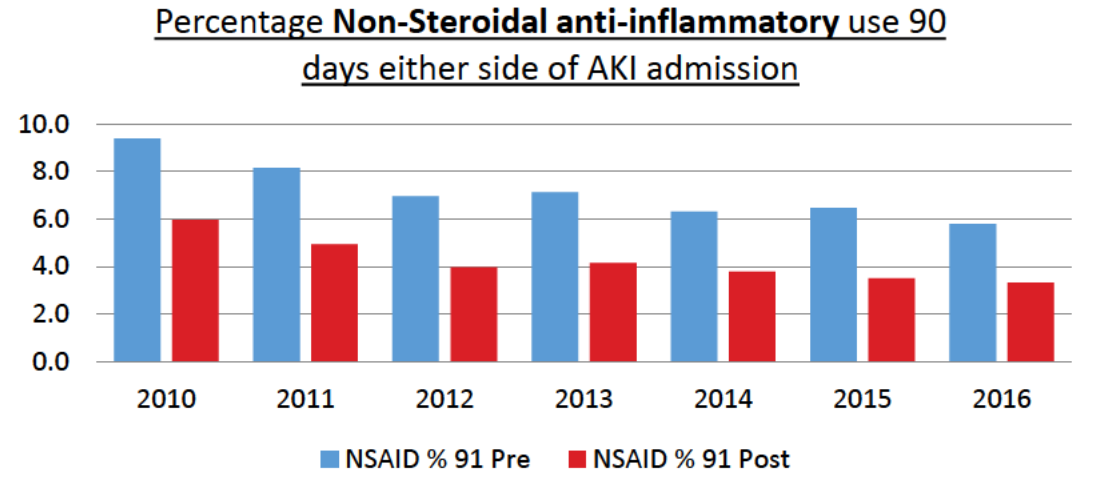


Understandably the longer the time period the more prescriptions there are, nevertheless, the proportional change between 90-days and 1-year is less than that of 30 to 90-days. This is not the same with the reviews, where the difference between 90-days and a year seems more striking.

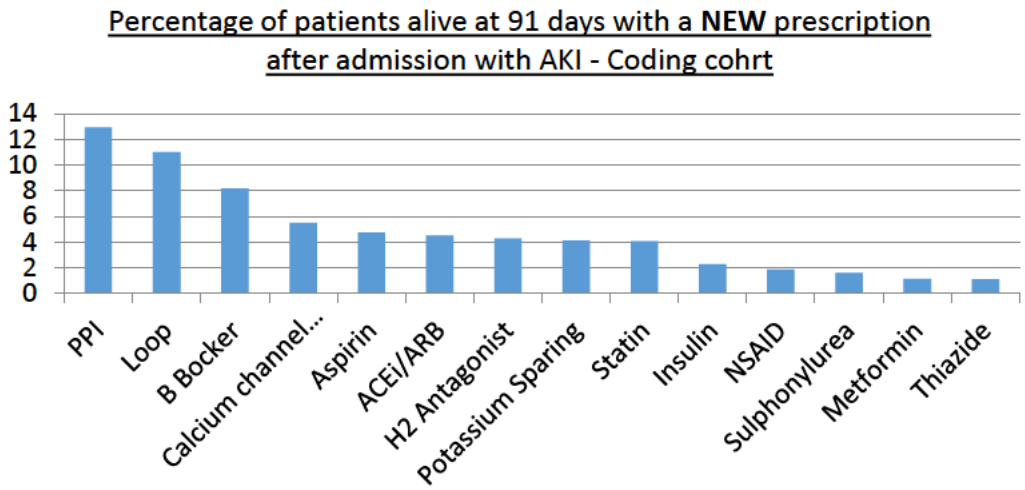


Following reviewing these aspects, I chose 90-days as the period for assessing the reviews and prescription. 1-year would select the most patients, however a lot can change medically in 1-year, and a blood pressure review or a short non-steroidal prescription almost a year before or after an AKI is unlikely to affect the AKI.

Over time there was a year on year fall in NSAID use;



As established this cohort of patients represents an AKI cohort with a higher mortality than those with AKI by serum creatinine, therefore we may not expect the data to be exactly the same, nevertheless we see a very similar trend, the first graph is from the coding AKI and the second is from the main study;



Graph – ICD-10 study

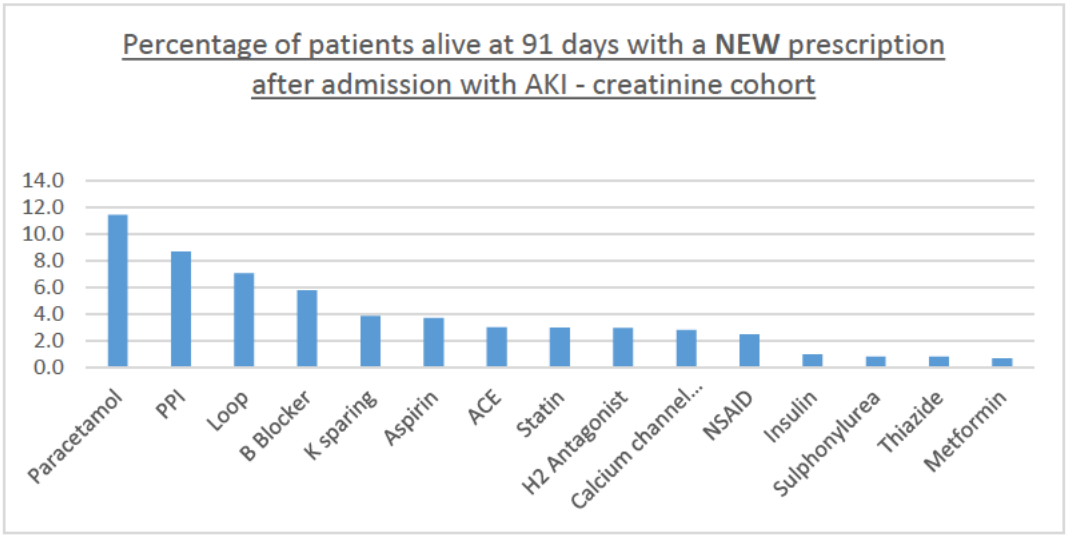


Table – From Chapter 7 - Prescriptions and reviews in primary care following AKI

As can be seen the trends are very similar between the two methods (this pilot study on the left and the main chapter on the right).

Prescription	ICD-10 coding 2010-2015		Creatinine between 2013-2016 (chapter 7)	
	90-days before	90-days after	90-days before	90-days after
ACEi/ARB	49.1	42.5	43.3	30.7
Loop	40.4	46.5	34.6	31.9
B blocker	34.5	42.7	31.9	31.2
Calcium channel blocker	24.6	25.5	21.2	16.7
Potassium sparing diuretic	10.4	11.4	8.3	9.2
Thiazide	10.4	6.5	9	4.7
Metformin	14.5	12.9	13	9.3
Sulphonylurea	9.4	10.3	7.5	6
Insulin	6.2	8.9	4	4.7
NSAID	7.1	4.2	5.6	2.4

As can be seen the trends remain similar, albeit the numbers slightly different as a result of a difference in selection of the AKI (therefore a different cohort) and a difference in time. These results help understand the changes seen in patients with AKI, if we look at the admitted population as a whole, we see that the AKI population have a higher percentage of medication use as a whole, but particularly cardiovascular medications;

GP Event	Whole Population (%)	AKI (%)
NSAID	14.3	12.6
ACEi/ARB	12.8	55.1
Loop Diuretics	3.4	45.1
Beta Blocker	7.4	37.3
K Sparing	0.6	12.2
Calcium Channel Antagonist	7.9	29.9
Thiazide	4.9	14.0
Statin	13.9	52.3
Aspirin	7.2	38.8
Paracetamol	10.7	39.9
Metformin	3.5	16.8
Sulphonylurea	1.6	7.3
Insulin	0.9	11.0
PPI	16.0	52.7
H2 Antagonist	1.6	6.0

Findings

- In patients that survive hospital admission with coding for AKI, almost a **third** of these patients will **die in the next 12 months**.
- The patients identified with AKI by coding often represent severe AKI and have a higher 1-year mortality than patients identified by AKI serum creatinine based algorithm (5).
- As you may expect, an episode of AKI often results in a change in prescribing practice by general practice.
- **Who initiates** this change (hospital clinicians or general practitioners) we are **unable to determine in this study**.
- The largest **increases** in usage was seen in H2 receptor antagonists, insulin, proton pump inhibitors, beta blockers and loop diuretics (76.1, 43.5, 25.2, 23.8 and 14.9% increase respectively).
- The largest **decrease** in medication was in NSAIDs and thiazide use following AKI (40.8 and 37.5% respectively).
- We have observed an **increase** in the percentage prescription of medications used to help facilitate **fluid removal** (loop and potassium sparing). This is likely to be related to the interrelationship between chronic kidney disease, heart failure and AKI, all of which frequently result in a water imbalance.

- It is beyond the ability of this study to understand whether the changes in medication use are correct. However, with non-steroidal anti-anti-inflammatories, there is a stronger argument for ongoing cessation following AKI yet almost **1/5** of patients on **NSAIDS** before admission, continued the medication after admission.
- We are unable to tell if there was a dose change.
- Reassuringly there was an **increase** in the percentage of these patients having chronic disease monitoring after AKI, however some patients do not.
- A major question here is, **do the general practitioners know about the episode of AKI?** (i.e. are the discharge summaries being done and do they mention AKI). Wales has not had a commissioning for quality and innovation care (CQUIN) necessitating the mentioning of AKI on discharge summaries, unlike England.
- The **coding** for **AKI** is **specific** but **not sensitive**, as such there will be patients with AKI during admission not included in this study.
- We also can not infer that this is sample is representative of all of Wales as almost **30**% of the patients **do not** have **primary care records available** for the period in SAIL.

This pilot study was presented as a poster presentation at UK kidney week in 2018.

Renal Registry AKI report 2022

Publications based on UK Renal Registry (UKRR) data presented in this report must include the citation detailed above and the following disclaimer:

The data reported here have been supplied by the UKRR of the Renal Association. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy or interpretation of the UKRR or the Renal Association.