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1 **Reduction in postoperative Acute Kidney Injury following a change in antibiotic**
2 **prophylaxis policy for orthopaedic surgery – an observational study**

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20 **Short running title:** Reduced AKI in orthopaedic surgery

21

22 **Abstract**

23 Objectives: Evidence has shown that a prophylactic antibiotic regimen of flucloxacillin and
24 gentamicin for orthopaedic surgery was associated with increased rates of post-operative
25 acute kidney injury (AKI). This resulted in changes in national antibiotic policy
26 recommendation for orthopaedic surgical prophylaxis. This study aimed to assess whether
27 this change from flucloxacillin and gentamicin to co-amoxiclav was associated with changes
28 in the rates AKI and *Clostridium difficile* infection (CDI).

29 Methods: An observational study and interrupted time series analyses were used to assess
30 rates of post-operative AKI separately in patients undergoing neck of femur (NOF) repair and
31 other orthopaedic operations which required antibiotic prophylaxis. Incidence rate ratios were
32 used to evaluate changes in CDI rates.

33 Results: Following the change in policy, from flucloxacillin and gentamicin to co-amoxiclav,
34 there was a relative change in rates of post-operative AKI of -63% (95% CI -77% to -49%) at
35 18 months in the other orthopaedic surgeries group. In the NOF repair group, there was no
36 change in the rate of post-operative AKI -10%, (95% CI -35% to 15%) at 18 months. The
37 incident rate ratio for CDI in other orthopaedic operations was 0.29 (95%CI 0.09 to 0.96) and
38 for NOF repair patients was 0.76 (95%CI 0.28 to 2.08).

39 Conclusions: The use of co-amoxiclav for antibiotic prophylaxis in orthopaedic surgery was
40 associated with a decreased rate of post-operative AKI compared to flucloxacillin and
41 gentamicin and was not associated with increased rates of CDI.

42

43 **Introduction**

44 Surgical site infections (SSI) are a preventable healthcare associated infection. They are
45 associated with a significant increase in morbidity, mortality, length of hospital stay and both
46 socioeconomic and health related costs.^{1, 2} Prophylactic antibiotics have been shown to
47 reduce the rate of SSI in patients undergoing joint replacement surgeries³ and are
48 recommended for orthopaedic implant surgeries.⁴ However, their use can also have
49 associated adverse effects and unintended consequences, such as allergy,⁵ the development of
50 antibiotic resistance among organisms,⁶ acute kidney injury (AKI)⁷⁻¹⁰ and *Clostridium*
51 *difficile* infection (CDI).^{11, 12}

52 AKI is reported to be an independent risk factor for mortality, as well as being a marker of
53 co-existing pathologies,¹³⁻¹⁶ and is a predictor of poor prognosis in hospitalised patients.¹⁷⁻¹⁹
54 AKI is associated with increased risk of the development and progression of chronic kidney
55 disease (CKD), increased risk of readmission,²⁰ longer hospital stays and higher long term
56 mortality rates,¹⁹ even in patients with transient changes in renal function.²⁰ AKI therefore has
57 associated important long term socioeconomic and public health effects.

58 CDI is a healthcare-associated infection with significant associated morbidity and mortality²¹
59 that has been under mandatory surveillance in Scotland since 2006,²² and in England since
60 2004.²³ Antibiotic use is associated with an increased risk of CDI for at least 3 months
61 following administration.²⁴ In order to restrict the use of antibiotics associated with high risk
62 of CDI²⁵ NHS Tayside orthopaedic antibiotic prophylaxis was changed from cefuroxime to
63 gentamicin and flucloxacillin in October 2008. Following this, several studies indicated that
64 prophylaxis with flucloxacillin and gentamicin in orthopaedic patients was associated with a
65 significant increased rate of post-operative AKI.⁷⁻¹⁰ Most of these were uncontrolled before
66 and after studies, but one was a robust quasi-experimental analysis that found the same

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67 effect.⁷ In June 2012 within NHS Tayside, policy was changed from flucloxacillin and
68 gentamicin to co-amoxiclav.

69 This study aimed to assess whether the change in orthopaedic antibiotic prophylaxis policy
70 from flucloxacillin and gentamicin to co-amoxiclav was associated with changes in the rates
71 of post-operative AKI and CDI in adult patients undergoing orthopaedic surgery. The study
72 also aimed to assess the effect of post-operative AKI on length of hospital stay and one year
73 post-operative mortality.

74 **Ethical Approval**

75 Anonymised record linkage was conducted according to the Health Informatics Centre (HIC)
76 standard operating procedure. The Tayside Research Ethics Committee does not require
77 submission of individual studies that follow this standard operating procedure.

78 **Methods**

79 This study included all adults aged ≥ 18 years who resided, or died, in the NHS Tayside
80 region and, who underwent an orthopaedic surgical procedure requiring antibiotic
81 prophylaxis, between 1st October 2008, and 31st December 2013. Patients were identified by
82 the Office of Population, Censuses and Surveys Classification of Surgical Operations and
83 Procedures 4th revision (OPCS-4) codes²⁶ from hospital admissions data (Supplementary
84 Material, Table 1).

85 Table 1 shows the recommended antibiotics and doses in NHS Tayside before and after the
86 2012 policy change. Patients who underwent repair of a neck of femur (NOF) fracture
87 received co-amoxiclav as antibiotic prophylaxis throughout the period of observation
88 described here because of concerns raised by orthopaedic surgeons with regard to
89 administering gentamicin in this particular patient group.

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90 This study period encompassed 63 months between October 2008 and December 2013. The
91 study design was an interrupted time series (ITS) with segmented regression analysis²⁷ using
92 44 monthly time points before and 19 monthly time points after the intervention in June 2012.

93 **Definitions**

94 The definition of postoperative renal impairment used the Kidney Disease Improving Global
95 Outcomes (KDIGO) criteria.²⁸ (Supplementary Material Table 2) Patients with postoperative
96 AKI were classified according to their most severe degree of AKI. This was applied using
97 baseline serum creatinine as the pre-measurement (most recent in the year prior to surgery)
98 and maximal serum creatinine during the first 7 post-operative days as the post-measurement.

99 The definition of post-operative CDI was any case with a *Clostridium difficile* toxin positive
100 stool sample and/or polymerase chain reaction (PCR) for *Clostridium difficile* positive result
101 within 12 weeks post-operatively. Cases were excluded if there had been another positive
102 sample for *Clostridium difficile* toxin or PCR in the 12 weeks prior to this, due to the
103 possibility of this being a recurrence of CDI.

104 **Data Sources**

105 Data were provided by HIC²⁹ at the University of Dundee. Data were linked between the
106 following datasets: Community Health Index (CHI) register, Scottish Morbidity Record of
107 hospital admissions (SMR01), OPCS-coded procedures, laboratory results database,
108 medicines dispensed by community pharmacies, General Register Office death database and
109 Scottish Care Information – Diabetes Collaboration (SCI-DC).

110 Age, to the nearest year in the year of surgery, sex and social deprivation, the Scottish Index
111 of Multiple Deprivation (SIMD) which is linked to residential postal code, were obtained
112 from the CHI register. A Charlson Comorbidity Index (CCI)³⁰ score was calculated for each

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113 patient from hospital discharge codes and the number of medication types dispensed from
114 community pharmacies in the previous three months was applied as an additional measure of
115 comorbidity.

116 Exposure to medicines that predispose to renal impairment (NSAIDs, cyclooxygenase-2
117 inhibitors, angiotensin-converting enzyme inhibitors (ACE I), angiotensin II receptor
118 antagonists (ARB), diuretics, β -blockers, metformin, other hypoglycaemics and lipid
119 regulating medications), in the three months prior to the operation was ascertained from
120 dispensed prescribing data.

121 Baseline renal function was obtained from the laboratory database. This was the most recent
122 preoperative serum creatinine measurement in 12 months prior to and including the date of
123 operation, which could include preoperative samples taken during the current admission. The
124 median was calculated if there was more than one serum creatinine measurement taken on the
125 same day. Only patients with both preoperative and postoperative creatinine measurements
126 could be included. The completeness of creatinine data in each group was measured and
127 reported (Table 2). Patients already established on renal replacement therapy pre-operatively
128 were excluded from the analysis. In cases where a patient had a subsequent operation within
129 7 days of another operation, the second operation was excluded from the analysis.

130 **Statistical Analysis**

131 Monthly rates of AKI were defined by the number of patients with AKI as a proportion of all
132 patients aged ≥ 18 years undergoing orthopaedic surgery in each month. Rates were plotted
133 over time for descriptive purposes and the functional form of the relationship before and after
134 the intervention was assessed for linearity with splines. Kolmogorov - Smirnov test³¹ and the
135 Shapiro – Wilk test³² were used to check data were normally distributed. Segmented
136 regression analysis of ITS data was used to assess intervention effects on total AKI at 1, 6, 12
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137 and 18 months after the policy change, with 95% confidence intervals (95%CI)^{27, 31} and
138 models were assessed for first order autocorrelation using the Durbin–Watson statistic,³³ with
139 adjustment for autocorrelation using lag terms as required. The effect size at each time point
140 was converted to a relative percentage difference between the observed and predicted (if the
141 intervention had not happened) AKI rate.

142 To assess for the effect of factors other than policy change on total AKI rates multiple linear
143 regression was used to determine the effects of exposure to medicines that predispose to renal
144 disease, age, sex and CCI on all rates of AKI in the time periods before and after policy
145 change.

146 The monthly rates of CDI were too small to undergo ITS analysis. Due to there being no or
147 few cases in some months, rates of CDI were calculated using incidence rate ratios³⁴ (IRR)
148 and 95% CIs.

149 The median length of stay with IQR was calculated from data extracted from SMR01 data.

150 Death within 1 year of surgery was calculated as a percentage of all patients who had
151 undergone operations within each group, in patients with and without post-operative AKI.

152 All analyses were carried out in IBM SPSS (version 21) and SAS (version 9.2.1) software. A
153 p-value of <0.05 was considered statistically significant.

154 The analysis plan included information that addressed the common risks of bias in ITS
155 studies (Supplementary Material, Table 3).

156 **Results**

157 Data were provided for 14,563 potentially eligible orthopaedic operations in the study period
158 of October 1, 2008 to December 31, 2013. Of these, five duplicate cases were excluded.

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159 Cases were split into two groups, Group 1 (n=12707): patients who underwent orthopaedic
160 operations other than NOF repair, as identified by the International Statistical Classification
161 of Diseases and Related Health Problems ICD9/10 main condition codes, and Group 2
162 (n=1851): patients who underwent a NOF repair operation. Patients were excluded if they
163 were on the renal replacement register (Group 1 n=33 (0.26%), Group 2 n=8 (0.43%)), if the
164 operation was within 7 days of a previous operation (Group 1 n=22 (0.17%), Group 2 n=0) or
165 if creatinine data were missing (Group 1 n=3410 (26.8%), Group 2 n=81 (4.38%)). In total,
166 11,004 cases were included (Figure 1).

167 Compared to patients in the other orthopaedic operation group, patients in the NOF group
168 were older, were more likely to be female and had higher CCI scores (Table 1). However,
169 baseline creatinine was no worse in NOF patients compared with the other orthopaedic
170 operation group, median creatinine 69 $\mu\text{mol/L}$ (IQR 53-94) versus 68 $\mu\text{mol/L}$ (IQR 57-80)
171 respectively.

172 Table 1 includes the percentage of missing creatinine data within each sub-group. The
173 majority of missing creatinine measurements were post-operative. There were fewer missing
174 creatinine data for patients with NOF repair operations. An examination of the characteristics
175 of patients included *versus* patients who were excluded due to missing data showed that the
176 included patients were, on average, older patients with higher CCI comorbidity scores
177 (Supplementary Material, Table 4).

178 **Acute Kidney Injury**

179 The majority of AKI was mild (Stage 1) AKI (Table 2). Overall, AKI was more common in
180 the NOF repair patients (Group 2) and affected a slightly higher proportion overall in the
181 second study period, while Group 1 had a slightly lower proportion of patient with AKI in the
182 second study period (after prophylaxis changed).

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183 All other orthopaedic surgeries (Group 1)

184 The monthly proportion of patients with any stage of post-operative AKI in Group 1 fell
185 following the intervention (Figure 2A) and interrupted time series analysis indicated a
186 relative change of -63% (95% CI -77% to -49%) 18 months after the policy change (Table 3).

187 Multiple linear regression analyses were performed to assess for the effects of sex, age, CCI
188 and the use of other nephrotoxic drugs. In addition to the policy change only ACE I/ARB
189 were significantly associated with an increase in rates of post-operative AKI ($\beta=0.186$; 95%
190 CI, 0.03 to 0.342; $p=0.02$).

191 Neck of Femur repair (Group 2)

192 Over the whole period of observation AKI rates in this group were highest, and they had most
193 variation in the year preceding the change in antibiotic policy for the other group (Figure 2B).
194 From interrupted time series analysis, there were statistically significant reductions in AKI
195 rates in the following year but these were much smaller relative changes than in Group 1 and
196 there was no significant change at 18 months after the policy change -10%, (95% CI -35% to
197 15%, Table 3).

198 Multiple linear regression analyses were performed to assess for the effects of sex, age, CCI
199 and the use of other nephrotoxic drugs. Only ACE I/ARB were significantly associated with
200 an increase in rates of post-operative AKI ($\beta=0.2520$; 95% CI, 0.04 to 0.464; $p=0.02$).

201 **Other outcomes**

202 Death within 1 year of surgery

203 A higher proportion of patients with AKI died within 1 year of surgery compared with
204 patients without AKI in both the NOF operations group 36.63% (n=89) versus 25.15%

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205 (n=382), respectively (chi-square=14.09 df=1 p<0.001) and the other orthopaedic operations
206 group 10.48% (n=108) versus 5.18% (n=425), respectively (chi-square=47.33 df=1 p<0.001).

207 Length of hospital stay

208 In the other orthopaedic operations group the median length of hospital stay was 6 days (IQR
209 11-3) in patients with post-operative AKI compared with 5 days (IQR 9-3) in patients without
210 post-operative AKI. In the NOF repair operation group was 7 days (IQR 11-4) in patients
211 with post-operative AKI compared with 6 days (IQR 10-3) in patients without post-operative
212 AKI.

213 *Clostridium difficile* infection and SSI Rates

214 There was no change in the rate of CDI before and after the policy change in either group.
215 The CDI IRR (95% CI) for the NOF repair group was 0.76 (0.28 to 2.08) and for other
216 operations was 0.29 (0.09 to 0.96).

217 Audits of SSI rates were not done consistently for all types of surgery in the study population
218 throughout the study period; however the SSI rates among the procedures audited were low
219 throughout the study period with no apparent change in rate accompanying the policy
220 changes

221 **Discussion**

222 This large observational study of >14,500 patients, found that a change in prophylactic
223 antibiotic policy from flucloxacillin and gentamicin to co-amoxiclav was associated with
224 decreased rates of post-operative AKI in patients undergoing orthopaedic surgeries
225 (excluding NOF repairs) in the NHS Tayside Region of Scotland, with the majority of
226 patients developing mild (Stage 1) AKI. The association with the change in antibiotic policy

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227 is strengthened because there were much smaller reductions in monthly AKI rates among
228 patients who underwent NOF repair, who received co-amoxiclav throughout the study period,
229 and the change at 18 months post policy change was not significant in this group. There was
230 no change in CDI rates associated with the change in antibiotic policy.

231 We have shown a reduction in all stages of post-operative AKI by -63% (95% CI -77%,-
232 49%) at 18 months post antibiotic policy change statistically significantly associated with that
233 change in policy. There are likely to be other factors also contributing to the change in rates
234 of AKI, supported by the (smaller magnitude and not significant at 18 months) reduction in
235 NOF patients who were not affected by the policy change. Such factors include anaesthetic
236 practice and post-operative care, such as the Enhanced Recovery Programme, which aims to
237 optimise pre- and post-operative care including reducing the physical stress of the operation,
238 promoting effective analgesia and encouraging early mobilisation and oral nutrition. This
239 programme may lead to an increase in rates of post-operative AKI, as patients may be
240 exposed to more nephrotoxic analgesics and less fluid replacement in the post-operative
241 period than before. There has also been ongoing work throughout our institutions, educating
242 healthcare professionals around recognition, prevention and management of AKI.

243 The causes of AKI are multifactorial and reported incidence varies dependent on the
244 definition used, as well variations in population groups and settings³⁵. The incidence of AKI
245 in acute hospitalised patients is 5-7.5%, with 30-40% of cases occurring in the surgical
246 perioperative period.^{36, 37} This is an important contributor to post-operative morbidity and
247 mortality³⁵ and research suggests that up to 30% of AKI is iatrogenic and/or potentially
248 preventable.³⁸ The KDIGO AKI guidelines state that major surgery and trauma are exposures
249 for non-specific AKI, where there is no specific kidney disease causing AKI.²⁸ Therefore, it
250 is important that these patients have their serum creatinine and urine output measured

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251 alongside their clinical status. In line with previous recommendations⁷ patients receiving
252 surgical antibiotic prophylaxis are generally undergoing major surgery and, as a minimum,
253 should have serum creatinine measured both pre-operatively and at least 24 hours post-
254 operatively.

255 The unadjusted one year post-operative mortality was higher in patients who had undergone
256 an NOF repair surgery when compared with those having undergone other orthopaedic
257 surgeries. Within each subgroup crude 1 year post-operative mortality was higher among
258 those with post-operative AKI than those without. This is consistent with the previous
259 findings, including this cohort that AKI contributes to higher mortality.^{16, 19, 36-38} We did not,
260 however, find any difference in length of hospital stay, when comparing patients with and
261 without AKI, which may be because the majority of AKI were stage 1 and it is possible that
262 AKI was not detected until after the patient was discharged so did not impact on inpatient
263 management. The potential implications of reduced rates of AKI include reduced mortality,
264 readmission to hospital, progression to CKD and the subsequent socio-economic costs, that
265 have previously been identified in the literature.²⁰

266 There was no change in CDI rates in either group, suggesting that this is not related to
267 changes in surgical prophylactic antibiotic policy. Restrictions on the use of therapeutic
268 antibiotics considered high-risk for CDI, which are used for longer durations, have
269 contributed, alongside infection control procedures and a change in circulating strains and
270 virulence of *Clostridium difficile*,^{12, 39} to a reduction in rates of CDI.⁴⁰

271 Effective restrictions on the use of therapeutic antibiotics associated with high risk for CDI
272 have also been shown in the orthopaedic surgery population, without a subsequent effect on
273 rates of deep SSI.⁴¹ Rates of CDI across the UK have fallen. By 2013, in Scotland there had

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274 been reductions in CDI of greater than 79% since 2007/08⁴² and in 2013/14, England
275 reported a reduction in CDI of 76% compared with 2007/08.⁴³

276 Prophylactic antibiotics in orthopaedic implant surgery reduces the risk of SSI.³ In an ageing
277 population, it is likely that the number of orthopaedic operations is going to increase,
278 exposing more individuals to prophylactic antibiotics. Any prophylactic antibiotic should aim
279 to reduce SSI rates, providing cover for commonly implicated pathogens and considering
280 local resistance patterns, while also minimising the associated risks of AKI, CDI, antibiotic
281 resistance and allergies. SSI, AKI and CDI are interlinked. The management of SSI is
282 antibiotic therapy. SSI in severe cases can lead to sepsis. Both exposure to certain antibiotics
283 and sepsis have been identified as risk factors for non-specific AKI.²⁸ Further antibiotic
284 exposure would also put patients at an increased risk of CDI,²⁴ which itself may result in a
285 patient becoming dehydrated, another susceptibility for non-specific AKI.²⁸ It is therefore
286 important to ensure that intended and unintended consequences of changes in policy are
287 balanced.

288 The strengths of our study are that we used a robust quasi-experimental study design to
289 evaluate a real-world policy change, addressed risks of bias for ITS studies in our analysis
290 plan (Supplementary Material, Table 2), defined operations using OPCS-4 operation
291 procedure codes (Supplementary Material, Table 3), defined NOF cases using ICD9/10
292 codes, and used the KDIGO definition of AKI.

293 We addressed the issues common to all non-randomised studies, including potential
294 ascertainment and selection biases. Data were prospectively entered into electronic databases
295 and were not subject to manipulation or bias. ITS is the strongest quasi-experimental design
296 to assess intervention effects in non-randomised setting. It allows for control of trends that

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297 exist before the intervention being studied, by using multiple time points before and after the
298 intervention.^{44, 45}

299 A weakness of our study is that we were unable to adjust for potential effects of
300 intraoperative events and other medications prescribed during in-patient stay on AKI rates
301 because these data are not collected electronically. Furthermore, it is possible that the
302 changes in diagnostic criteria and methods could have masked a true decrease in CDI
303 incidence over the study period.

304 Rates of post-operative AKI were not assessed in 4% of the NOF repair surgery group and
305 27% of the other orthopaedic operations group because of missing pre-operative and post-
306 operative creatinine data. These patients were younger and had less comorbidity when
307 compared with patients who were included in the study. This could bias the results in either
308 direction of estimating the rates of AKI. However, there were similar percentages of missing
309 creatinine data in the pre-intervention and post-intervention groups.

310 Previous literature showed that a prophylactic antibiotic regimen of flucloxacillin and
311 gentamicin in orthopaedic patients was associated with a significant increased rate of AKI.
312 From the previous research carried out by our group it is not clear whether gentamicin or
313 flucloxacillin or both antibiotics increased the risk of post-operative AKI, or by what
314 mechanism.⁷ However, this study has shown that using co-amoxiclav for antibiotic
315 prophylaxis in orthopaedic surgery is associated with a decreased rate of post-operative AKI
316 compared to flucloxacillin and gentamicin and is not associated with an increased rate of
317 CDI. This study also raises the importance of monitoring the intended and unintended
318 consequences of policy change within healthcare.

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326 **Transparency declaration**

327 None to declare.

328

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Table 1. Baseline characteristics and missing creatinine data

Characteristic	Operations other than NOF repair		NOF repair operations	
	Before 2012 policy change	After 2012 policy change	Before 2012 policy change	After 2012 policy change
Recommended antibiotics (dose)	Flucloxacillin (1g) x 4 doses + one dose Gentamicin (4mg/kg)	3 doses Co-amoxiclav (1.2g)	3 doses Co-amoxiclav (1.2g)	3 doses Co-amoxiclav (1.2g)
Patients (n)	6267	2975	1250	512
Mean Age (yr) (SD)	68.5 (14)	68.9 (13.6)	80 (11.4)	80.6 (10.2)
Median Baseline SCr ($\mu\text{mol/L}$) (IQR)	74 (62-88)	68 (57-80)	72 (57-94)	69 (53-94)
Sex n(%)				
Female	3619 (57.7)	1774 (59.6)	914 (73.1)	372 (72.7)
Male	2648 (42.3)	1201 (40.4)	336 (26.9)	140 (27.3)
SIMD n(%)				
1-3 (most deprived)	1212 (19.3)	573 (19.3)	244 (19.5)	113 (22.1)
4-7	2679 (42.7)	1299 (43.7)	545 (43.6)	217 (42.4)

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8-10 (least deprived)	2269 (36.2)	1044 (35.1)	444 (35.5)	171 (33.4)
CCI n(%)				
Low (0)	5282 (84.3)	2317 (77.9)	789 (63.1)	303 (59.2)
Medium (1 or 2)	870 (13.9)	584 (19.6)	400 (32)	183 (35.7)
High (≥3)	115 (1.8)	74 (2.5)	61 (4.9)	26 (5.1)
Patients before missing creatinine exclusions n(%)*	8515	4137	1304	539
Missing pre-operative creatinine	453 (5.32)	192 (4.64)	7 (0.54)	4 (0.74)
Missing post-operative creatinine	1995 (23.43)	1039 (25.11)	49 (3.76)	22 (4.08)
Missing both pre and post-operative creatinine	405 (4.76)	173 (4.18)	4 (0.31)	2 (0.37)

* Data are presented as n (%) of all patients after exclusion of duplicates, patients on RRT and subsequent operation within 7 days

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Table 2. AKI rates by each stage

AKI Stage n(%)	Operations other than NOF repair		NOF repair operations	
	Before 2012 policy change	After 2012 policy change	Before 2012 policy change	After 2012 policy change
1	618 (9.86)	239 (8.03)	153 (12.24)	67 (13.09)
2	95 (1.52)	22 (0.74)	16 (1.28)	4 (0.78)
3	45 (0.72)	12 (0.4)	2 (0.16)	1 (0.2)
None	5509 (87.9)	2702 (90.8)	1079 (86.32)	440 (85.94)

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Table 3. ITS analyses intervention effects at 1, 6, 12 and 18 months post-policy change for other orthopaedic operations and NOF repair operations, all AKI Stages (Rate per 100 patients)

	Operations other than NOF repair				NOF repair operations			
	1 month	6 months	12 months	18 months	1 month	6 months	12 months	18 months
Absolute difference	-6.1	-8.2	-10.6	-13.1	-4.7	-3.8	-2.8	-1.8
95% CI	(-9.7,-2.6)	(-11.2,-5.2)	(-13.9,-7.4)	(-17.3,-8.9)	(-8.8,-0.5)	(-7.3,-0.4)	(-6.5,0.8)	(-6.6,3.0)
Relative change	-36.0%	-45.2%	-54.8%	-63.2%	-28.7%	-22.8%	-16.1%	-10.0%
95% CI	(-54.6%,-17.4%)	(-57.7%,-32.6%)	(-65.3%,-44.3%)	(-77.3%,-49.1%)	(-52.2%, -5.3%)	(-40.8%, -4.8%)	(-34.6%, 2.3%)	(-34.7%, 14.8%)

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Figure 1: Summary of case groupings and exclusions

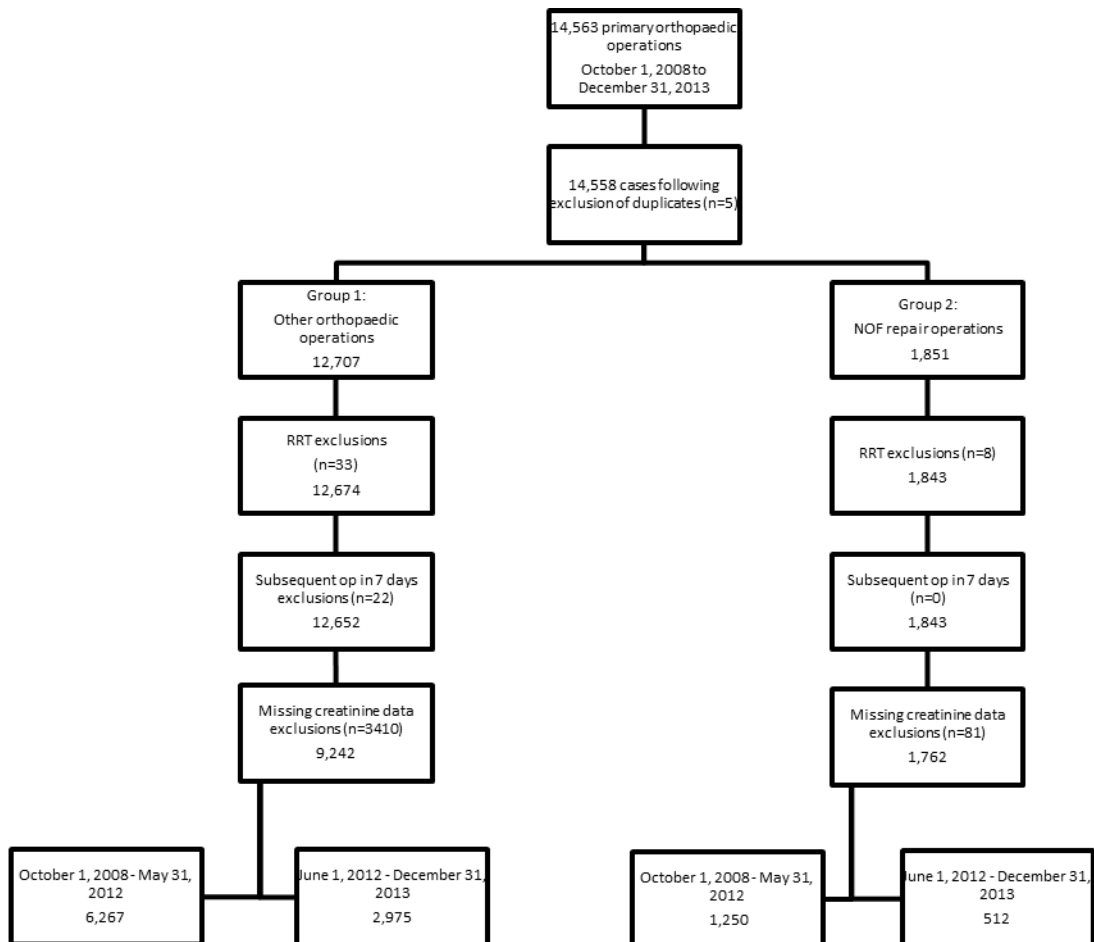


Figure 2A: AKI (Stages 1-3 combined) in orthopaedic operations other than NOF repair from October 2008 to December 2013. The Policy Change was from flucloxacillin plus gentamicin to co-amoxiclav for antibiotic prophylaxis.

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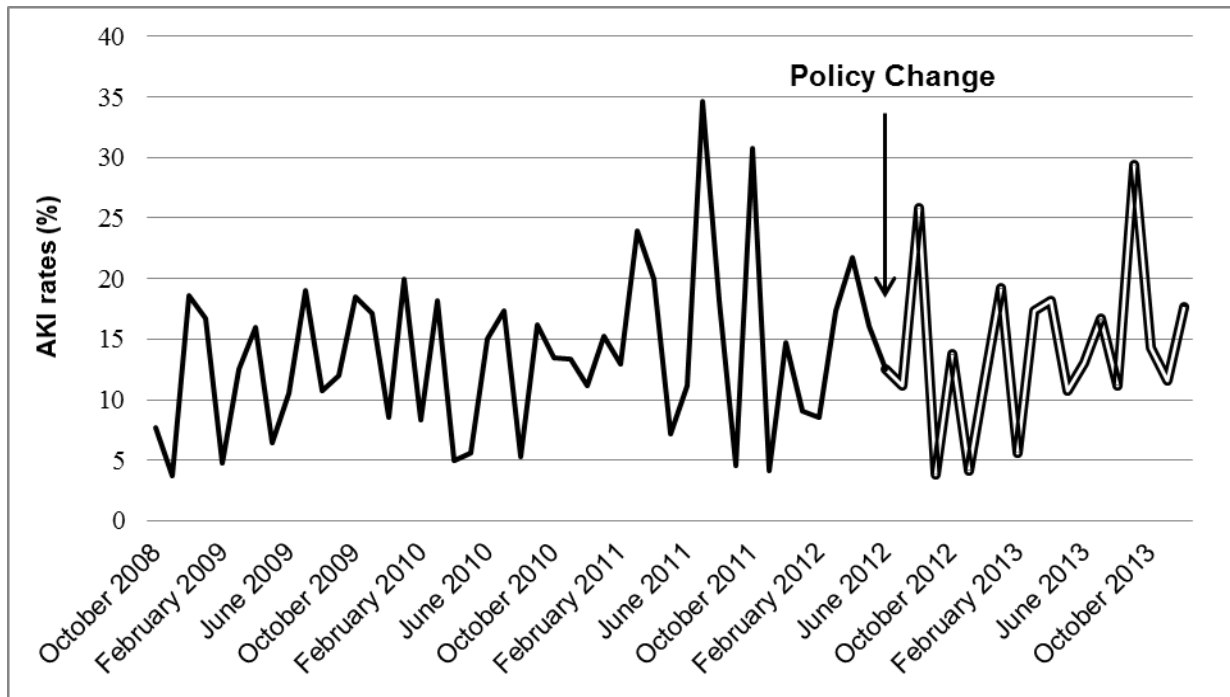


Figure 2B: AKI (Stages 1-3 combined) in NOF repair operations from October 2008 to December 2013 with co-amoxiclav the recommended antibiotic prophylaxis throughout. The Policy Change was for operations other than NOF repair.