Trends in orthopaedic antimicrobial prophylaxis in the UK between 2005 and 2011

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ABSTRACT

INTRODUCTION  Antimicrobial prophylaxis remains the most powerful tool used to reduce infection rates in orthopaedics but the choice of antibiotic is complex. The aim of this study was to examine trends in antimicrobial prophylaxis in orthopaedic surgery involving the insertion of metalwork between 2005 and 2011.

METHODS  Two questionnaires (one in 2008 and one in 2011) were sent to all National Health Service trusts in the UK using the Freedom of Information Act.

RESULTS  In total, 87% of trusts that perform orthopaedic surgery responded. The use of cefuroxime more than halved between 2005 and 2011 from 80% to 36% and 78% to 26% in elective surgery and trauma surgery respectively. Combination therapy with flucloxacillin and gentamicin rose from 1% to 32% in elective and 1% to 34% in trauma surgery. Other increasingly popular regimes include teicoplanin and gentamicin (1% to 10% in elective, 1% to 6% in trauma) and co-amoxiclav (3% to 8% in elective, 4% to 14% in trauma). The majority of changes occurred between 2008 and 2010. Over half (56%) of the trusts stated that Clostridium difficile was the main reason for changing regimes.

CONCLUSIONS  In 2008 a systematic review involving 11,343 participants failed to show a difference in surgical site infections when comparing different antimicrobial prophylaxis regimes in orthopaedic surgery. Concerns over C difficile and methicillin resistant Staphylococcus aureus have influenced antimicrobial regimes in both trauma and elective surgery. Teicoplanin would be an appropriate choice for antimicrobial prophylaxis in both trauma and elective units but this is not reflected in its current level of popularity.

KEYWORDS  Antimicrobial prophylaxis – Infection – Orthopaedics

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Infection prevention in orthopaedic surgery is a multifactorial process. Strict theatre protocols, antimicrobial use systemically or in bone cement, ultraclean air/laminar flow theatres, body exhaust suits and bacteriologically occlusive gowns are all methods used to reduce infection rates. This is particularly the case in orthoplastic surgery. Given the low incidence of prosthetic joint infections, it has been difficult to prove effectiveness of any of these measures but evidence suggests that antimicrobial prophylaxis is the most powerful method for preventing infection.

Antimicrobial prophylaxis has been used in orthopaedic surgery since the 1950s but it was not until 1970, when Fogelberg et al demonstrated a reduction in postoperative infections, that clinical evidence supported the accepted theory. This clinical evidence was further substantiated by two randomised double blinded clinical trials proving that antimicrobial prophylaxis, with sodium nafcillin or cephaloridine, reduced postoperative infection rates in orthopaedic surgery when compared directly with placebos. More recently, a systematic review involving 26 randomised controlled trials (11,343 participants) failed to show superiority of any particular antimicrobial prophylaxis regime.

Cephalosporins remain the first choice of many international guidelines for antimicrobial prophylaxis in orthopaedic surgery. This has been due to their safety profile, broad spectrum, tissue penetration, price and their early proven effectiveness in clinical trials. Some have cited marketing and habit as reasons for widespread use of cephalosporins. The American Academy of Orthopaedic Surgeons recommends either cefuroxime or cefazolin as the first line antimicrobial for patients undergoing arthroplasty procedures. Cephalosporins are active against many Gram positive and anaerobic organisms with subsequent generations expanding its Gram negative coverage. Their broad range of microbial cover includes the most common microorganisms encountered in orthopaedic surgery.

A survey by Leach and Wilson in 1990 revealed that 86% of Scottish orthopaedic surgeons were using cephalosporins.

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as prophylaxis for elective hip replacements. A similar survey of Canadian orthopaedic surgeons during 2004–2005 revealed that 97% of respondents employed a first generation cephalosporin in total joint arthroplasty. The aim of this study was to examine trends in antimicrobial prophylaxis regimes in elective and trauma orthopaedic surgery (involving the insertion of metalwork) from 2005 to 2011, and to identify factors (if any) that precipitated changes in prophylactic regimes.

Methods
Using the Freedom of Information Act, two separate questionnaires were sent to all 195 acute care National Health Service (NHS) trusts in the UK. The first was distributed during 2008 and the second during 2011. The questions included were:

1. Which antimicrobial regime is used for routine prophylaxis in trauma orthopaedic surgery? Please specify dose(s) and time(s) of administration.
2. Which antimicrobial regime is used for routine prophylaxis in elective orthopaedic surgery? Please specify dose(s) and time(s) of administration.
3. Has there been any change in antibiotic or regimen used in the last three years? If ‘yes’:
   - When was it changed?
   - Why was it changed?
   - What was the previous regimen?
4. Which antimicrobial regime is used if the patient is allergic to penicillin? Please specify dose(s) and time(s) of administration.

This information was used to create a timeline of which antimicrobial prophylaxis regimes were used between 2005 and 2011 across all UK trusts conducting elective and trauma orthopaedic surgery.

Results
Information collected was divided to define regimes used across a seven-year period encompassing three checkpoints (2005, 2008 and 2011). Of all the UK trusts conducting elective orthopaedic surgery, defined regimes were identified for 152/172 (88%) in 2005, 157/172 (91%) in 2008 and 136/173 (79%) in 2011. For trusts conducting trauma orthopaedic surgery, responses were 151/166 (91%) in 2005, 155/166 (93%) in 2008 and 135/166 (81%) in 2011. The cumulative response rate was 87% of UK trusts.

Elective orthopaedic surgery
Table 1 shows all elective orthopaedic regimes used during 2005, 2008 and 2011. In 2005, 15 different regimes were employed. The top three regimes used were cefuroxime alone (79.6%), other cephalosporins (5.3%) and co-amoxiclav (2.6%). At this time, regimes using fluocoxacillin or teicoplanin were in the minority. Two trusts had no formal antimicrobial prophylaxis regime defined in 2005. In 2008, the number of different potential regimes used increased to 18. The top three were cefuroxime alone (59.9%), fluocoxacillin plus gentamicin (15.9%) and co-amoxiclav (5.1%). In 2011, 18 different regimes were used. The top three regimes were cefuroxime alone (56.0%), fluocoxacillin plus gentamicin (32.4%) and teicoplanin plus gentamicin (9.6%).

Fifty-eight trusts did not change their elective orthopaedic antimicrobial prophylaxis regime across the seven-year period. Between 2005 and 2011, elective antimicrobial prophylaxis regimes changed a total of 88 times (Table 2). The most popular regime adopted was fluocoxacillin plus gentamicin (35.7%) while 12.5% changed to teicoplanin plus gentamicin and 11.4% changed to co-amoxiclav alone. The majority of the trusts that changed regimes moved away from cefuroxime (63/88, 71.6%).

During the study period, 2008 proved to be the year that had the most changes of elective antimicrobial prophylaxis regimes, with 27 trusts (31%) changing their antimicrobial prophylaxis policy (Fig 1). In 2010, 19 trusts (22%) changed their policy. Owing to poor response quality, it was unclear when five of the trusts changed their regime.

Trauma orthopaedic surgery
Table 3 shows all trauma orthopaedic surgery antimicrobial prophylaxis regimes used during 2005, 2008 and 2011. In 2005, 15 different regimes were used. The top three regimes used were cefuroxime alone (77.5%), other cephalosporins (4.6%) and co-amoxiclav (4.0%). During this time, antimicrobial prophylaxis using fluocoxacillin or teicoplanin was infrequent. Two trusts had no formal antimicrobial prophylaxis regime defined during 2005.

The total number of different antimicrobial prophylaxis regimes increased in 2008 to 20. The top regimes were cefuroxime alone (55.3%), fluocoxacillin plus gentamicin (15.5%) and co-amoxiclav (9.7%).

In 2011, 25 different regimes were used. The top three regimes were fluocoxacillin plus gentamicin (54.1%), cefuroxime alone (25.9%) and co-amoxiclav (14.1%).
Forty-one trusts did not change their trauma orthopaedic antimicrobial prophylaxis regime across the seven-year period. During this time, the use of cefuroxime or other cephalosporins alone reduced from 82.1% to 26.6%. The use of flucloxacillin plus gentamicin rose from 1.3% in 2005 to 34.1% in 2011 and was the most popular antimicrobial prophylaxis regime.

Trauma orthopaedic surgical antimicrobial prophylaxis regimes changed a total of 100 times during the study period (Table 2). The most popular regime adopted was flucloxacillin plus gentamicin (50.0%) while 18.0% changed to co-amoxiclav alone and 6.0% to teicoplanin plus gentamicin. The majority of trusts that changed regimes moved away from cephalosporins (83/100, 83.0%).

As for elective surgery regimes, 2008 also proved to be the year that had the most changes of trauma antimicrobial prophylaxis regimes (Table 1). The most common reported reason was association/fear of Clostridium difficile. This was reported by 55.5% of elective and 56.0% of trauma units. The desire to reduce cephalosporin use (11.4% elective, 10.0% trauma) and advice from microbiology departments (8.0% elective, 8.0% trauma) were the second and third most common reasons.

Reasons for changing orthopaedic antimicrobial prophylaxis regimes varied across elective and trauma units (Table 4). The most common reported reason was association/fear of Clostridium difficile. This was reported by 55.5% of elective and 56.0% of trauma units. The desire to reduce cephalosporin use (11.4% elective, 10.0% trauma) and advice from microbiology departments (8.0% elective, 8.0% trauma) were the second and third most common reasons.

Penicillin allergy
Table 5 shows all the antimicrobial prophylaxis regimes used in 2008 and 2011 for patients with penicillin allergy. In 2008 in elective surgery, the most popular regime was teicoplanin plus gentamicin (21.2%). This increased to 41.5% in 2011. In trauma surgery, a similar pattern was evident with teicoplanin plus gentamicin used most frequently in 2008 (20.8%) and in 2011 (39.4%). Vancomycin and cefuroxime use reduced over this time period. In 2011 teicoplanin alone or in combination with gentamicin constituted 60.2% of elective and 65.8% of trauma antimicrobial prophylaxis regimes.
Discussion

During the late 1990s and up to the early 2000s, 86–97% of hospitals across the developed world were using cephalosporins as antimicrobial prophylaxis for elective orthopaedic surgery.16–19 This study shows a gradual decline in the use of cephalosporins in the UK, in both elective orthopaedics (85% to 38%) and trauma orthopaedic surgery (82% to 27%).

Systematic reviews of randomised controlled trials have not shown any difference in prosthetic joint infection rates when comparing cephalosporin, teicoplanin and penicillin derivatives as antimicrobial prophylaxis.11,20 These may be essential findings to justify the use of new antimicrobial prophylaxis regimes in arthroplasty surgery but issues including resistance patterns, methicillin resistant Staphylococcus aureus (MRSA) and C difficile infections may also affect antibiotic choice. Studies have highlighted cost and local availability as other key concerns when selecting an antimicrobial prophylaxis regime.11,20

Concluding studies have advised against single centre comparisons of orthopaedic antimicrobial prophylaxis given the large number of patients required to show any significant difference in surgical site infection (SSI) rates.11 For example, to demonstrate a reduction in infection rate from 2% to 1% with a power of 90%, at the 95% confidence interval, a study would need over 5,000 patients per group.

MRSA

Patients colonised with MRSA have a higher risk of SSI than other orthopaedic admissions.21 Cephalosporins are of little use in the prevention of MRSA infections22 and the American Academy of Orthopaedic Surgeons recommendations advise the addition of vancomycin in patients who are known to be colonised with MRSA or in response to an MRSA outbreak.15

Over the past decade, an increase in acquired MRSA skin and soft tissue infections has been demonstrated in American communities.23,24 In contrast, according to European Antimicrobial Resistance Surveillance Network reports, the propor-
tion of MRSA infections has remained static across Europe since 2009.25,26 The UK Health Protection Agency’s microorganism breakdown also shows that over two separate time periods the percentage of MRSA prosthetic joint infections has remained static.27 In the UK between 2004 and 2008, 26.6% of prosthetic joint infections were due to MRSA, and between 2008 and 2010 the incidence was 26.0%. This suggests that infection control measures, in hospitals and in the community, have successfully controlled the growth of MRSA infections. However, given the morbidity and mortality associated with infection, MRSA remains a significant pathogen against which orthopaedic surgeons must remain vigilant.

There have been doubts regarding the accuracy of prescreening for MRSA in elective admissions. One study showed that almost 10% of elective orthopaedic patients who were MRSA negative at preassessment were in fact MRSA positive on admission to the ward.28 In the trauma setting, its has been shown that up to 86% of neck of femur fracture patients reach the operating theatre before MRSA screening results are obtained.29

### Table 3. Antimicrobial prophylaxis regimes used by UK NHS trusts for trauma orthopaedic surgery (involving prosthetic joint insertion/insertion of metalwork)

| Antimicrobial regime used                        | Number of trusts |
|------------------------------------------------|------------------|
| **2005**                                        | **2008**         | **2011**        |
| Cefuroxime                                      | 117 (77.5%)      | 83 (53.5%)      | 35 (25.9%)      |
| Cefuroxime + gentamicin                        | 3 (2.0%)         | 1 (0.6%)        | 1 (0.7%)        |
| Cefuroxime +/- teicoplanin                      | –                | 1 (0.6%)        | 1 (0.7%)        |
| Cefuroxime + metronidazole                      | 3 (2.0%)         | 3 (1.9%)        | –               |
| Cefuroxime + teicoplanin + metronidazole        | 1 (0.7%)         | 1 (0.6%)        | –               |
| Other cephalosporins                            | 7 (4.6%)         | 5 (3.2%)        | 1 (0.7%)        |
| Flucloxacillin                                  | 1 (0.7%)         | 3 (1.9%)        | 5 (3.7%)        |
| Flucloxacillin + gentamicin                     | 2 (1.3%)         | 24 (15.5%)      | 46 (34.1%)      |
| Flucloxacillin + benzylpenicillin               | –                | –               | 1 (0.7%)        |
| Flucloxacillin + teicoplanin                    | –                | –               | 1 (0.7%)        |
| Flucloxacillin + teicoplanin + metronidazole    | 1 (0.7%)         | 1 (0.6%)        | 1 (0.7%)        |
| Flucloxacillin + benzylpenicillin + gentamicin  | –                | 1 (0.6%)        | 1 (0.7%)        |
| Flucloxacillin + gentamicin + metronidazole     | –                | 1 (0.6%)        | 1 (0.7%)        |
| Teicoplanin                                     | –                | –               | 1 (0.7%)        |
| Teicoplanin + gentamicin                        | 2 (1.3%)         | 3 (1.9%)        | 8 (5.9%)        |
| Teicoplanin + metronidazole                     | –                | –               | 1 (0.7%)        |
| Teicoplanin + ceefadine                         | –                | 1 (0.6%)        | –               |
| Co-amoxiclavit                                  | 6 (4.0%)         | 15 (9.7%)       | 19 (14.1%)      |
| Co-amoxiclavit + gentamicin                     | 1 (0.7%)         | 4 (2.6%)        | 3 (2.2%)        |
| Amoxicillin + gentamicin                        | 1 (0.7%)         | 1 (0.6%)        | 1 (0.7%)        |
| Piperacillin/tazobactam + gentamicin            | –                | –               | 1 (0.7%)        |
| Ertapenem                                       | –                | 1 (0.6%)        | 1 (0.7%)        |
| Vancomycin                                      | –                | –               | 1 (0.7%)        |
| Vancomycin + gentamicin                         | 1 (0.7%)         | 2 (1.3%)        | –               |
| Cefuroxime or flucloxacillin                    | 1 (0.7%)         | 1 (0.6%)        | 1 (0.7%)        |
| Cefuroxime or flucloxacillin + gentamicin       | –                | –               | 1 (0.7%)        |
| Cefuroxime or teicoplanin                       | –                | –               | 1 (0.7%)        |
| Cefuroxime or co-amoxiclavit                     | 2 (1.3%)         | 2 (1.3%)        | 1 (0.7%)        |
| Flucloxacillin or vancomycin or co-amoxiclavit   | –                | –               | 1 (0.7%)        |
| Nil formal                                      | 2 (1.3%)         | 1 (0.6%)        | –               |
| **Total responses**                             | **151**          | **155**         | **135**         |
Clostridium difficile

It was during the 1980s that an association between antimicrobial prophylaxis in orthopaedic surgery and the development of *C difficile* associated diarrhoea was noted.30–32 Higher numbers of *C difficile* infections were noted in institutes using clindamycin or cephalosporins as antimicrobial prophylaxis.33 The widespread use of these antibiotics was criticised by the microbiology community and their use was restricted in hospital settings. Studies revealed that the use of cephalosporins was an important predisposing factor for the development of *C difficile* infections and the restriction of cephalosporins has reduced *C difficile* outbreaks.33,34

The overall incidence of *C difficile* infection in orthopaedic trauma patients has been reported as being 0.6%35 but incidences of 4–6% have been reported in the fractured neck of femur cohort.36,37 *C difficile* is far less of a problem among elective orthopaedic patients than trauma orthopaedic patients, with reported incidences of 0.1–0.17%.35,38 Jenkins *et al* concluded that, given the low incidence of *C difficile* in arthroplasty patients, cephalosporins were a safe option as antimicrobial prophylaxis in elective surgery.38

*C difficile* continues to be an important cause of morbidity and mortality in orthopaedic trauma patients and measures must be put in place to reduce risk factors.39 We have demonstrated previously how trusts changing away from cephalosporins reduced their *C difficile* infection rates in orthopaedic surgery significantly.39 Al-Obaydi *et al* mirrored this message after a change away from cefuroxime in a single unit reduced *C difficile* infections.39

Teicoplanin

Teicoplanin is a glycopeptide antimicrobial agent that offers high soft tissue and bone penetration. Concentration of teicoplanin in bone reaches 65% of serum concentration, with a peak occurring between 0.5 and 6 hours after intravenous administration.40

Four randomised controlled trials have compared joint infection rates in patients undergoing total hip and knee arthroplasty who received teicoplanin versus a cephalosporin (cefaclorin, cefamandole or cefuroxime).41–44 No individual trial showed a significant difference in infection rates and a summarising study that pooled data also showed there was no significant difference in infection rates.40 Furthermore, the regional use of teicoplanin in total knee arthroplasty following tourniquet inflation has been proven to be effective.45

We have shown that the use of teicoplanin alone or in combination with gentamicin increased from 2.0% to 10.3% in elective surgery and from 1.3% to 6.7% in trauma surgery between 2005 and 2011. This regime is not as popular as one may have envisaged given the ease of use, effectiveness against SSI, coverage of common orthopaedic pathogens and benefits in treating MRSA. These clinical advantages are also mirrored with a financial change with a reduction in the price of teicoplanin from £52.40 in 199546 to £6.00 in 2011.47

Study limitations

Our study was based on a national questionnaire distributed, via the Freedom of Information Act, to all UK NHS trusts. Consequently, the information presented is dependent on the quality and accuracy of responses received. The average response rate across the three checkpoint years was 87%. Failure of some hospitals to respond does reduce the accuracy of our results but we feel that an 87% response rate from across the UK provides an acceptable representation of current UK practice. The trends in antimicrobial prophylaxis...
TRENDS IN ORTHOPAEDIC ANTIMICROBIAL PROPHYLAXIS IN THE UK BETWEEN 2005 AND 2011

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Conclusions

Over the past seven years, the use of cephalosporin as orthopaedic antimicrobial prophylaxis has declined in the UK. This is likely to be due to multiple factors but in orthopaedic trauma surgery concerns over C difficile appear to have driven this change. MRSA and antimicrobial resistance patterns will continue to affect antimicrobial prophylaxis regimes in the future. Flucloxacillin or teicoplanin based regimes are becoming more popular, with teicoplanin having the added advantage of MRSA coverage. No regime has been proven to reduce SSI over any other and this may be a target for future research to provide evidence for the ideal prophylaxis regime.

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Table 5

The antimicrobial prophylaxis regimes used in orthopaedic surgery (involving the insertion of metalwork) in patients with penicillin allergy

| Antimicrobial regime | Number of elective trusts | Number of trauma trusts |
|----------------------|---------------------------|-------------------------|
|                      | 2008  | 2011  | 2008  | 2011  |
| Vancomycin           | 25 (17.1%) | 12 (9.2%) | 25 (17.4%) | 11 (8.7%) |
| Vancomycin + gentamicin | 6 (4.1%) | – | 4 (2.8%) | – |
| Teicoplanin          | 26 (17.8%) | 36 (27.7%) | 24 (16.7%) | 31 (24.4%) |
| Teicoplanin + gentamicin | 31 (21.2%) | 54 (41.5%) | 30 (20.8%) | 50 (39.4%) |
| Teicoplanin + gentamicin + metronidazole | – | – | 1 (0.7%) | 2 (1.6%) |
| Erythromycin         | 11 (7.5%) | 4 (3.1%) | 11 (7.6%) | 4 (3.1%) |
| Clarithromycin       | 2 (1.4%) | 5 (3.8%) | 2 (1.4%) | 3 (2.4%) |
| Clarithromycin + gentamicin | – | – | – | 1 (0.8%) |
| Clindamycin          | 2 (1.4%) | 2 (1.5%) | 2 (1.4%) | 3 (2.4%) |
| Clindamycin + gentamicin | 1 (0.7%) | 2 (1.5%) | 1 (0.7%) | 3 (2.4%) |
| Gentamicin           | 8 (5.5%) | 4 (3.1%) | 8 (5.6%) | 4 (3.1%) |
| Ertapenem            | 1 (0.7%) | 1 (0.8%) | 1 (0.7%) | 1 (0.8%) |
| Cefuroxime           | 24 (16.4%) | 4 (3.1%) | 25 (17.4%) | 5 (3.9%) |
| Cefuroxime + gentamicin | 1 (0.7%) | – | 1 (0.7%) | – |
| Ceftriazone + gentamicin | 2 (1.4%) | – | 2 (1.4%) | – |
| Aztreonam + vancomycin + metronidazole | – | – | – | 1 (0.8%) |
| Gentamicin + metronidazole | – | – | – | 1 (0.8%) |
| Clarithromycin or teicoplanin | 1 (0.7%) | – | 1 (0.7%) | – |
| Vancomycin or gentamicin | 1 (0.7%) | – | 1 (0.7%) | – |
| Vancomycin or teicoplanin | 1 (0.7%) | – | 1 (0.7%) | – |
| Clindamycin or teicoplanin | – | 1 (0.8%) | – | 1 (0.8%) |
| Teicoplanin or erythromycin | – | 1 (0.8%) | – | 1 (0.8%) |
| Microbiology advice | 2 (1.4%) | 2 (1.5%) | 3 (2.1%) | 3 (2.4%) |
| Surgeon’s choice     | 1 (0.7%) | 2 (1.5%) | 1 (0.7%) | 2 (1.6%) |
| Total responses      | 146   | 130   | 144   | 127   |
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