

Supplemental file 2: Summary of '4C' antibiotic stewardship intervention

Overview:

As part of a national response to increasing rates of *C.difficile* infections in Scotland, Aberdeen Royal Infirmary (ARI) introduced a mixed persuasive and restrictive antibiotic stewardship (ABS) intervention in May 2009 limiting use of '4C' antibiotics (Clindamycin, cephalosporins, ciprofloxacin (fluoroquinolones) and co-amoxiclav). Although not part of the primary ABS intervention, long-term efforts to limit macrolide were on-going pre-and post-intervention. Given previous evidence linking a number of these antibiotics to the emergence of resistant *S.aureus* infections, [37] we integrated hospital-wide antibiotic use data (defined daily doses, DDDs / 1000 AOBs) into multivariate time-series analysis to explain variation in rates of SAB.

Components of the ABS intervention:

Persuasive elements	
Hospital-wide promotion of revised empirical antibiotic therapy guidelines avoiding use of '4C' antibiotics	<ul style="list-style-type: none"> Recommended first and second-line regimens for common acute presentations incorporated: <ol style="list-style-type: none"> increased use of narrower-spectrum antibiotics, including amoxicillin, aminoglycosides (gentamicin) and β-lactamase-resistant penicillin, substitution of doxycycline co-trimoxazole and piperacillin/tazobactam for co-amoxiclav and cephalosporins. reservation of 3rd or 4th generation cephalosporins for severe infections. Greater emphasis was also placed on considering appropriate antibiotics for potentially resistant HCAs
Reminders for clinical staff	Posters in clinical areas, written information and trust-wide email communications.
Audit and feedback	<ul style="list-style-type: none"> Root cause analysis for all episodes of MRSA infection, Weekly ward-based auditing of antimicrobial prescribing in 'high-risk' environments (defined as those wards with higher than usual rates of <i>C.difficile</i> or with high usage of '4C' antibiotics pre-intervention) Results of compliance reported to clinical staff responsible for reviewing performance and improving practice
Restrictive elements	
Removal of stocks	'4C' antibiotics removed from 'high-risk' clinical areas and wards unable to limit consumption by persuasive means accompanied by advice on therapeutic substitutions
Prior authorisations	Prescriptions for '4C' antibiotics, even where indicated by empirical guidelines and available on wards, required prior authorisation from medical microbiology or ward pharmacists on a case-by-case basis.
Organisational elements	
Leadership and oversight	The antibiotic Pharmacists, medical microbiology and infectious disease specialists reinforced the policy, with strong support from hospital leadership. The intervention was overseen by the hospital antibiotic management team and Strategic Infection Control Committee.

Details of regimen changes

Important changes in first-line regimens included substitutions of penicillins with β -lactamase inhibitor (piperacillin/tazobactam) for 3rd generation cephalosporins in the management of sepsis of unknown origin and severe hospital-acquired pneumonia (HAP), amoxicillin and gentamicin (+/- metronidazole) or co-trimoxazole in place of ciprofloxacin, co-amoxiclav or ceftriazone (for upper urinary tract infections, biliary or intra-abdominal sepsis). There was notable diversification in 2nd line regimens with introduction of tetracyclines (doxycycline) and an increase in use of glycopeptides for SSTIs, bone and joint infections and sepsis given the concentration of MRSA in these presentations.

Trends in antibiotic use

Abrupt and permanent reductions in the use of all '4C' antibiotics were seen within 3 months of the ABS intervention. Use was 50% lower than forecasted at 32 months of intervention. There was also a reversal of an increasing trend in use of therapeutics for common healthcare-associated infections (including MRSA) and an abrupt increase in antibiotics substituted for '4C' antibiotics in empirical guidelines. An overall increasing trend in antibiotic use was not reversed during the '4C' interventions although total costs were reduced.