A Strategy for the Control of
Antimicrobial Resistance in Ireland

SARI

Guidelines for Antimicrobial Stewardship in Hospitals in Ireland

SARI Hospital Antimicrobial Stewardship Working Group

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Contents

Foreword

In 2001, the Minister for Health and Children, Micháel Martin launched the Strategy for the Control of Antimicrobial Resistance in Ireland (SARI). In that report, there was significant emphasis on the importance of careful and appropriate antibiotic use, so called antimicrobial stewardship and in 2003, a working group produced recommendations on stewardship in Irish hospitals. Since then, antimicrobial resistance has emerged as a major threat to public health and is recognised as such by the World Health Organisation (WHO), the European Commission and the Centers for Disease Control (CDC).

During the last six years, there has been a considerable focus on antimicrobial stewardship and the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America have updated their guidance on the issue and there have been significant publications by the British Society for Antimicrobial Chemotherapy (BSAC) and the European Society for Clinical Microbiology and Infectious Diseases (ESCMID). In consequence, the Hospital Antimicrobial Stewardship Guidance has been updated to reflect recent knowledge and changing trends.

The Department of Health and Children and the Health Service Executive have recognised the importance of antimicrobial resistance and considerable resources have been deployed in appointing additional consultant microbiologists, infectious diseases physicians, antimicrobial pharmacists, surveillance scientists, and infection prevention and control nurses. This has been accompanied by a heightened public and political awareness of the importance of hospital hygiene and infection prevention and control and in consequence significant progress has been made.

In order to further optimise the use of antimicrobials, a working group of the National SARI Committee was convened and updated the stewardship recommendations. These should act as an aid for hospitals and healthcare institutions, both large and small, in putting in place measures to ensure the appropriate use of this precious resource. It is fair to say that antimicrobials are one of the great medical advances of the 20th century and today form a cornerstone for the practice of medicine. It is everybody's responsibility to protect this legacy for future generations and these guidelines will undoubtedly be helpful in that endeavour.

As Chair, I would like to acknowledge the contribution of all members of the subcommittee but I would particularly like to thank the honorary secretary, Dr Robert Cunney whose diligence and enthusiasm has ensured the efficient and timely publication of this comprehensive document. I believe that patients, hospitals and healthcare institutions across the state will benefit from this guidance.

Dr Edmond Smyth,
Chair,
SARI Hospital Antimicrobial Stewardship Working Group

Introduction

A working group of the Strategy for the control of Antimicrobial Resistance in Ireland (SARI) produced recommendations for development of antimicrobial stewardship programmes in hospitals in 2003. These recommendations have been updated, in light of more recent evidence and international guidelines. The updated guidelines outline:

1. Rationale for antimicrobial stewardship in hospitals
2. Resources and structures that need to be in place to develop stewardship programmes
3. Specific guidance on stewardship interventions.

These updated guidelines support recommendations made in the SARI report (2001), the SARI Strategy 2009 – 2011, and the HSE's National Strategy for Healthcare Associated Infection and Antimicrobial Resistance (2007). Antimicrobial stewardship is included as a standard within the National Standards for the Prevention and Control of Healthcare Associated Infections, produced by the Health Information and Quality Authority (HIQA). Healthcare institutions will be required to implement antimicrobial stewardship programmes, in order to comply with this standard.

Membership of the SARI working group is listed in Appendix 1.

Implementation of the Guidelines

- Antimicrobial stewardship is a key component in the prevention and control of antimicrobial resistance. Infection prevention and control interventions are also key components, by reducing the transmission of antimicrobial-resistant pathogens, and thus the requirement for antimicrobial therapy. These guidelines should therefore be implemented in parallel with local infection prevention and control programmes.
- The recommendations included in these guidelines are primarily designed for acute hospital settings. However, many of the recommendations are also applicable to non-acute residential healthcare settings. Specific recommendations for such settings are given in section D.
- The recommendations included in these guidelines are based on antimicrobial stewardship interventions that have been shown to be successful. It is not the intention of these guidelines that every stewardship intervention listed be implemented in every institution. The Working Group recognises that this would not be possible, even for large institutions, and that not every intervention is appropriate to every institution. Rather, the intention of the guidelines is to indicate how stewardship programmes should be structured and organised, followed by a list of interventions to be considered for implementation.
- The Working Group recommends the following approach to implementing these guidelines at institutional level:
    - All acute hospitals should ensure the recommendations included in section A2 ("Structure and organisation of stewardship programmes at acute hospital level") are implemented
    - Antimicrobial stewardship teams should ensure the core, high-impact, interventions (section C1) are developed and implemented
    - Antimicrobial stewardship teams should implement as many of the recommendations included in sections C2 to C4 as possible and as are relevant to their institution
- The Working Group, when reviewing the literature and the evidence, undertook to provide guidelines according to what is currently consistent with best practice. However, it is acknowledged that in many healthcare settings in Ireland, it will not be possible to implement much of what follows despite the best efforts of all healthcare professionals, because of inadequate resources, sub-optimal infrastructure and a lack of access to relevant expertise locally. Nonetheless, these are guidelines that all healthcare facilities should aspire to implement. Where it is not possible to implement some or part of the recommendations, the reasons for this should be highlighted to senior management. In this way, it is hoped that these guidelines will facilitate the provision of the appropriate resources.

Executive Summary

Antimicrobial resistance is well recognised as a global threat to human health. Infections caused by antimicrobial-resistant micro-organisms in hospitals are associated with increased morbidity, mortality and healthcare costs. Antimicrobial resistance is closely linked to antimicrobial use, and it is estimated that 50% or more of hospital antimicrobial use is inappropriate. In addition to promoting antimicrobial resistance, excessive or inappropriate antimicrobial use is associated with avoidable adverse drug reactions, with implications for patient safety.

Antimicrobial stewardship is a systematic approach to optimising antimicrobial therapy, through a variety of structures and interventions. Antimicrobial stewardship includes not only limiting inappropriate use but also optimising antimicrobial selection, dosing, route, and duration of therapy to maximise clinical cure or prevention of infection, while limiting the unintended consequences, such as the emergence of resistance, adverse drug events, and cost.[1] Antimicrobial stewardship programmes have been shown to reduce inappropriate antimicrobial use, with resulting reductions in antimicrobial resistance, and also lead to more appropriate antimicrobial therapy for infections where therapy is required, with improved clinical outcomes for patients. Antimicrobial stewardship programmes are highly cost effective, and are capable of saving hospitals many multiples of the cost required to staff and run the programme.

The following summarises the recommendations for development of high quality, evidence-based hospital antimicrobial stewardship programmes in Ireland:

A: Structure and Organisation of Antimicrobial Stewardship

- Development of hospital antimicrobial stewardship programmes, along with provision of appropriate resources, should be a priority for the Health Services Executive (HSE)
- All acute hospitals should have an annually-assessed antimicrobial stewardship programme
- National treatment guidelines for common infections in hospital should be developed, for adaptation at local level
- Undergraduate and postgraduate education of health professionals should include principles of prudent antimicrobial prescribing
- All acute hospitals must have on-site presence of a medical microbiologist or infectious diseases physician, with responsibility for leading the antimicrobial stewardship programme, and 24-hour access to expert advice for management of infections
- All acute hospitals must have one or more clinical pharmacists with responsibility for antimicrobial stewardship
- All pharmacists with responsibility for antimicrobial stewardship should have access to a structured training programme delivered at a national level
- All hospitals should have appropriate administrative and information technology support for antimicrobial stewardship, including an appropriate pharmacy information technology system
- The hospital chief executive/manager must ensure promotion of rational antimicrobial use is a strategic goal for the hospital
- All acute hospitals should have a multi-disciplinary Drugs and Therapeutics Committee

B: Roles and Responsibilities for Prescribers

- All prescribing of antimicrobials, either for treatment or prophylaxis, should follow the principles of prudent antimicrobial prescribing (Appendix 2)
- Rational antimicrobial prescribing should be included in clinical governance requirements for all clinicians
- Patients, or their legal guardians, should be informed of the rationale for prescribing antimicrobials, and informed of any associated risks or adverse effects

C: Antimicrobial Stewardship Interventions

- The recommended core, high impact interventions to promote prudent antimicrobial use are:
    - Clinical review of patients receiving antimicrobials by an antimicrobial stewardship team (microbiologist/infectious diseases physician/pharmacist), with direct advice and feedback to prescribers
    - Regular surveillance/audit of antimicrobial use, with interactive feedback of results to prescribers
    - Limiting the use of specific antimicrobial agents through restricting availability, restricting use to specified clinical settings, or requiring pre-authorisation by a member of the antimicrobial stewardship team prior to prescribing

- The recommended therapeutic interventions to improve the quality of antimicrobial use are:
  - Ensuring antimicrobial therapy is optimised to the individual patient including, where necessary, therapeutic drug monitoring
  - Ensuring empiric antimicrobial therapy is streamlined as soon as possible, to ensure therapy is directed against the causative pathogen(s)
  - Having an effective programme for timely conversion of parenteral antimicrobial therapy to oral therapy
  - Antimicrobial stewardship teams should promote the management of patients in Outpatient Parenteral Antimicrobial Therapy (OPAT) programmes, for selected clinical situations

- The recommended educational interventions and prescribing aids to improve the quality of antimicrobial use are:
  - All hospitals should have a programme of ongoing education for prescribers
  - All hospitals should have local/regional antimicrobial prescribing guidelines, which are regularly updated and are based, whenever possible, on local antimicrobial resistance data
  - All hospitals should consider using specific order forms, or designate a section of the prescription chart for prescribing of antimicrobials.
  - Consideration should be given to using prescribing aids, such as standardised documentation of treatment decisions and information technology-based prescribing supports
  - Commercial promotion of antimicrobials should follow the Code of Marketing Practice, produced by the Irish Pharmaceutical Healthcare Association, and local guidelines approved by the hospital's Drugs and Therapeutics Committee

- The recommended laboratory interventions to improve the quality of antimicrobial use are:
  - All acute hospitals should have 24-hour access to an accredited microbiology laboratory
  - Laboratories should carry out local surveillance of antimicrobial resistance, including annual review of antibiograms where appropriate.
  - Laboratories should report antimicrobial susceptibilities in a restrictive manner, and reports should include interpretative comments to guide prescribers
  - Laboratories should develop, or provide access to, rapid diagnostic methods and key inflammatory markers

D: Recommendations for Non-Acute Residential Healthcare Institutions

- Structure and organisation:
  - All non-acute residential healthcare institutions should have an antimicrobial stewardship programme, appropriate to local requirements
  - Each institution should have access to antimicrobial stewardship advice from a consultant microbiologist or infectious diseases physician, and antimicrobial pharmacist
  - Each institution should have a designated person, or team, responsible for antimicrobial audit and implementation of stewardship interventions

- Stewardship interventions:
  - Where possible, institutions may implement any of the recommended interventions listed in Section C
  - All institutions should have local or regional guidelines for empiric antimicrobial therapy of commonly encountered infections
  - All institutions should carry out point prevalence surveys of antimicrobial use

Background

Antimicrobial Stewardship
Antimicrobial stewardship is a systematic approach to optimising antimicrobial therapy, through a variety of structures and interventions. Antimicrobial stewardship includes not only limiting inappropriate use but also optimising antimicrobial selection, dosing, route, and duration of therapy to maximise clinical cure or prevention of infection, while limiting the unintended consequences, such as the emergence of resistance, adverse drug events, and cost.[1] Specifically, the goals of antimicrobial stewardship programmes are:

1. To ensure the best clinical outcome, for treatment or prevention of infection
2. To minimise unintended consequences of antimicrobial use including
    a. Adverse drug reactions
    b. Selection of pathogenic organisms e.g. *Clostridium difficile*
    c. Emergence of antimicrobial resistance
3. To minimise healthcare costs without compromising quality of care

Comprehensive stewardship programmes have consistently demonstrated a decrease in antimicrobial use of 22% to 36%, with annual cost savings of €130,000 to €600,000 in both large academic and smaller community hospital settings.[1] In England the Hospital Pharmacy Initiative (HPI) facilitated the employment of Antimicrobial Pharmacists in 88% of Hospital Trusts and consequently experienced a reduction in overall expenditure on antimicrobials, with a projected decrease of £30million (€34 million) in 1 year; almost three times the outlay for the HPI provided from central funds.[2]

Antimicrobial Consumption & Antimicrobial Resistance
Antimicrobial consumption in hospitals is a key factor in the emergence of antimicrobial-resistant hospital pathogens, such as meticillin-resistant *Staphylococcus aureus* (MRSA), vancomycin-resistant enterococci (VRE), *C. difficile* and multiple-resistant Gram-negative bacteria. Use of certain broad spectrum antibiotic classes appears to be particularly strongly associated with the emergence of such pathogens. For example, a 2006 study of 204 hospitals in 32 European countries showed that overall antimicrobial consumption and, in particular, the level of consumption of quinolone, macrolide and third generation cephalosporin antibiotics were independent predictive factors for the prevalence of MRSA.[3] Use of cephalosporins (particularly third generation agents), glycopeptides and, more recently, quinolones, have been shown to be independent risk factors for emergence of VRE.[4-6]

The prevalence of resistance to multiple antibiotic classes among Gram-negative hospital pathogens, such as *Escherichia coli*, *Klebsiella pneumoniae* and *Pseudomonas aeruginosa*, has increased in recent years, and has been closely linked to levels of antimicrobial consumption.[7-9] Prior exposure to beta-lactam antibiotics has been shown to be a risk factor for acquisition of extended-spectrum beta-lactamase (ESBL) producing strains of *E. coli* and *K. pneumoniae* in hospitalised adults and children.[10-12] Development of antimicrobial resistance (AMR) has also been demonstrated at individual patient level. For example, in one study 12.2% of patients who received piperacillin/tazobactam became colonised with Gram-negative bacilli resistant to the drug.[13]

Most cases of *C. difficile* associated disease (CDAD) are associated with prior antibiotic use. Although most classes of antibiotics have been identified as risk factors for CDAD, penicillins, cephalosporins, clindamycin and quinolones are the most frequently implicated agents.[14-15] The recent emergence of a hyper-virulent strain of *C. difficile* has been linked to use of quinolone antibiotics.[16,17]

Impact of Antimicrobial Resistance
Infections caused by antimicrobial resistant pathogens are associated with increased morbidity, mortality and long-term socio-economic impact for patients.[18] For example, a review of over 100 articles concluded that the incidence of death, likelihood for hospitalisation, and the average length of hospital stay were at least two-fold higher for infections caused by antimicrobial resistant pathogens, compared to those caused by susceptible pathogens.[19]

A study of over 1900 patients in 93 European intensive care units examined the impact of AMR on bloodstream infections and ventilator-associated pneumonia. After adjusting for risk factors and severity of illness, mortality for infections caused by antimicrobial resistant pathogens, compared to susceptible pathogens, was approximately two-fold higher for MRSA (odds ratio (OR) 1.9) and quinolone-resistant *Enterobacter sp.* (OR 2.3), and three-fold higher for ceftazidime-resistant *Pseudomonas sp.* (OR 3.1).[20] A systematic review of 31 studies of *S. aureus* bloodstream infections found a 2-fold increase in attributable mortality for infections caused by MRSA versus those caused by meticillin-sensitive *S. aureus* (MSSA).[21] An analysis of Irish European Antimicrobial Resistance Surveillance System (EARSS) data also found a two-fold difference in attributable mortality for MRSA versus MSSA bloodstream infections, with meticillin resistance identified as an independent predictor of 14-day mortality on multivariate analysis.[22]

AMR is associated with significant excess healthcare costs. A 2003 study found that the median post-operative hospital stay and associated healthcare costs were 14 days and US$52,791 for surgical site infections caused by MSSA, compared to 23 days and US$92,363 for infections caused by MRSA.[23] In another study, surgical patients with infections due to antimicrobial resistant Gram-negative bacilli had higher median hospital costs (US$80,500 vs. US$29,604), higher median antibiotic costs (US$2,607 vs. US$758) and longer median hospital length of stay (29 vs. 13 days), compared to those with infections due to antimicrobial sensitive strains.[24] A study by the US Office of Technology Assessment estimated that AMR cost the US healthcare system US$4 billion per year (1995 dollars).[25]

Antimicrobial Consumption & Antimicrobial Resistance in Ireland

Hospital antimicrobial consumption in Ireland is high, compared to most European countries. In 2007 the median antimicrobial consumption for acute inpatient admissions in Ireland was 80.6 defined daily doses per 100 bed days (DBD), an increase from 78.5 DBD in 2006.[26] This compares with a median of 55.2 DBD among 140 hospitals across Europe in 2006.[3]

Ireland participates in EARSS, which allows standardised surveillance of national levels of AMR among selected key pathogens and comparison between participating European countries. Compared to most other European countries, Ireland has a moderate to high level of AMR among the pathogens included in EARSS. Recent data has shown that the level of AMR among most of these pathogens in Ireland is increasing.[27] For example:

- Although the proportion of meticillin resistance among bloodstream isolates of *S. aureus* decreased from 42% in 2006 to 34% in 2008, Ireland continues to have one of the highest proportions of MRSA among countries participating in EARSS.
- The proportion of vancomycin resistance among isolates of *Enterococcus faecium* (VREfm) increased from 11% in 2002 to 36% in 2008. In 2007 Ireland had the second highest proportion of VREfm in Europe.
- Quinonlone resistance among isolates of *E. coli* increased from 5.4% in 2002 to 23% in 2008, while gentamicin resistance increased from 2.7% to 10.2% over the same time period. ESBL production was detected in 1.2% of *E. coli* isolates tested in 2002, and this increased to 5% in 2008.

Evidence for the Effectiveness of Antimicrobial Stewardship Programmes

A systematic review and meta-analysis of high quality studies on antimicrobial stewardship programmes, published from 1980 to 2003, was carried out on behalf of the Cochrane Collaboration.[28] Of 52 studies reporting on appropriateness of antibiotic use, 81% demonstrated an improvement. For example, in one randomized control trial the intervention resulted in a 69% decrease in the number of participants receiving antibiotics for more than three days, and was associated with a significant decrease in the risk of colonisation or infection by antimicrobial resistant bacteria (RR 0.36, 95% CI 0.14 to 0.89).[29] Likewise data from Bradley *et al* showed that changes in prescribing were associated with a significant decrease in the probability of being colonised with VRE after removal of ceftazidime, followed by a significant increase after ceftazidime was re-introduced.[30] Meyer *et al* showed that restriction of ceftazidime was associated with a significant reduction in cases of ceftazidime resistant *K. pneumoniae*.[31]

Among the studies included in the Cochrane review, the most consistent evidence of an impact on antimicrobial-resistant pathogens was provided by studies designed to reduce the incidence of CDAD: four out of five such studies demonstrated a significant reduction, while the remaining study showed a

non-significant trend towards reduction. The review authors were able to pool the results of four of these studies, demonstrating that the antimicrobial stewardship interventions were associated with a mean immediate reduction of 15 CDAD cases per quarter (range 6 to 26) and a median sustained reduction of 3.2 cases per quarter (range 1 to 6).[28]

In addition to the evidence showing a reduction in CDAD, numerous studies of antimicrobial stewardship programmes have demonstrated significant reductions in other antimicrobial-resistant pathogens. For example, a programme combining education, antibiotic order forms and bedside review of antimicrobial prescribing in a 250-bed teaching hospital in Argentina demonstrated an 80% reduction in third-generation cephalosporin-resistant *Enterobacter cloacae*, 100% reduction in carbapenem-resistant *P. aeruginosa*, and 36% reduction in MRSA, over an 18 month period.[32] Development of antimicrobial prescribing guidelines and regular education sessions in a French intensive care unit (ICU) resulted in a 79% reduction in MRSA and a 52% reduction in ceftazidime-resistant Gram-negative bacteria, over four years.[33] A similar intervention in a German neurosurgical ICU resulted in a 62% reduction in MRSA over two years.[34] The combination of education, bedside review and automatic stop orders led to a 75% reduction in cephalosporin resistance and a 78% reduction in quinolone resistance among isolates of *K. pneumoniae* over three years, in a 900-bed community teaching hospital in Texas.[35]

There is a considerable body of evidence to show that antimicrobial stewardship programmes result in cost savings that are many times greater than the cost of implementing the programme. For example, a clinical pharmacist-led programme of guideline development, education and review and feedback, at a 900-bed university hospital in Scotland, resulted in a £133,296 (€169,000) reduction in antimicrobial drug costs over two years. The cost of implementing the programme, over the same time period, was £20,133 (€25,000).[36] A programme based on antimicrobial prescribing review and feedback at a 200-bed community hospital in Boston resulted in a $293,000 (€200,000) reduction in antimicrobial drug costs per year. The cost of the programme, which required the full-time involvement of an antimicrobial pharmacist and a quarter-time involvement of an infectious diseases physician, was $43,000 (€29,000) per year.[37] Many studies reporting the economic benefit of antimicrobial stewardship programmes focus on drug acquisition costs. However, when all costs associated with using a particular antibiotic are included, the cost per dose may be three to five times higher than the drug acquisition cost alone.[38] Thus the direct cost savings from stewardship programmes are likely to considerably higher than estimates based on published literature.

Concern is sometimes expressed that stewardship programmes that reduce overall antimicrobial use may lead to under-treatment of serious infections, with resulting adverse outcomes for patients. However, this concern is not supported by the literature. In the Cochrane review six studies designed to improve the adequacy of antimicrobial treatment resulted in improved clinical outcomes. However, no adverse patient effects were found in studies that restricted access to antimicrobials.[28] For example, a study of automatic stop orders for vancomycin therapy found that inappropriate discontinuation of therapy was rare, and no adverse clinical consequences were found.[39]

Persuasive Versus Restrictive Interventions

The Cochrane review was unable to directly compare different types of interventions. Overall rates of success for persuasive interventions (e.g. direct clinical review with intervention and feedback) were 64-75%, and 66-87% for restrictive interventions (e.g. formulary restriction and pre-authorisation requirements for specific agents). However, restrictive interventions had, on average, a more than three-fold greater effect compared to persuasive interventions.[28]

Direct feedback to prescribers on their antibiotic prescribing practices has been shown to improve antimicrobial use. In one study, non-consultant hospital doctors were randomised to receive either no intervention or one-on-one education by a clinical specialist ("academic detailing") on a patient-specific basis. This resulted in a 37% reduction in the number of days of unnecessary levofloxacin or ceftazidime use.[40] At a 600-bed tertiary teaching hospital, inpatients receiving parenteral antimicrobials chosen by their primary care physician were randomised to an intervention group that received antimicrobial-related suggestions from an infectious diseases fellow and a clinical pharmacist versus no antimicrobial suggestions. Eighty-five percent of the suggestions were implemented, resulting in 1.6 fewer days of parenteral therapy and a direct cost savings of $400 (€270) per patient, with no adverse impact on clinical response, compared with the control group.[41]

A 120-bed community hospital used an infectious diseases physician and clinical pharmacist three days per week to review patients receiving multiple, prolonged, or high-cost courses of antimicrobial therapy. Sixty-nine percent of 488 recommendations were implemented, resulting in a 19% reduction in antimicrobial expenditures for an estimated annual savings of $177,000 (€120,000), compared with the pre-intervention period.[42]

Antimicrobial restriction—either through formulary limitation or by the requirement of pre-authorisation and justification before use—is the most effective method of achieving the process goal of controlling antimicrobial use.[28] Restrictive policies have demonstrated significant initial decreases in the use of the targeted antimicrobials, with annual antimicrobial cost savings ranging upwards of $800,000 (€550,000).[1] Both formulary restriction and pre-authorisation requirements for use of clindamycin during nosocomial outbreaks of *C. difficile* infection have led to prompt cessation of the outbreaks.[43,44] Pre-approval restriction of broad spectrum antimicrobials led to increased susceptibilities among Gram-negative pathogens, such as *P. aeruginosa, K. pneumoniae,* and *E. cloacae,* during a 6–12-month period.[45,46] In one centre, restriction of vancomycin and third-generation cephalosporins in response to increasing rates of vancomycin-resistant enterococci (VRE) was associated with a decrease in the faecal VRE point prevalence from 47% to 15% during six months.[44] A crossover study of two neonatal intensive care units showed that a narrow-spectrum (penicillin plus tobramycin) regimen for empirical treatment of early- and late-onset suspected sepsis was associated with a markedly lower prevalence of colonisation with resistant Gram-negative bacilli, compared to a broad-spectrum (ampicillin plus cefotaxime) regimen.[47]

Outpatient Parenteral Antimicrobial Therapy (OPAT)

Patients with infections that require a lengthy duration of parenteral antimicrobial therapy, such as osteomyelitis, infective endocarditis or acute exacerbations of cystic fibrosis, may be suitable for OPAT. OPAT programmes have been shown to be cost effective, allow earlier discharge of patients requiring parenteral therapy, and may allow some patients to avoid hospital admission. A review of an OPAT programme in Singapore found that the mean cost per day for care including an OPAT episode was US$278, compared to US$457 per day for inpatient-only care.[48] A cost analysis of an OPAT programme in Canada concluded that the programme resulted in savings of CAN$1,730,520 to the hospital, and a further CAN$1,009,450 to the provincial Ministry of Health, over a three year period.[49] Another study concluded that the costs associated with an OPAT programme were 6.5 times less than for inpatient hospital care, and four times less than for nursing home care.[50] OPAT programmes have been shown to be safe, when compared to inpatient hospital care, and are associated with a high level of patient satisfaction.[51,52]

Microbiology Laboratory Interventions

Appropriate management of infections, and containment of antimicrobial resistance, requires access to a high quality diagnostic microbiology laboratory.[53] Such diagnostic services provide appropriate identification of microbial pathogens, antimicrobial susceptibility testing and, where necessary, additional testing such as strain typing and identification of virulence factors. Numerous studies have shown that timely clinical application of such data (the "bench to bedside" approach) by medical microbiologists or infectious diseases physicians results in improved clinical outcomes for patients, and reduction in inappropriate antimicrobial use.[54-56] The provision of clinically relevant laboratory reports, and inclusion of interpretative comments to assist clinicians in applying the laboratory result to patient care, can have a positive impact on appropriate antimicrobial use.[57]

Restricted Reporting of Antimicrobial Susceptibilities

Reporting of susceptibility to specific antimicrobial agents has been shown to increase the use of these agents.[58] Such increased use may be inappropriate, as was shown in one study where routine reporting of rifampicin susceptibilities for Gram-positive bacteria resulted in unnecessary, and potentially harmful, prescribing of the agent.[59] Conversely, reporting of antimicrobial susceptibility results in a selective manner (e.g. only reporting susceptibilities to "first line" antimicrobials, or withholding susceptibility results for isolates that are unlikely to be clinically significant) has been shown to improve the appropriateness of antimicrobial use.[60]

Antibiograms

Provision of aggregate antibiograms, which include susceptibility data for key pathogens within a hospital

over a given time period (usually one year) can be a valuable tool for guiding empiric antimicrobial therapy.[61] Antibiograms for specific patient care areas, such as intensive care units, may allow identification of local antimicrobial resistance problems and, thus, focus antimicrobial stewardship and infection control interventions.[62] Antibiograms based on specific units or culture types may also be used to guide the development of local empiric antimicrobial prescribing guidelines.[63] However, local antibiograms are prone to selection biases that can lead to over-estimation of levels of antimicrobial resistance (e.g. urine cultures may be more likely to be submitted from patients who have already received antimicrobial therapy, or multiple isolates may be included from the same patient), potentially promoting inappropriate antimicrobial prescribing. Thus, antibiograms should be produced in a standardised fashion, and data only disseminated to prescribers with appropriate interpretation.[61,64]

Rapid Diagnostic Methods and Inflammatory Markers

Provision of rapid microbiological diagnostic tests has been shown to improve appropriate antimicrobial prescribing.[65-67] For example, a landmark study comparing rapid same-day bacterial identification and susceptibility testing with traditional overnight methods found that patients in the rapid test group had a shorter time to institution of appropriate antimicrobial therapy, decreased mortality (8.8%, versus 15.3% for the overnight test group), and decreased hospital costs.[68] Rapid detection of viral or atypical bacterial pathogens using molecular or antigen detection-based methods, have also been shown to reduce inappropriate antimicrobial use.[69,70] A systematic review of antimicrobial stewardship programmes in paediatric settings found that rapidly available tests to identify viral pathogens, or to measure a variety of inflammatory markers, were associated with the greatest reduction in inappropriate antimicrobial use.[71] For example, in one study, rapid measurement of C-reactive protein (CRP) and interleukin (IL)-8 was associated with a 73% reduction in antimicrobial use in neonates with suspected bacterial infection.[72]

Recommendations

A: Structure and organisation of antimicrobial stewardship

1: National development of hospital antimicrobial stewardship

- Rational antimicrobial use in hospitals should be a key strategic goal within the HSE risk management programme.
- All acute hospitals should be required to have an antimicrobial stewardship programme in place. Hospital managers/chief executives should be required to provide evidence, on an annual basis, to show that such a programme is in place, that clear targets and objectives for the programme have been set, and that these targets and objectives are being realised.
- The HSE must prioritise and fund the appointment of key personnel required to implement antimicrobial stewardship programmes in hospitals, including medical microbiologists, infectious diseases physicians and antimicrobial pharmacists.
- All pharmacists with responsibility for antimicrobial stewardship should have access to a structured training programme delivered at a national level
- The SARI National Committee should establish working groups to develop guidelines relating to rational antimicrobial use, including management of common infections in the community, hospital and non-acute residential care settings.
- There should be a national programme to further advance clinical pharmacy services in hospitals
- The HSE should prioritise the provision of pharmacy information technology systems, which are capable of providing the audit and surveillance requirements outlined in these guidelines, as part of the national information technology strategy.
- The HSE should prioritise the development of electronic patient records, electronic prescribing and computer-based surveillance in hospitals; all of which will enhance the implementation of antimicrobial stewardship programmes.
- Academic and professional bodies should provide undergraduate and postgraduate training to ensure that all healthcare professionals who recommend, prescribe, handle and administer antimicrobials receive adequate training and education in the proper use of antimicrobials, in line with the principles of prudent antimicrobial prescribing detailed in Appendix 2. Principles of prudent antimicrobial prescribing should be a mandatory core module for postgraduate training and be included in postgraduate examinations.

2: Structure and organisation of stewardship programmes at acute hospital level

2.1: Key personnel and resources

- All acute hospitals must have a consultant medical microbiologist or infectious diseases physician with a formal on-site commitment, including designated hours for managing the antimicrobial stewardship programme. Consultant medical microbiologist staffing levels should be in line with the recommendations developed by the Royal College of Pathologists.[73]
- Prescribers should have ready access to clinical microbiology or infectious diseases expertise on a 24-hour basis. Such contact should be encouraged for all serious or complicated infections.
- All acute hospitals must have at least one clinical pharmacist with dedicated responsibility for antimicrobial stewardship. One or more full-time positions will be required for tertiary referral centres and regional hospitals, where the antimicrobial pharmacist will oversee and co-ordinate the delivery of antimicrobial stewardship strategies by the clinical ward pharmacists, where available. Smaller hospitals should have at least one pharmacist with part time responsibility for antimicrobial stewardship. Antimicrobial pharmacists should have appropriate training in antimicrobials and infectious diseases.
- All acute hospitals should have access to a laboratory-based surveillance scientist.
- All acute hospitals should have administrative and information technology personnel available to support the antimicrobial stewardship programme.

- All acute hospitals should have a pharmacy information technology system that is capable of providing antimicrobial prescribing data, in line with local and national surveillance requirements.
- The hospital manager/chief executive, or a designated senior member of the hospital management team, should have corporate responsibility for ensuring an effective antimicrobial stewardship programme is in place, including the provision of funding for appropriate personnel, information technology and educational initiatives.
- The control and prevention of antimicrobial resistance, the reduction of medication-related adverse events, and the reduction of unnecessary financial costs, through having an effective antimicrobial stewardship programme, should be a strategic goal for all acute hospitals.
- An overview of the key responsibilities for personnel involved in antimicrobial stewardship is given in Appendix 3.

2.2: Drugs and Therapeutics Committee

- All acute hospitals should have a multidisciplinary Drugs and Therapeutics Committee. Larger hospitals require their own in-house committee, while regional committees may be set up to service smaller institutions or develop regional guidelines.
- Larger hospitals may consider having a designated Antimicrobial Advisory Committee, as a subcommittee of the local/regional Drugs and Therapeutics Committee
- Membership of the Antimicrobial Advisory Committee may include (where available):
    - Consultant medical microbiologist
    - Consultant infectious diseases physician
    - Chief pharmacist
    - Antimicrobial pharmacist
    - Surveillance scientist
    - Infection prevention and control nurse
    - Consultant surgeon
    - Consultant physician
    - Non-consultant hospital doctor
    - Consultant in emergency medicine
    - Nursing administrator
    - Registered nurse prescriber (where established)
    - Hospital manager/chief executive (or designated senior member of management team)
    - Representatives from other specialist areas, as appropriate (e.g. intensive care, transplant unit etc.)
- The role of the Antimicrobial Advisory Committee in relation to antimicrobial stewardship, includes:
    - Authorising the introduction of new antimicrobials within the hospital/region.
    - Development and regular updating of a local/regional antimicrobial formulary, as appropriate
    - Development and regular updating of local/regional antimicrobial prescribing guidelines
    - Development and management of an antimicrobial stewardship programme
    - Production of an annual report, summarising levels of antimicrobial use, antimicrobial resistance, and the impact of stewardship initiatives
    - Production of an annual service plan for antimicrobial stewardship
- The Antimicrobial Advisory Committee should meet at least twice per year (or at least quarterly, for large tertiary and regional hospitals)
- Minutes from the Antimicrobial Advisory Committee meetings should be fed back to the Chair of the Drugs & Therapeutics Committee

2.3: Antimicrobial stewardship team

- All acute hospitals should have an antimicrobial stewardship team, which should be lead by a medical microbiologist or infectious diseases physician
- Where there is no on-site presence of a microbiologist or infectious diseases physician, the antimicrobial stewardship team may be led by a senior clinician on an interim basis, pending the appointment of a microbiologist or infectious diseases physician.
- The antimicrobial pharmacist should be a core member of the team, and in some situations may co-direct the antimicrobial stewardship programme (with the microbiologist or infectious diseases physician)
- Infection prevention and control nurse specialists should be members of the antimicrobial stewardship team, particularly in institutions where they are directly involved in antimicrobial stewardship activities
- The antimicrobial stewardship team should also include microbiology and infectious diseases non-consultant hospital doctors where present.
- The clinical ward pharmacists, where present, should link with the antimicrobial stewardship team, helping them to target their activities efficiently.
- The antimicrobial stewardship team should have sufficient administrative and information technology support, to allow it to implement stewardship initiatives
- The role of the team is to implement the antimicrobial stewardship programme, which may include:
    - Pre-authorisation of restricted antimicrobials
    - Review of patients on intravenous antimicrobials, for potential switch to oral therapy
    - Review of patients receiving antimicrobials with duplicate spectra, or other potentially inappropriate drug combinations
    - Review of patients on selected broad spectrum antimicrobials
    - Review of patients with documented sterile site infections (e.g. bloodstream infection, meningitis), to ensure appropriate antimicrobial therapy is in place
    - Review of patients receiving antimicrobials for a duration that exceeds recommendations in the hospital antimicrobial guidelines
    - Participation in the infection prevention and control programme
    - Provision of education on prudent antimicrobial use to consultant, non-consultant and nurse prescribers
- The antimicrobial stewardship team should work closely with the institution's infection prevention and control team to ensure that prevention of healthcare associated infection and antimicrobial resistance are integrated with the antimicrobial stewardship programme. In many institutions the antimicrobial stewardship team and infection prevention and control team will share membership in common, and may be lead by the same individual.

B: Roles and responsibilities of prescribers

- All prescribing of antimicrobials should follow the principles of prudent antimicrobial prescribing, outlined in Appendix 2.
- Prescribing of antimicrobial prophylaxis for surgical procedures should follow the principles outlined in Appendix 4.
- The principles of prudent antimicrobial prescribing (Appendix 2) should be a core component of undergraduate and postgraduate training of prescribers and those who influence antimicrobial prescribing (including clinicians, nurses and pharmacists), and be included in undergraduate and postgraduate examinations.
- New appointees should be able to provide evidence of completion of specific training in antimicrobial prescribing (e.g. e-learning programme), prior to taking up a clinical post.
- Rational antimicrobial prescribing, along with other measures to control or prevent antimicrobial resistance in hospital settings, should be part of clinical governance requirements for all clinicians. Evidence of implementation of such measures should be included in the performance monitoring of clinicians by clinical directors (e.g. using the process indicators detailed in Appendix 7).

- Where antimicrobials are included in a nurse prescriber's collaborative practice agreement, compliance with the principles of prudent antimicrobial prescribing (Appendix 2) should be included in the regular prescribing audits required by An Bord Altranais.
- Patients, or their legal guardians, should be informed when they are being prescribed an antimicrobial of the reason why the antimicrobial is necessary
- Information on antimicrobial prescribing, including risks and side effects associated with antimicrobial treatment, should be available to patients or their legal guardians

C: Antimicrobial stewardship interventions

1: Core, high-impact, interventions

1.1: Clinical review and direct prescriber feedback*

- Members of the antimicrobial stewardship team should have a high clinical profile in the hospital, including regular bedside review of patients and regular interaction with prescribers.
- The antimicrobial stewardship team should have a system for timely identification of patients who are receiving, or likely to require, antimicrobial therapy, and who are likely to benefit from an antimicrobial stewardship intervention (see flow chart in Appendix 5).
    - The decision on which patients require bedside review may be based on formal requests for consultation, laboratory results (in particular, positive cultures from normally sterile sites), regular ward rounds in high risk areas (such as intensive care units), or lists of patients receiving restricted antimicrobials, prolonged duration or unusual combinations of antimicrobials.
- The antimicrobial stewardship team should carry out a clinical review of selected patients, and, where necessary, provide advice on optimal antimicrobial therapy to the clinician/team responsible for the patient's care. This advice may be provided via:
    - Direct conversation with the clinician/team (preferred)
    - The clinical ward pharmacist attending the antimicrobial stewardship team round
    - Written record in the patient's medical record (in addition to direct conversation, particularly in the setting of a formal clinical consultation by members of the antimicrobial stewardship team)
    - Written advice on a standardised advice form (an example of such a form is given in Appendix 6)
- Advice provided to prescribers, arising from such clinical review, should:
    - Be seen as optional advice, which does not interfere with the presciber's clinical autonomy
    - Be delivered in a non-confrontational and non-critical manner
    - Be used as an opportunity to educate precribers on the principles of prudent antimicrobial use.

1.2: Antimicrobial prescribing surveillance and audit

- The antimicrobial stewardship team in each hospital should have a system of regular surveillance and audit of antimicrobial use.
- Quantitative measurement of antimicrobial use, expressed as defined daily dose (DDD) per 100 bed days used, should be reported to hospital management and prescribers on a quarterly basis. Where possible, the data should be broken down to the level of individual wards/units, as detailed in Appendix 7
- Regular (yearly or 6 monthly) point prevalence studies of antimicrobial use should be undertaken and further in-depth audit performed if necessary. Options and methodology for such audit are detailed in Appendix 8.

*Note: Guidelines produced by the Infectious Diseases Society of America (IDSA) employ the term "prospective audit" to describe clinical review and direct presciber feedback.[1] The term "prospective audit", as used in reports from IDSA and others, should not be confused with surveillance and audit of antimicrobial prescribing, as detailed in Appendix 7.

- The results of antimicrobial use audits should be fed back to prescribers and to clinical directors on a regular basis. Members of the antimicrobial stewardship team should discuss the results of targeted audits in face-to-face meetings with relevant prescribers.

1.3: Restricted availability of antimicrobials and pre-authorisation

- Each hospital's antimicrobial prescribing guidelines should include a list that stipulates which antimicrobials are unrestricted, restricted (approval of a specialist is required) or permitted for specific conditions. Criteria for restricted antimicrobials include spectrum of activity, potential toxicity, misuse or cost.
- The list of restricted antimicrobials should be reviewed on a regular basis, in light of the hospital's antimicrobial usage data and rates of antimicrobial resistance. Restrictions may have to be reinforced, or applied to additional antimicrobial agents, in the setting of outbreaks caused by antimicrobial-resistant pathogens (e.g. *C. difficile*, VRE, MRSA).
- Restricted antimicrobials should only be available from the hospital pharmacy, and not included in ward drug stocks of those areas where access is restricted. However, hospitals should ensure that there is a mechanism for accessing restricted agents, when required, outside of normal working hours.
- Where possible, each hospital should have a process in place to allow pre-authorisation for the use of restricted antimicrobials by a member of the antimicrobial stewardship team. Details of how a pre-authorisation system may be established are given in Appendix 9.
- Where pre-authorisation is not possible, there should be a system for identifying when restricted antimicrobials have been prescribed, and early review of such prescriptions by a member of the antimicrobial stewardship team.

2: Therapeutic interventions

2.1: Optimisation of therapy

- Antimicrobial stewardship teams, with the support of clinical ward pharmacists where available, should ensure that antimicrobial therapy is given at the optimal dose, frequency and duration, based on individual patient characteristics (e.g. age, weight, renal function), likely causative organism, site of infection, and pharmacokinetic and pharmacodynamic characteristics of the antimicrobial agent(s).
- Antimicrobial stewardship teams, with the support of clinical ward pharmacists where available, should ensure that serum levels of antimicrobials requiring therapeutic drug monitoring (e.g. aminoglycosides) are measured appropriately, and the results acted upon in a timely manner.

2.2: Streamlining or de-escalation of therapy

- Empiric antimicrobial therapy should be streamlined on the basis of ongoing clinical review, laboratory results, and diagnostic imaging, as soon as possible.
- All empiric antimicrobial therapy should be reviewed on a daily basis by the clinician responsible for the patient's care.
- Antimicrobial stewardship teams should have a mechanism in place (eg. liaising with the clinical ward pharmacist, where possible) to identify antimicrobial regimens that are likely to require streamlining, such as:
    - Antimicrobial combinations with overlapping spectrum of activity
    - Prolonged use of broad spectrum antimicrobials
    - Unauthorised use of restricted agents
    - Antimicrobial agents, or combinations of agents, that are not in accordance with hospital prescribing guidelines

2.3: Parenteral to oral conversion

- Hospital antimicrobial prescribing guidelines should include clinical criteria and guidelines for converting parenteral antimicrobial therapy to oral therapy, once the patient's condition allows.
- Antimicrobial stewardship teams should have a system in place for identifying patients whose antimicrobial therapy is suitable for parenteral to oral conversion. An example of such a system is given in Appendix 10.

2.4: Outpatient Parenteral Antimicrobial Therapy (OPAT) programmes

- Antimicrobial stewardship teams should promote the use of OPAT, where available, and identify patients who are suitable for entry into OPAT programmes.
- Details of suggested models for delivery of an OPAT programme are given in Appendix 11

3: Educational interventions and prescribing aids

3.1: Prescriber education

- All acute hospitals should have a programme of ongoing education for prescribers on prudent antimicrobial use, in accordance with the principles outlined in Appendix 2.
- The principles of prudent antimicrobial prescribing should be included in induction training for all new medical, nursing and pharmacy staff.

3.2: Guidelines and clinical pathways

- All acute hospitals should have local or regional antimicrobial prescribing guidelines, based where possible on local antimicrobial resistance data, in accordance with the framework outlined in Appendix 12.
- Guidelines should be evidence-based, and developed in collaboration with hospital clinicians.
- Guidelines should be updated at least every two years.
- Guidelines should be distributed to all prescribers and where possible, made available in electronic format.
- Consideration should be given to providing laminated cards to prescribers, summarising prescribing guidelines for common infections. Such cards should be pocket sized, or designed to be attached to staff identification badges, include the date created, and reference the current edition of the hospital antimicrobial guidelines.
- Audits of antimicrobial prescribing should include the proportion of antimicrobial use in accordance with hospital guidelines, and should be carried out at least annually.
- User surveys should be carried out to ensure guidelines are acceptable, being used, and meet the requirements of prescribers.

3.3: Prescribing aids

- Hospitals should consider introducing antimicrobial order forms, or designate a section of the prescription chart for antimicrobial prescribing, which include a requirement for clinical indication and a required duration before order renewal. Order forms should distinguish between antimicrobials used for prophylaxis, and those used for active therapy. Consideration should be given to having separate order forms for peri-operative antimicrobial prophylaxis. Examples of antimicrobial order forms are given in Appendix 13.
- Hospitals should introduce educational aids to guide prescribers at the point of prescribing. These may include clinical algorithms for the diagnosis of infection, or methods to standardise documentation of treatment decisions, such as infection stamps or stickers to be included in the clinical notes.
- Where possible, information technology support for prudent antimicrobial use should be introduced. This includes electronic patient records, computerised prescribing and clinical decision support software.
- Hospitals should use computer-based surveillance to target antimicrobial stewardship interventions, track antimicrobial resistance patterns, and identify healthcare-associated infections and treatment-related adverse events.

3.4: Pharmaceutical promotion

- Commercial promotion of antimicrobials should be carried out in an ethical manner, in line with the Irish Pharmaceutical Healthcare Association (IPHA) Code of Marketing Practice (available from www.ipha.ie).
- The Pharmacy Department and/or the hospital Drugs and Therapeutics Committee (or Antimicrobial Advisory Committee) should be informed of any promotional activities directed towards hospital staff, relating to antimicrobial agents, and provided with copies of relevant promotional or scientific literature.

- Pharmaceutical representatives should not promote antimicrobial agents in an acute hospital that are not included in the hospital prescribing guidelines or formulary, without the approval of the hospital Drugs and Therapeutics Committee (or Antimicrobial Advisory Committee).
- IPHA should be informed if a pharmaceutical company is found to be carrying out promotional activities that are in breach of the IPHA Code of Marketing Practice.

4: Laboratory interventions

4.1: Access to high quality laboratory service

- All acute hospitals should have 24-hour access to an accredited microbiology laboratory.
- There should be prompt clinical liaison for critical results, such as positive sterile site cultures.
- The laboratory should use a standardised method for antimicrobial susceptibility testing, such as the method produced by the Clinical Laboratory Standards Institute (CLSI).
- The laboratory should carry out surveillance of antimicrobial resistance, with feedback of standardised data to local prescribers.
- Annual antibiograms for common pathogens or conditions (e.g. antibiotic susceptibilities for organisms causing urinary tract infection), or for specific units or patient groups (e.g. intensive care unit), should be reviewed according to local requirements.
- The susceptibility data included in the annual antibiogram should be based on the first clinical isolate of a given pathogen per patient.
- The production and feedback of the annual antibiogram report should be in line with the relevant CLSI guidelines.[74]
- The laboratory should ensure that appropriate specimens are taken, for the investigation of possible infections, through prescriber education and direct clinical liaison.

4.2: Restrictive and interpretative laboratory reporting

- Laboratories should report antimicrobial susceptibilities only where clinically indicated, and these should be restricted to agents included in the antimicrobial formulary.
- Where susceptibility results are reported, these should be restricted to the narrowest spectrum agents to which the organism is susceptible. Susceptibility results for broad spectrum agents should be restricted, but may be made available to clinicians following appropriate clinical liaison.
- Laboratories should include interpretative comments on reports, to guide prescribers in deciding whether or not antimicrobial therapy is required and, if so, what drug to prescribe.
- Laboratory results should be reported in a way that encourages prescribers to discuss the results with a microbiologist, or other member of the antimicrobial stewardship team, before deciding to prescribe an antimicrobial agent. Examples of restrictive and interpretative reporting are given in Appendix 14.

4.3: Rapid diagnostics and inflammatory markers

- Laboratories should develop, or provide access to, rapid diagnostic methods that can rapidly confirm the presence of a bacterial pathogen (e.g. polymerase chain reaction (PCR) identification of *Neisseria meningitidis* in blood or cerebro-spinal fluid), or help to rule out a bacterial infection (e.g. PCR identification of respiratory viruses in children with lower respiratory tract infection).
- Laboratories should provide rapid testing for inflammatory markers that can help to confirm or rule out serious bacterial infection, monitor response to therapy, and guide the duration of antibiotic therapy (e.g. C-reactive protein, procalcitonin, Interleukin-8).

D: Antimicrobial Stewardship in Non-Acute Residential Healthcare Institutions

1: Structure and organisation

- All non-acute residential healthcare institutions should have an antimicrobial stewardship programme
    - The manager/director of each institution should provide evidence to show that antimicrobial use is being audited, and that there are mechanisms to promote prudent antimicrobial use, within their institution. This should be provided at least annually to the HSE Regional Director of Operations and Regional SARI Committee for review.
- Each institution should have access to a consultant medical microbiologist or infectious diseases physician, and to an antimicrobial pharmacist, to assist with the development of local or regional antimicrobial stewardship programmes
    - Larger institutions may require a regular formal commitment from a medical microbiologist or infectious diseases physician, to review the stewardship programme and provide clinical review, where needed.
- Each institution should have a designated person, or team, with responsibility for audit of antimicrobial use and implementation of stewardship interventions. This may include (depending on the size of the institution):
    - Physician with on-site clinical commitment (or medical director, where present)
    - General practitioner, with regular on-site commitment
    - Hospital or community pharmacist
    - Infection prevention and control nurse specialist
    - Registered nurse prescriber (where present)
- The roles and responsibilities of prescribers, listed in section B, apply to non-acute healthcare settings, as well as to acute healthcare settings.

2: Stewardship interventions

Where possible, non-acute residential institutions may implement any of the stewardship recommendations listed in section C. However, the following interventions are considered most appropriate to this setting:

- All institutions should have guidelines for empiric antimicrobial therapy for infections commonly encountered in that institution, using the template in Appendix 12. These guidelines may be produced locally (within the institution) or regionally.
- Institutions should carry out point prevalence surveys of antimicrobial use at least annually. The surveys should indicate whether or not antimicrobial therapy was given in accordance with local/regional prescribing guidelines. The results of these surveys should be reported to all antimicrobial prescribers in the institution, the HSE Regional Director of Operations and the Regional SARI Committee.

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Appendix 1: Membership of the SARI Hospital Antimicrobial Stewardship Working Group

Dr Edmond Smyth (Chair)
Consultant Microbiologist, Beaumont Hospital

Dr Robert Cunney (Honorary Secretary)
Consultant Microbiologist, Children's University Hospital, Temple Street, and Health Protection Surveillance Centre, Dublin

Dr Colm Bergin
Consultant Infectious Diseases Physician, St. James's Hospital, Dublin

Dr John Lambert
Consultant Infectious Diseases Physician, Mater Misericordiae University Hospital, Dublin

Ms Audrey O'Reilly
Antimicrobial Pharmacist, St. James's Hospital, Dublin

Ms Marie Philbin
Antimicrobial Pharmacist, Midlands Regional Hospital, Tullamore

Dr Bernard Silke
Consultant Physician, St. James's Hospital, Dublin

Appendix 2: Principles of prudent antimicrobial prescribing

The following is adapted from recommendations produced by the UK Specialist Advisory Committee on Antimicrobial Resistance (SACAR)[75]

- Antimicrobials should be used after a treatable infection has been recognised or there is a high degree of suspicion of infection. In general, colonisation or contamination should not be treated. Antimicrobials should be used for the prevention of infection where research has demonstrated that the potential benefits outweigh the risks. Long-term prophylaxis should be avoided unless there is a clear clinical indication (for example, rheumatic fever and post-splenectomy).
- The choice of antimicrobial should be determined by the sensitivity of the identified causative organism when this is known. Empiric therapy, for the likely causative organism (s) should be governed by local guidelines that have been informed by recent information about trends in antimicrobial sensitivities.
- Targeted therapy should be used in preference to broad-spectrum antimicrobials unless there is a clear clinical reason (for example, mixed infections or life-threatening sepsis). The prescription of broad-spectrum antimicrobials should be reviewed as soon as possible and promptly switched to narrow-spectrum agents when sensitivity results become available. Mechanisms should be in place to control the prescribing of all new broad-spectrum antimicrobials.
- The timing, regimen, dose, route of administration and duration of antimicrobial therapy should be optimised and documented. The indication for which the patient is being prescribed the antimicrobials should be documented in the drug chart and case notes by the prescriber.
- Wherever possible, antimicrobials should be given orally rather than intravenously. Clear criteria should be defined for when intravenous therapy is appropriate. As soon as possible the prescription should be switched to an oral equivalent. The intravenous prescription should be reviewed after 48 hours as a minimum.
- Antimicrobial treatment should be stopped as soon as possible. A stop date or review date should be recorded by the prescriber on the drug chart. In general, antimicrobial courses should be reviewed within five days.
- To ensure rapid treatment and infection control, mechanisms should be in place to ensure that patients receive antimicrobial drugs in a timely manner.

Appendix 3: Responsibilities of key personnel involved in antimicrobial stewardship

Hospital Chief Executive/Manager

- Ensuring an effective antimicrobial stewardship programme is in place, including the provision of funding for appropriate personnel, information technology and educational initiatives.
- Ensuring control and prevention of antimicrobial resistance, minimisation of medication-related adverse events, and reduction of unnecessary financial costs, through having an effective antimicrobial stewardship programme, is a key strategic goal for the hospital.
- Regular review of antimicrobial surveillance and audit reports, to ensure strategic goals are being met.
- Annual management review of antimicrobial stewardship programme (with director of programme), to review progress and agree goals to be included in the hospital's annual service plan

Director of Antimicrobial Stewardship Programme

(Note: this will normally be an infectious diseases physician or medical microbiologist, but for hospitals without an on-site infection specialist the programme may be lead by a senior clinician from another speciality)

- Lead the antimicrobial stewardship team
- Member of Drugs and Therapeutics Committee
    - Chair Antimicrobial Advisory Committee, where one exists
- Planning and management of antimicrobial stewardship programme
- Development of an annual service plan for antimicrobial stewardship, including review of progress to date and strategic goals/targets
- Agreement of annual service plan with hospital manager/CEO
- Submission of regular surveillance/audit reports to hospital executive (and board of management, where present)
- Antimicrobial education initiatives, in collaboration with other members of the antimicrobial stewardship team

Antimicrobial Pharmacist*

- Lead on the implementation of antimicrobial stewardship policies / initiatives as recommended by the Antimicrobial Advisory / Drugs and Therapeutics Committee
- Clinical role in conjunction with other members of the Antimicrobial Stewardship Team
    - Member of antimicrobial or drugs and therapeutics committee
        - Policy development / review, clinical practice guidelines and new antimicrobials review
    - Identification of patients for stewardship interventions
    - Initiation of streamlining or sequential therapy
    - Dose adjustments
    - Therapeutic drug monitoring
    - Approval of restricted antimicrobials, in conjunction with microbiologist or infectious diseases physician
- Provision of expert advice on antimicrobial use, to promote the safe, effective and cost efficient use of antimicrobials
- Surveillance of antimicrobial use
    - Collection and analysis of local consumption and expenditure
    - Feedback on antimicrobial prescribing trends to the Antimicrobial Advisory Committee / Drugs and Therapeutics Committee and prescribers
    - Compliance with policies
    - Prescribing errors
    - Provision of data to regional/national surveillance programmes
- Audit and feedback
    - E.g. evaluation of impact of clinical guidelines, patient outcomes, financial outcomes, antimicrobial resistance patterns
- Education of:
    - Clinicians (formal education sessions and point of prescribing interventions)
    - Nursing and allied health professionals
    - Patients

    - Pharmacists
- Infection prevention and control
    - Integration of antimicrobial stewardship and infection prevention and control
    - Member of local infection control committee
- Participation in OPAT programme (where established)

Medical Director of Microbiology Laboratory

(Note: this will normally be a medical microbiologist and, in many hospitals, will also be the director of the antimicrobial stewardship programme)

- Ensuring there is access to a high quality diagnostic microbiology service
- Provision of antibiograms and antimicrobial resistance surveillance reports to clinicians, if deemed appropriate.
- Ensuring there is restrictive reporting of antimicrobial susceptibilities and interpretative reporting of microbiology test results
- Provision of appropriate rapid diagnostic tests

Clinical Directors and Medical Boards

- Ensuring rational antimicrobial prescribing is part of clinical governance requirements for all clinicians.
- Inclusion of rational antimicrobial prescribing in performance monitoring of clinicians.
- Ensuring rational antimicrobial prescribing is included in post-graduate education for both senior clinicians and clinicians in training.

*Adapted from reference[76]

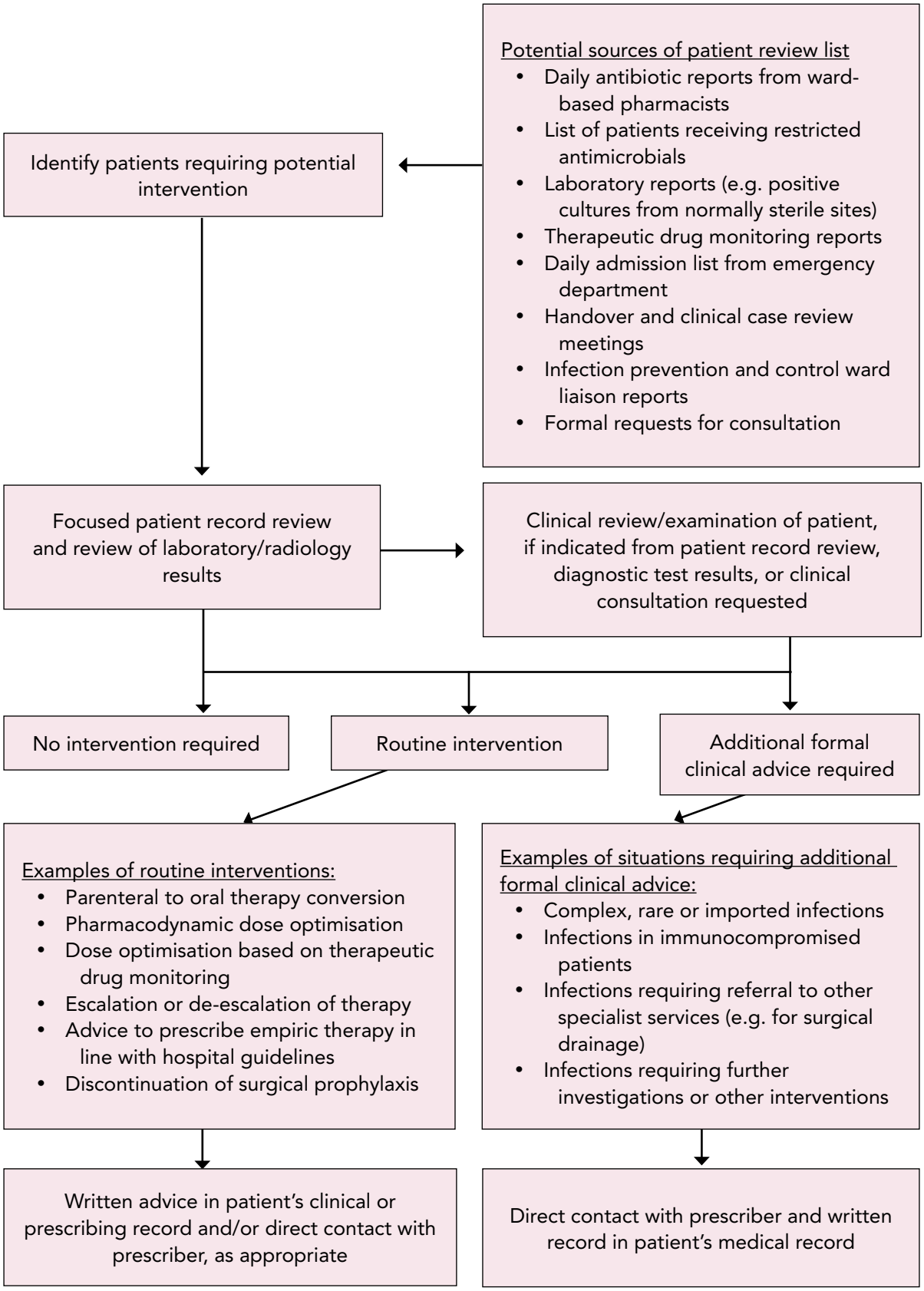
Appendix 4: Principles of antibiotic prophylaxis in surgery

The following recommendations are adapted from the Scottish Intercollegiate Guidelines Network (SIGN) report "Antibiotic prophylaxis in surgery: a national clinical guideline" (July 2008)[77]

- Patients with a history of anaphylaxis, laryngeal oedema, bronchospasm, hypotension, local swelling, urticaria or pruritic rash, occurring immediately after a penicillin therapy, are potentially at increased risk of immediate hypersensitivity to beta-lactams and should not receive prophylaxis with a beta-lactam antibiotic.
- The duration of prophylactic antibiotic therapy should be single dose, except in special circumstances such as prolonged surgery, major blood loss or for the following procedures:
    - Duration of prophylaxis not more than 24 hours:
        - Open reduction and internal fixation of compound mandibular fractures
        - Orthognathic surgery
        - Complex septorhinoplasy (including grafts)
        - Head and neck surgery (contaminated or clean-contaminated wound class)
        - Arthroplasty
    - Duration of prophylaxis not more than 48 hours:
        - Open heart surgery
- A single dose of antibiotic with a long enough half-life to achieve activity throughout the operation is recommended.
- The antibiotics selected for prophylaxis must cover the expected pathogens for that operative site.
- Prophylactic antibiotic treatment during surgery solely for the prevention of urinary or respiratory tract infection is not recommended.
- Intranasal mupirocin should be used prophylactically for adult patients undergoing surgery with a high risk of major morbidity who are identified as carrying meticillin-sensitive or meticillin-resistant *Staphylococcus aureus*.
- A glycopeptide should be considered for antibiotic prophylaxis in patients undergoing high risk surgery who are colonised with MRSA.
- Intravenous prophylactic antibiotics should be given ≤ 30 minutes before the skin is incised.

Appendix 5:
Suggested workflow diagram for clinical review and prescriber feedback by Antimicrobial Stewardship Team

Adapted from reference[78]



Appendix 6:
Example of standardised advice form

Adapted from reference[78]

Hospital Name	(Patient details/addressograph label)

This patient's antimicrobial therapy has been reviewed by a member of the Antimicrobial Stewardship Team and the advice given below is suggested to provide optimal antimicrobial therapy

These recommendations are not mandatory. If you wish to discuss the recommendations further, please contact a member of the Antimicrobial Stewardship Team (contact details below)

Date:	Time:	Allergies:

Based on a review of this patient's antimicrobial therapy, the following changes are suggested:

Rationale/supporting evidence for above recommendations:

Reviewer name	Signature	Bleep no.

(Contact details for members of antimicrobial stewardship team)

Notes:

- Rationale/supporting evidence may include reference to relevant section in local antimicrobial prescribing guidelines, national guidelines, published literature, websites etc.
- Form may be designed as a two part carbonless form, with one copy placed in the medical/ prescribing record and one retained by the antimicrobial stewardship team

Appendix 7: Options and methodology for antimicrobial surveillance, audit and feedback

Antimicrobial prescribing analysis may be quantitative (consumption reporting) or qualitative (audit of appropriateness of prescribing, e.g. point prevalence studies).

Antimicrobial consumption surveillance is one of the key recommendations of the 2001 SARI report. Hospital pharmacies currently report data on antimicrobial consumption to HPSC. Antimicrobial consumption is reported using the anatomic, therapeutic, chemical (ATC) classification and expressed as defined daily doses (DDD) per 100 bed-days used. The ATC/DDD system was devised by the World Health Organisation (WHO) as a standardised method of measuring antimicrobial consumption. Details of the ATC/DDD system can be found at www.hpsc.ie.

The primary value of the data is to the individual data providers, allowing hospitals to compare trends over time, assess the impact of interventions, and identify targets for future interventions. Direct comparison between hospitals should be undertaken with caution due to differences in case mix and limitations of the ATC/DDD system.

1: Quarterly antimicrobial consumption report

The quarterly report on antimicrobial use for each hospital should be based on the WHO ATC/DDD classification. The report should be submitted to the hospital Chief Executive/Manager, the Board of Management (where one exists) and circulated to all clinicians. The report should include the following data:

- Graph of total cost of antibiotics per quarter
- Graph of total cost of antifungals per quarter
- Antibiotic/antifungal cost per bed day per quarter
- Total antibiotic consumption, expressed as DDDs per 100 bed days per quarter
- Total antibiotic consumption, expressed as DDDs per 100 inpatient admissions or discharges per quarter
- Graph of antibiotic consumption, expressed as DDDs per 100 bed days and/or per 100 inpatient discharges or admissions per quarter, for:
    - Specialist anti-Gram positive agents, such as:
        - Vancomycin
        - Linezolid
        - Teicoplanin
        - Tigecycline
        - Quinupristin/Dalfopristin
    - Other specific alert antimicrobials, such as
        - Second generation cephalosporins
        - Third generation cephalosporins
        - Flouroquinolones
        - Beta-lactam/beta-lactamase combinations (e.g. amoxicillin/clavulanate)
        - Carbapenems
        - Clindamycin
    - Alternatively, antibiotic risk groups may be reported, where the degree of risk relates to the propensity to promote antimicrobial resistance, or predispose patients to superinfection with *C. difficile* or MRSA. For example:
        - ***High Risk:*** cephalosporins, flouroquinolones, clindamycin, co-amoxiclav
        - ***Intermediate Risk:*** amoxicillin, azithromycin, clarithromycin, erythromycin
        - ***Low Risk:*** aminoglycosides, rifampicin, benzylpenicillin, chloramphenicol, co-trimoxazole, tetracyclines, flucloxacillin, fusidic acid, metronidazole, nitrofurantoin, penicillin V, sulphonamides, teicoplanin, trimethoprim, vancomycin

        - ***Specialist:*** aztreonam, colistin, daptomycin, linezolid, quinopristin - dalfopristin, tigecycline
        - ***Ultra-broad spectrum:*** ertapenem, imipenem, meropenem, piperacillin/tazobactam
    - Total IV and oral, for antimicrobials that have excellent oral bioavailability and should normally be prescribed via the oral route, such as:
        - Ciprofloxacin
        - Levofloxacin
        - Linezolid
        - Fusidic acid
        - Clindamycin
        - Metronidazole
        - Rifampicin
        - Fluconazole
        - Clarithromycin

2: Annual antimicrobial report

This should include all of the data fields included in the quarterly antimicrobial report, with quarterly trends and comparison with previous years' data (where available). In addition, the annual report should include:

- Comparison of individual data fields with corresponding national hospital antimicrobial consumption data.
- Antibiotic/antifungal consumption data by individual ward/unit/department, expressed as:
    - DDD per 100 bed days and/or inpatient admissions or discharges for each ward/unit/department per quarter (or per month, if available)
    - Total antibiotic/antifungal cost for each ward/unit/department per quarter
- Antimicrobial resistance surveillance data, such as:
    - Data on bloodstream isolates, submitted to EARSS
    - Rates of detection of selected antimicrobial resistant bacteria (e.g. new isolates of extended spectrum beta-lactamase (ESBL) producing Gram negative bacteria)
    - Antibiograms for selected pathogens (e.g. urinary tract isolates), or for specific high-risk units (e.g. intensive care unit)
    - Rates of *C. difficile* associated disease (CDAD)
    - Use of specific agents by ward or unit

3: Point prevalence surveys

A point prevalence survey is an audit of antimicrobial prescribing, which examines the use of antimicrobials at a single point in time (ideally on a single day). The aims of point prevalence studies include:

- Establishing baseline antimicrobial use data for the hospital
- Examining prescribing patterns (e.g. use of reserved antimicrobials, route of administration and potential for intravenous/oral switch, duration of use, combinations prescribed, review date, indication etc.)
- Identifying areas for intervention
- Providing data to target antimicrobial stewardship initiatives
- Benchmarking practice over time in each hospital and with other hospitals.

Prevalence surveys of antimicrobial use should be carried out at least every twelve months, and ideally every six months. Prevalence surveys should focus on high risk areas, or on aspects of antimicrobial use that are likely to be targeted for stewardship interventions. The data set should be kept to a minimum, to facilitate completion of the surveys, and only include data that is likely to be acted upon. Surveys should follow the methodology developed by the European Surveillance of Antimicrobial Consumption (ESAC) network (see example in Appendix 8), or similar. Options for such surveys include:

- Global antimicrobial use in selected wards or units
- Global antimicrobial use by selected speciality or service
- Antimicrobial use for selected conditions, such as community-acquired pneumonia, ventilator-

associated pneumonia or central-venous catheter related infections
- Use of specific agents by ward/unit or clinical service

4: Prescribing audits

Detailed audits of antimicrobial use may be carried out by ward-based pharmacists. The frequency with which such audits are carried out will vary according to local resources and needs. Examples of such audits include:

- Audit of peri-operative antimicrobial prophylaxis (using the Scottish Intercollegiate Guidelines Network methodology (see below), or similar)
- Audit of antimicrobial use on selected wards or units where an increase in antimicrobial resistant organisms has been identified (e.g. ESBL-producing Gram negative bacteria, VRE, CDAD)
- Monthly audit of antimicrobial use on selected high risk units (e.g. ICU, transplant unit)
- Audit of use of restricted antimicrobials
- Audit of parenteral to oral conversion programmes
- Audit of therapeutic drug monitoring

5: Process indicators

A variety of measurements, taken from prevalence surveys or prescribing audits, may be used that can act as process indicators for the success of antimicrobial stewardship programmes. Examples of useful process indicators include

- Quarterly measure of overall antimicrobial consumption, or consumption of selected agents, expressed as DDD per 100 bed days
- Proportion of single dose peri-operative antimicrobial prophylaxis for clean surgery
- Proportion of patients receiving aminoglycoside therapy with toxic or sub-therapuetic serum levels with review/adjustment before next dose
- Proportion of restricted antimicrobial use that is in accordance with hospital prescribing guidelines
- Proportion of patients with community-acquired pneumonia who have been assessed using a validated measure of severity
- Proportion of patients with community-acquired pneumonia who have received antimicrobial therapy in concordance with hospital prescribing guidelines

6: Feedback of antimicrobial use data to individual clinical services or consultants

Data on antimicrobial prescribing should be fed back to each clinical service or consultant on a regular basis, when pharmacy IT system allows. For consultants with large teams, high numbers of admissions or high antimicrobial prescribing rates, data should be fed back quarterly. For other consultants, data should be fed back every 6-12 months. The feedback report should be accompanied by a face-to-face meeting to discuss the data, where possible. Where pharmacy information technology systems allow, the feedback report should include:

- Antimicrobial use, expressed as DDD per 100 inpatients admitted or discharged under that consultant's care per quarter
- Antimicrobial costs for inpatients admitted or discharged under that consultant's care per quarter
- Comparison of antibiotic and antifungal use and cost with overall data for hospital and, where appropriate, with overall data for the relevant discipline (e.g, medicine, surgery, paediatrics etc.)
- Where available, analysis of dose and duration of antibiotic and antifungal use
- Where available, an indication of the proportion of antimicrobial use that was in line with hospital prescribing guidelines
- Breakdown of antimicrobial use by risk groups and iv/oral route, as detailed under quarterly report (item 1 above)

Where pharmacy information technology systems do not allow antimicrobial prescribing data to be reported to the level of individual clinical team or consultant, feedback of data should be based on periodic prevalence surveys or prescribing audits.

7: Audit of surgical antibiotic prophylaxis

(The following is adapted from the Scottish Intercollegiate Guidelines Network (SIGN) report "Antibiotic prophylaxis in surgery, a national clinical guideline" (July 2008))[77]

A: Documentation

All aspects of antibiotic prophylaxis, for example, where prophylaxis is not given when recommended, should be clearly recorded in the case records.

Locally agreed protocols should clearly indicate where to document antibiotic prophylaxis in the patient records *(for example, the "once only" section of the drug chart, integrated care pathway or anaesthetic chart).*

B: Minimum data set for auditing surgical antibiotic prophylaxis

The following should be routinely recorded, to document the administration of surgical antibiotic prophylaxis:

- Date
- Operation performed
- Classification of operation (clean/clean-contaminated/contaminated)
- Elective or emergency
- Patient weight (especially children)
- Any previous adverse reactions/allergies to antibiotics
- Justification for giving prophylaxis (eg, evidence of a high risk of SSI), if given for an operation where prophylaxis is not routinely indicated
- Justification for not giving prophylaxis (eg, procedure not in local guideline, patient on antibiotic treatment)
- Time of antibiotic administration
- Name of antibiotic
- Dosage of antibiotic
- Route of administration
- Time of surgical incision
- Duration of operation
- Second dosage indicated?
- Second dosage given?
- Postoperative antibiotic prophylaxis indicated?
- Postoperative antibiotic prophylaxis given?
- Antibiotic prophylaxis continued for > 24hrs
- Documentation recorded appropriately (in correct place, clarity)
- Name of anaesthetist
- Name of surgeon

C: Core indicators for audit

Process measures:

- Was prophylaxis given for an operation included in local guidelines?
- If prophylaxis was given for an operation not included in local guidelines, was a clinical justification for prophylaxis recorded in the case notes?
- Was the first dosage of prophylaxis given in the 30 minutes before the start of surgery?
- Were the choice, dosage and route of administration consistent with local guidelines for the procedure?
- Was the prescription written in the "once-only" section of the drug prescription chart?
- Was the duration of prophylaxis greater then 24 hours?

Outcome measures:

- Surgical site infection (SSI) rate (i.e. number of SSIs occurring postoperatively, divided by the number of operative procedures)
- Rate of SSIs occurring postoperatively in patients who received inappropriate prophylaxis

compared with rate of this infection in patients who receive appropriate prophylaxis, expressed as a ratio.

- Rate of *C. difficile* infections occurring postoperatively in patients who receive inappropriate prophylaxis compared with rate of this infection in patient who receives appropriate prophylaxis, expressed as a ratio.

For audit, surgical site infections should be described following the CDC criteria[79]

D: Audit and feedback methodology

- Ensure the minimum data set is recorded in the clinical record, to facilitate audit of the appropriateness of surgical antibiotic prophylaxis
- Short period audits held at regular intervals, with feedback to surgical teams, are recommended
- Statistical process control is recommended, to achieve affective, embedded change
    - An example of statistical process control is the PDSA (Plan, Do, Study, Act) cycle. Measurement of compliance (for example, using run and control charts) to give timely feedback to healthcare professionals is recommended by the Patient Safety Alliance (www.patientsafetyalliance.scot.nhs.uk) to achieve effective, embedded change. Further information on PDSA is available from NHS-Scotland Clinical Governance (www.clinicalgovernance.scot.nhs.uk/section2/pdsa.asp).

Appendix 8:
Example of antimicrobial consumption point prevalence survey methodology

(Adapted from European Surveillance of Antimicrobial Consumption (ESAC) methodology)

Point Prevalence Survey: Ward details

Date of survey				
Auditor code				
Ward				
Specialty: In the case of mixed wards, tick all relevant specialities	**Medicine**	**Surgery**	**Intensive Care**	**Other** (specify)
	☐	☐	☐	☐
Denominator: total patients in the ward at 8am. In case of mixed wards, indicate total number of patients in each of the relevant specialities				

Include in survey: All patients who are receiving non-topical antibacterials and antifungals (ATC codes: J01, J02, A07AA, P01AB, D01AB, J04AB02). All patients who are in the hospital at 8 am on the days of survey should be included in the study.

Prophylaxis: any patient who received one or more doses in the 24h prior to 8 am on the day of the survey. Check doses received on the previous day as well in order to code as either 1 dose, 24hours or >24hours.

Diagnosis Group: by anatomical site of infection treated (or prevented, in the case of prophylaxis).

Site	Codes	Examples
CNS	Proph CNS	Prophylaxis for central nervous system (CNS) infections (neurosurgery, meningococcal)
	CNS	Infections of the Central Nervous System
EYE	Proph EYE	Prophylaxis for eye operations
	EYE	Endophthalmitis
ENT	Proph ENT	Prophylaxis for ear, nose or throat (surgery or medical)
	ENT	Infections of ear, mouth, nose, throat or larynx
RESP	Proph RES	Pulmonary surgery, prophylaxis for respiratory pathogens
	Bron	Acute bronchitis or exacerbations of chronic bronchitis
	Pneu	Pneumonia
CVS	Proph CVS	Cardiac or vascular surgery, endocarditis prophylaxis
	CVS	Cardiovascular infections: endocarditis, vascular graft
GI	Proph GI	Surgery of the GI tract, liver or biliary tree, GI prophylaxis in neutropenic patients or hepatic failure
	GI	GI infections (salmonellosis, antibiotic associated diarrhoea)
	IA	Intra-abdominal sepsis including hepatobiliary
SSTBJ	Proph SBJ	Prophylaxis for plastic or orthopaedic surgery (bone or joint)
	SST	Cellulitis, wound, deep soft tissue not involving bone
	BJ	Septic arthritis (including prosthetic joint), osteomyelitis
UTI	Proph UT	Prophylaxis for urological surgery, recurrent UTI
	Cys	Lower UTI
	Pye	Upper UTI
GUOB	Proph GyOb	Prophylaxis for obstetric or gynaecological surgery
	OBGY	Obstetric or gynaecological infections, STI (sexually transmitted infection) in women
	GUM	Prostatitis, epididymo-orchitis, STI in men

Not Defined	BAC	Bacteraemia (not endocarditis) with no clear anatomical site
	SIRS	Systemic inflammatory response with no clear anatomic site
	UND	Completely un-defined site with no systemic inflammation

Point Prevalence Survey: Details of Patients Receiving Antimicrobials

Ward	Patient Identifier[a]	Survey Number[b]	Age[c] Year	Age[c] Month	Sex	Specialty[d]

[a] For example 10 digit unique hospital number, to allow local linkage to patient records for more detailed audit.
[b]A unique but non-identifiable number for each patient entered in the survey.
[c] If more than 2 years old, specify only the number of years. If less than 2 years old, specify only the number of months
[d] Specify speciality that the patient belongs to, regardless of where the patient is located

Essential Fields							
Drug	**Unit Dose[1]**	**Doses per day[2]**	**Route[3]**	**Diagnosis (site)[4]**	**Indication[5]**	**Culture pre-therapy[6]**	**Reason in notes[7]**
1							
2							
3							
4							

[1]Dose per administration in grams: for combination of penicillins with inhibitors, record only the amount of penicillin (e.g. co-amoxiclav (amoxicillin 1g/clavulanate 0.125g) report 1g), for combinations of multiple antimicrobial substances report the total amount (e.g. co-trimoxazole (sulpha 0.8g/trimethoprim 0.16g), report 0.96g)
[2]Provide fractions of doses if necessary, e.g. every 16h = 1.5 doses per day, every 36h = 0.67 doses per day, every 48h = 0.5 doses per day
[3]Parenteral (injections), oral, rectal, inhalation (or **P**, **O**, **R**, **I**)
[4]See list
[5]Indication codes:

A Community acquired infection	Symptoms or antibiotics started <48h after patient was admitted		
B Hospital acquired infection Symptoms start 48h after admission to hospital	B1 Post-operative infection (within 30 days after surgery or 1 year after implant surgery)		
	B2 Other intervention related infections (IV catheter, VAP, CAPD)		
	B3 *C difficile* associated diarrhoea >48h after admission or <30 days after previous admission		
	B4 Other hospital acquired infection		
	B5 Infection present on admission from another hospital		
C Surgical prophylaxis	C1 Single dose	C2 one day	C3 >1 day
D Medical prophylaxis			

[6]Relevant culture taken before antibiotic treatment was started, (Yes or No)
[7]A diagnosis or indication for treatment was recorded in the notes at the start of antibiotic treatment, (Yes or No)

Appendix 9:
Example of a pre-authorisation system for restricted antimicrobials

Note: The following is given as an example of how a pre-authorisation system for restricted antmicrobials may be structured, and should be adapted according to local requirements.

Restricted antimicrobial list

Antimicrobials included on the hospital formulary are divided into three groups:

1. Unrestricted: may be prescribed by any clinician
2. Consultant only: may only be prescribed by a consultant
3. Restricted: may only be prescribed following prior discussion with, and approval by, the antimicrobial stewardship team

The antimicrobials included in each group are regularly reviewed and approved, by the Drugs and Therapeutics Committee

Procedure for requesting restricted antimicrobials

i. A member of the antimicrobial stewardship team will carry a designated pager and/or mobile phone 24 hours/seven days a week

ii. If a consultant or non-consultant hospital doctor is considering prescribing one or more restricted antimicrobial agents, he/she should contact the antimicrobial stewardship team member on-call. The prescriber should be able to provide the following information:
    a. Patient's name, hospital medical record number and location
    b. Clinical indication for antimicrobial therapy
    c. Drug allergies and side effects to previous antimicrobials
    d. Microbiology culture results, if available
    e. Renal and hepatic function
    f. Weight and height of the patient

iii. The antimicrobial stewardship team member will respond to the prescriber in a timely manner, discuss the case with the prescriber and, on the basis of the above information, may:
    a. Recommend the use of the restricted agent(s)
    b. Recommend an alternative therapeutic option
    c. Recommend further investigations or clinical follow-up

iv. The antimicrobial stewardship team member will fill out an information card for all restricted antimicrobials requests. The information card contains the following:
    a. Patient's name, medical record number and location
    b. Prescriber's name, pager number, clinical service and position
    c. The prescribing consultant's name and clinical service
    d. Reason for calling
    e. If for pre-authorisation, reason for authorisation
    f. Recommendations given
    g. Rationale for recommendations given
    h. Whether or not the infectious diseases or medical microbiology consultant was contacted

Appendix 10:
Example of a parenteral to oral conversion programme

Note: The following is given as an example of how a parenteral to oral conversion programme may be structured, and should be adapted according to local requirements.

Background:
Many intravenous agents have equivalent oral preparations. The administration of oral medications relies upon a functioning gastrointestinal tract for adequate absorption of the medication. Early switch from intravenous (IV) agents to the equivalent oral preparation (PO) offers several benefits: decreased total cost of therapy, decreased potential for line associated infections, a potential for decreased length of stay and patient preference, increased patient comfort and mobility, savings in nursing time spent preparing and administering intravenous doses.

A key factor in the conversion from IV to PO therapy is the bioavailability of the oral preparation. Bioavailability is expressed as a percentage of the drug concentration of the oral route compared to the IV route in the systemic circulation. An oral agent that is well absorbed is considered equivalent. Additionally, patient specific factors are also important determinants in the decision to switch from IV to PO therapy.

Implementation of parenteral to oral conversion programme

- A member of antimicrobial stewardship team, and/or a clinical pharmacist, will assess a patients ability to convert to oral antimicrobial therapy on the basis of the following criteria:

Inclusion and Exclusion Criteria

❖ Patient Inclusion Criteria ✓ Infection does not require prolonged course of intravenous antimicrobials ✓ A suitable oral antimicrobial is available ✓ Afebrile for the previous 24 to 48 hours ✓ Definite clinical improvements in signs and symptoms of infection ✓ White cell count returning towards normal ✓ The patient is receiving an oral diet, or is receiving tube feeds of at least 50% of their goal rate, or is receiving and tolerating oral medication
❖ Patient Exclusion Criteria ✓ Patients who are haemodynamically unstable ✓ The patient has a deep-seated or high risk infection, for which continued IV therapy is required (e.g. osteomyelitis, septic arthritis, deep tissue abscess, meningitis, intracranial abscess, endocarditis, severe or necrotising soft tissue infections) ✓ Patients designated 'nil by mouth' for any reason ✓ Patients receiving scheduled anti-emetics ✓ Patients with mucositis and/or receiving chemotherapy that causes mucositis ✓ Patients who are being treated for active gastrointestinal bleed

- The antimicrobial stewardship team member, and/or clinical pharmacist, will provide advice on converting patients meeting the above criteria from IV to equivalent oral dose and frequency, using a standardised form to be appended to the patient's prescribing record, as shown:

Conversion from parenteral to oral antimicrobial medication

The Drugs and Therapeutics Committee has an approved policy for conversion of selected parenteral antimicrobials to an equivalent oral dose. Your patient is receiving_____, which is one of the antimicrobials covered by this policy. By chart review the patient is tolerating an oral diet (or enteral feeding), or oral medication, and does not have any identifiable contraindications to oral antimicrobial therapy.

The antimicrobial stewardship team recommends converting the above agent to:

_____	_____	_____
Oral agent	Dose	Frequency

Notes (potential drug interactions, etc.):

_____

_____

Please contact us if you have any questions (refer to pager below).

_____	_____	_____
Signature (printed name	Date	Pager number

- If the IV agent has not been converted to the recommended oral equivalent within 24 hours of the recommendation being made, a member of the antimicrobial stewardship team will contact the clinical team responsible for the patient's care directly, to discuss the recommendation.
- Regular audits of compliance with parenteral to oral conversion recommendations will be carried out, and the results fed back to clinicians.

Appendix 11:
Outpatient Parenteral Antimicrobial Therapy (OPAT)

The following is based on practice guidelines for OPAT programmes, developed by the Infectious Diseases Society of America.[80] It is given as an example, to be adapted according to local requirements or to compliment existing OPAT services (where available)

The following aspects need to be considered in the establishment of an OPAT programme:

- The literature supports the effectiveness of OPAT for a wide variety of infections
- A thorough assessment of the patient's general medical condition, the infectious process, and the home situation is necessary before starting therapy
- Prescribing physicians should be aware of a number of aspects of OPAT which distinguish it from other forms of therapy. These include the required teamwork, communication, monitoring, and outcome measurements
- The physician has a unique role on the OPAT team, which may also include nursing, pharmacy, and social services. These responsibilities include establishing a diagnosis, prescribing treatment, determining the appropriate site of care, monitoring during therapy, and assuring the overall quality of care
- Antimicrobial selection for OPAT is different from that for therapy in the hospital. Once-daily drug administration has many advantages. Potential for adverse effects and the stability of an antimicrobial once it is mixed must be considered
- The first dose of an antimicrobial must be given in a supervised setting
- Regular clinical and laboratory monitoring of patients receiving OPAT is essential and varies with the antimicrobial chosen
- Outcomes measures should be an integral part of any OPAT programme, to assure the effectiveness and quality of care
- Children receiving OPAT must be considered differently because of their special needs.

The key elements required for an OPAT programme are:

- Health care team
  - An infectious diseases specialist or physician knowledgeable about infectious diseases and the use of antimicrobials in OPAT
  - Primary care or referring physicians available to participate in care
  - Nurse expert in intravenous therapy, access devices, and OPAT
  - Pharmacist knowledgeable about OPAT
  - Administrative support
  - Access to other allied health care professionals as required (e.g. physiotherapist, occupational therapist, dietician, social worker)
- Communications
  - Physician, nurse, and pharmacist available 24 hours per day, where appropriate
  - System in place for rapid communication between patient and team members
  - Patient education information for common problems, side effects, precautions, and contact lists
- Outline of guidelines for follow-up of patients with laboratory testing and intervention as needed
- Written policies and procedures
  - Outline of responsibilities of team members
  - Patient intake information
  - Patient selection criteria
  - Patient education materials
- Outcomes monitoring
  - Patient response
  - Complications of disease, treatment, or programme
  - Patient satisfaction

Specific considerations in evaluating patients for OPAT include:

- Is parenteral antimicrobial therapy needed?
- Does the patient's medical care needs exceed resources available at the proposed site of care?
- Is the home or outpatient environment safe and adequate to support care?
- Are the patient and/or caregiver willing to participate and able to safely, effectively, and reliably deliver parenteral antimicrobial therapy?
- Are mechanisms for rapid and reliable communications about problems and for monitoring of therapy in place between members of the OPAT team?

- Do the patient and caregiver understand the benefits, risks, and economic considerations involved in OPAT?
- Does informed consent need to be documented?

Appendix 12: Framework for development of antimicrobial prescribing guidelines

The following is adapted from recommendations produced by the UK Specialist Advisory Committee on Antimicrobial Resistance (SACAR)[75]

It is recommended that, as minimum, guidelines for treatment or prophylaxis should be available for the conditions listed below.

Treatment

- Urinary tract infections
- Upper respiratory tract infections
- Lower respiratory tract infections, including, community and health-care associated pneumonia and exacerbations of chronic obstructive pulmonary disease
- Soft tissue infections including injuries or bites, cellulitis, chronic ulcers and necrotising fasciitis
- Central nervous system infections: bacterial meningitis, viral encephalitis
- Gastro-intestinal infections: food poisoning and intra-abdominal sepsis
- Genital tract infections
- Blood stream infections
- Eye, ear, nose and throat infections
- Sepsis of unknown origin
- Specific confirmed infections: for example, treatment regimens for MRSA, *C. difficile* and tuberculosis
- Endocarditis

Prophylaxis

- Prevention of bacterial endocarditis (procedure-specific criteria should be agreed to identify which patients should receive prophylaxis)
- Endoscopic procedures (details should be given of which individuals, considered at high risk, should receive prophylaxis (for example neutropenic patients))
- Surgical prophylaxis (recommendations should be made for all common surgical interventions including timing of initial dose and exceptional circumstances for repeat doses)
- Splenectomy patients (provide details of both the immunization and antimicrobial prophylaxis requirements)

Template for local antimicrobial prescribing guidelines

Antimicrobial guidelines should be evidence-based and prepared in line with best practice recommendations for treatment guidelines. The provision of costing information within the guideline should be discussed locally. The following are additional recommendations for the content and detail of local antimicrobial policies.

Title page

- Name of policy
- Specify the condition and patient group where appropriate
- Date
- Version
- Review date
- Authors
- Contact details for enquiries for normal hours and out of hours
- Contact details for microbiological and pharmacological information
- Details of electronic availability

Introduction section

- Statement as to whether the guideline is mandatory or for guidance only
- Contents
- Guidance on the local procedure for microbiological samples
- Abbreviations used in the text
- Reference should be made to relevant national or international guidelines

Summary list of available antimicrobials

The antimicrobials that are recommended in the guidelines should be listed, with clear indications to the route of administration and should state whether they are:

- Unrestricted
- Restricted (approval of a specialist is required)
- Permitted for specific conditions (for example, co-trimoxazole for *Pneumocystis*)

Regimens for treatment of common infections

Treatment

- First-line recommendation
- Second-line recommendation
- Timing
- Dose
- Route of administration
- Duration of treatment
- Rules for intravenous to oral switch

Prophylaxis

- First-line recommendation for empirical therapy
- Second-line recommendation for empirical therapy
- Dose
- Timing of initial dose
- Route of administration
- Details of repeat dosing if required

Appendix 13:
Examples of designated sections of a prescription chart for antimicrobial prescribing

Regular antibiotic prescriptions

Patient name______________________

Parenteral medicines • Prior to prescribing antibiotics, please review all previous microbiological samples/data

Codes: A = given by B = checked by FDG=first dose given

Hospital no.______________

For medicines to be administered during regular medication rounds

Prescription Circle or enter other times required				Date →					
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				

Prescription Circle or enter other times required				Date →					
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				
Drug (approved name)			Dose	02:00	A B				
				06:00	A B				
Prescriber's signature			Frequency	10:00	A B				
				12:00	A B				
Route	Start date	Time fdg	Dr's sig	14:00	A B				
				18:00	A B				
Stop date	Indication	Pharmacist's signature		22:00	A B				
				24:00	A B				

Regular antibiotic prescriptions

Patient name____________________

Oral and other non-parenteral medicines

For medicines to be administered during regular medication rounds

Hospital no.____________________

Prescription Circle or enter other times required		Date →												
Drug (approved name)		Dose	02:00							STOP				
			06:00											
Route	Start date	Stop date	10:00											
			12:00											
Prescriber's signature		Frequency	14:00											
			16:00											
Pharmacist's signature	Indication		18:00											
			22:00											
			24:00											
Drug (approved name)		Dose	02:00							STOP				
			06:00											
Route	Start date	Stop date	10:00											
			12:00											
Prescriber's signature		Frequency	14:00											
			16:00											
Pharmacist's signature	Indication		18:00											
			22:00											
			24:00											
Drug (approved name)		Dose	02:00							STOP				
			06:00											
Route	Start date	Stop date	10:00											
			12:00											
Prescriber's signature		Frequency	14:00											
			16:00											
Pharmacist's signature	Indication		18:00											
			22:00											
			24:00											
Drug (approved name)		Dose	02:00							STOP				
			06:00											
Route	Start date	Stop date	10:00											
			12:00											
Prescriber's signature		Frequency	14:00											
			16:00											
Pharmacist's signature	Indication		18:00											
			22:00											
			24:00											
Drug (approved name)		Dose	02:00							STOP				
			06:00											
Route	Start date	Stop date	10:00											
			12:00											
Prescriber's signature		Frequency	14:00											
			16:00											
Pharmacist's signature	Indication		18:00											
			22:00											
			24:00											

(Source: MidWestern Regional Hospital, Ennis)

Appendix 14:
Restrictive and interpretative reporting of laboratory results

1: Example of unrestricted report (catheter specimen of urine)

Microscopy : Pus cells: 30/cm^3
Culture: *E. coli* 100 x 10^6/litre

Ampicillin	resistant
Trimethoprim	sensitive
Cephradine	sensitive
Gentamicin	sensitive

2: Examples of restricted reports, with interpretative comments

Catheter specimen of urine

Microscopy: Pus cells: 30/cm^3
Culture: *E. coli* 100 x 10^6/litre

The urine of patients with indwelling catheters frequently becomes colonised. Unless the patient becomes systemically unwell, treatment is not indicated. If clinical evidence of urinary tract infection, or bacteraemia, please contact (*contact details of medical microbiologist*) to discuss options for therapy. Antibiotic susceptibilities are available if clinical assessment suggests infection.

Sputum culture, from hospitalised patient

Culture: Moderate growth of *Enterobacter cloacae*

If clinical or radiological evidence of lower respiratory tract infection, antibiotic therapy may be indicated. Otherwise this probably represents upper airways colonisation, for which antibiotic therapy is not required. Please contact (*contact details of medical microbiologist*) to discuss options for therapy, if clinically indicated. Antibiotic susceptibilities are available if clinical assessment suggests infection.

Swab culture, from hospitalised patient

Culture: Moderate growth of *Staphylococcus aureus*

If cellulitis or deep-seated infection, antibiotic therapy may be indicated. Otherwise this represents colonisation, and likely to respond to topical antiseptic therapy alone. Please contact (*contact details of medical microbiologist*) to discuss options for therapy, if clinically indicated. Antibiotic susceptibilities are available if clinical assessment suggests infection.

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