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Start Smart - Then Focus

Antimicrobial Stewardship Toolkit for English Hospitals

Updated March 2015

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Published March 2015
PHE publications gateway number: 2014828

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Executive summary

This document is an update of the guidance published in 2011. It takes into account recommendations from the Annual Report of the Chief Medical Officer (CMO) 2011 (published in March 2013),[1] the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018,[2] the Cochrane Review - interventions to improve antibiotic prescribing practices for hospital inpatients 2013[3] and the English Surveillance Programme for Utilisation and Resistance (ESPAUR) report 2014.[4] It also acknowledges the forthcoming Cochrane update and draft antimicrobial stewardship guideline produced by the National Institute for Health and Care Excellence (NICE).[5,6]

The prevalence of antimicrobial resistance (AMR) has risen alarmingly over the last 40 years, and few truly novel antimicrobials have been developed. This has led to increased pressure on existing antibiotics and greater challenges in treating patients. Inappropriate use of antimicrobials increases the risk to patients of colonisation and infection with resistant organisms and subsequent transmission to other patients.

Antimicrobial stewardship is an important element of the both the UK Five Year Antimicrobial Resistance Strategy[2] and the 2011 CMO report.[1] The aims of such stewardship initiatives are to improve the safety and quality of patient care and to contribute significantly to reductions in the emergence and spread of AMR. These aims are ultimately achieved by improving antimicrobial prescribing through an organised antimicrobial management program. A ***Start Smart - then Focus*** approach is recommended for all antibiotic prescriptions.

Criterion 9 of the Health and Social Care Act 2008: Code of Practice on the prevention and control of infections and related guidance outlines the standards for compliance for registered organisations to provide evidence of prudent prescribing and antimicrobial stewardship.[7] The updated Code of Practice places greater emphasis on antimicrobial resistance and stewardship. The Code states: “Procedures should be in place to ensure prudent prescribing and antimicrobial stewardship. There should be an ongoing programme of audit, revision and update. In healthcare this is usually monitored by the antimicrobial management team or local prescribing advisors”.

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[1] Davies S. Annual Report of the Chief Medical Officer 2011: Volume Two. Infections and the Rise of Antimicrobial Resistance. http:// www.dh.gov.uk/health/2013/03/cmo-vol2/ (10 Aug 2014, date last accessed).
[2] UK Five Year Antimicrobial Resistance Strategy 2013 to 2018; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf (10 Aug 2014, date last accessed).
[3] Davey P, Brown E, Charani E, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. Cochrane Database Syst Rev 2013;(4):CD003543. http://dx.doi.org/10.1002/14651858.CD003543.pub3.
[4] PHE. English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) report 2014. https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report
[5] Davey P, Peden C, Brown E et al. interventions to improve antibiotic prescribing practices for hospital inpatients (updated protocol) http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD011236/full (27 Aug 2014 date last accessed)
[6] NICE guidance: Antimicrobial stewardship https://www.nice.org.uk/guidance/indevelopment/gid-antimicrobialstewardship (19 Feb 2015 date last accessed)
[7] The Health and Social Care Act 2008. Code of practice for the NHS on the prevention and control of health care associated infections and related guidance. Department of Health 2010. http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_122604

Outcome 8 of the CQC`s Essential Standards for Quality and Safety on cleanliness and infection control also points to the Code of Practice[8].

Improving antimicrobial prescribing and stewardship is dependent on strong clinical leadership. Within local Trusts, medical teams, in particular consultants should take a leadership role for antimicrobial quality improvement in their specialist areas. This should be done in collaboration with a consultant microbiologist/infectious diseases specialist and the antimicrobial pharmacist. Such initiatives should also seek to engage with junior doctors in order to develop a wider understanding of antimicrobial stewardship throughout the organisation.

This toolkit provides an outline of evidence-based antimicrobial stewardship in the secondary healthcare setting. It is recommended that the AMS management team/committee or equivalent use this toolkit along with the Code of Practice and *'Clostridium difficile:* how to deal with the problem'. This needs to be accompanied with a robust programme of auditing activities that promote safe and appropriate use of antimicrobials.[7,9]

These activities will form part of the quality improvement strategy for patient safety and help to reduce inappropriate prescribing and optimise antibiotic use. Implementation of this toolkit and the audit programme can be used as evidence of meeting criterion 9 of the Code of Practice on the prevention and control of infections when seeking registration with the Care Quality Commission.

Figures 1 and 2 show the Start Smart, Then Focus treatment algorithm and the antimicrobial stewardship surgical prophylaxis algorithm.

Start Smart - this means:

- do not start antimicrobial therapy unless there is clear evidence of infection
- take a thorough drug allergy history
- initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with severe sepsis or life-threatening infections. Avoid inappropriate use of broad-spectrum antibiotics
- comply with local antimicrobial prescribing guidance
- document clinical indication (and disease severity if appropriate), drug name, dose and route on drug chart and in clinical notes*
- include review/stop date or duration
- obtain cultures prior to commencing therapy where possible (but do not delay therapy)
- prescribe single dose antibiotics for surgical prophylaxis where antibiotics have been shown to be effective (figure 2)
- document the exact indication on the drug chart (rather than stating long term prophylaxis) for clinical prophylaxis

* Inclusion of these in both the drug chart and in clinical notes may clarify the patient treatment pathway thus aiding in the improvement of patient outcomes and in medico-legal outcomes such as for *C. difficile* apportionment.

[8] http://www.cqc.org.uk/sites/default/files/documents/gac_-_dec_2011_update.pdf
[9] Department of Health and the Health Protection Agency. Clostridium difficile infection: How to deal with the problem. London: Department of Health. 2008.
http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_093218.pdf

Then Focus – this means:

- reviewing the clinical diagnosis and the continuing need for antibiotics at 48*-72 hours and documenting a clear plan of action - the 'antimicrobial prescribing decision'
- the **five 'antimicrobial prescribing decision' options** are:
    1. **Stop** antibiotics if there is no evidence of infection
    2. **Switch** antibiotics from intravenous to oral
    3. **Change** antibiotics – ideally to a narrower spectrum – or broader if required
    4. **Continue** and document next review date or stop date
    5. Outpatient Parenteral Antibiotic Therapy (**OPAT**)[10]
- it is essential that the review and subsequent decision is clearly documented in the clinical notes and on the drug chart where possible eg stop antibiotic

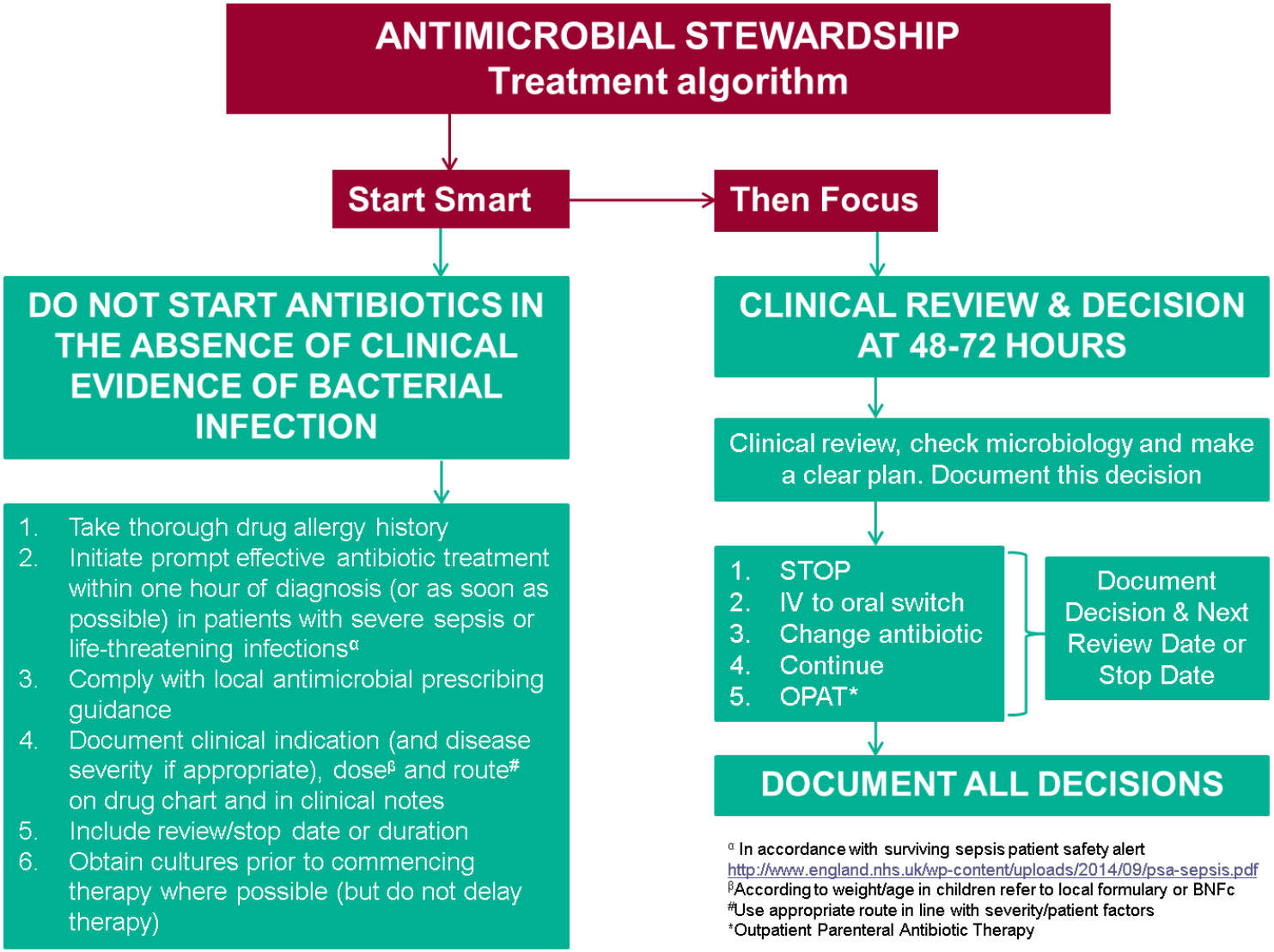
* Due to advances in rapid diagnostics it may be possible to review prior to 48 hours after first dose.

It is recommended that as a minimum, providers should develop an action plan and monitor adherence to Start Smart Then Focus principles regularly in all clinical areas (at least annually). In particular monitoring:

- evidence of documenting indication and duration (or review date) on the drug chart
- evidence of antimicrobial stewardship review of antibiotics at 48-72 hours after initiation and documentation of the antimicrobial prescribing decision (one of five options) on the drug chart (or in the clinical notes – see Figure 1)
- the time between the onset of sepsis related hypotension and administration of appropriate antibiotics (this may be part of 'Surviving Sepsis' related audits within the Trust)
- adherence with local guidance on the choice of antibiotic therapy (or documented reason for non-compliance)
- antimicrobial resistance and consumption trends

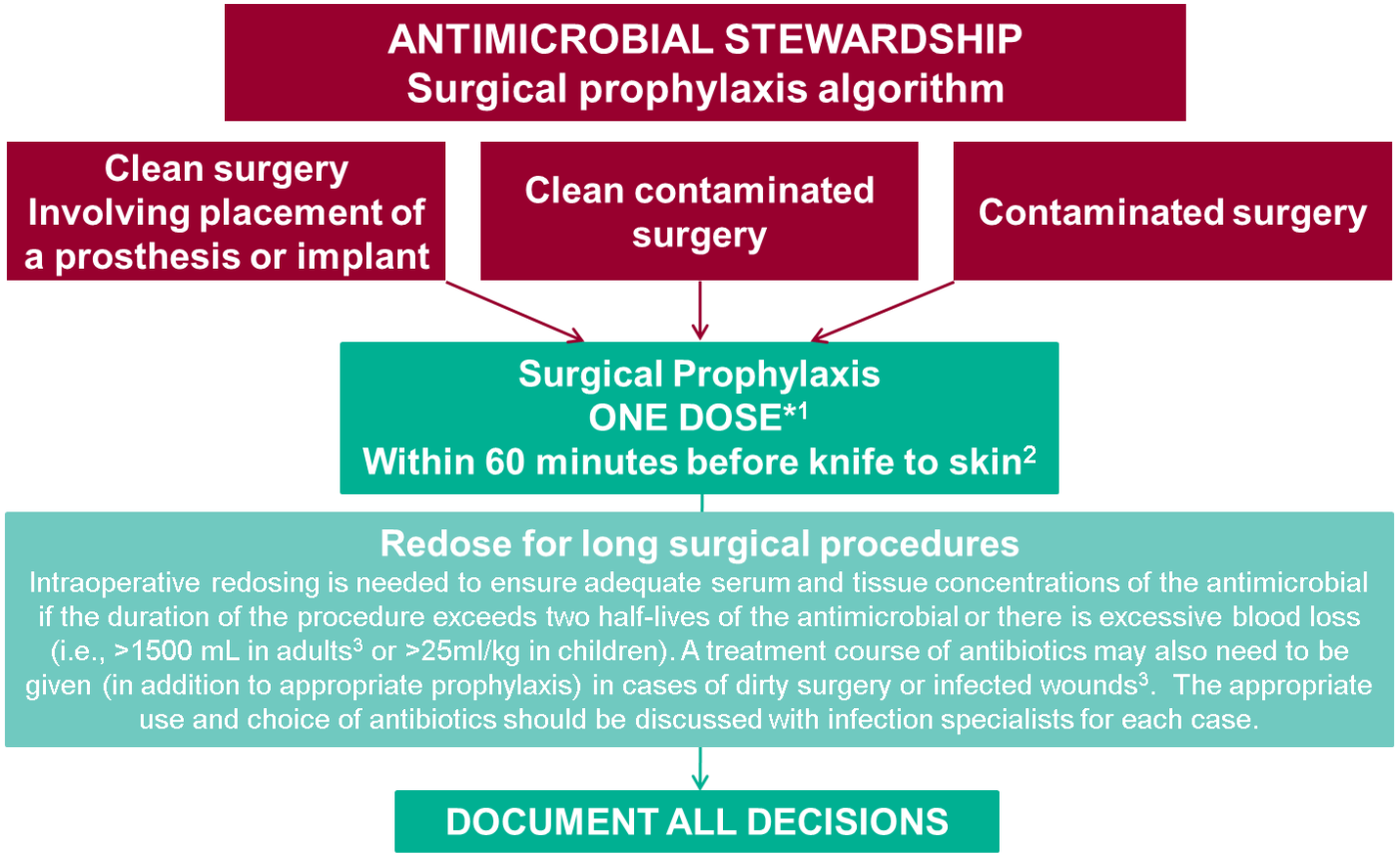
[10] British Society for Antimicrobial Chemotherapy. OPAT Good Practice Recommendations Available at: http://e-opat.com/opat-standards

Figure 1: Antimicrobial Stewardship (AMS) – Treatment algorithm



Advocating patient safety and auditing of antimicrobial stewardship in hospitals should be based around the principles stated in this AMS algorithm. Examples of audit tools are shared in Appendix 1

Figure 2: Antimicrobial Stewardship (AMS) – Surgical prophylaxis algorithm



References:
1. NICE clinical guideline 74: Surgical site infection – Prevention and treatment of surgical site infection http://www.nice.org.uk/Guidance/CG74
2. World alliance for Patient Safety. WHO surgical safety checklist June 2008 http://www.who.int/patientsafety/safesurgery/tools_resources/SSSL_Checklist_finalJun08.pdf?ua=1
3. Bratzler DW, Dellinger EP, Olsen KM et al. (2013). Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013; 70(3): 195-283

Advocating patient safety and auditing of antimicrobial stewardship in hospitals should be based around the principles stated in this AMS algorithm. Examples of audit tools are shared in Appendix 1. Deviations from the NICE guideline should be evidence based, with prolonged prophylaxis needing evidence of benefit.

Introduction

Aim

The aim of this toolkit is to provide an evidence-based outline for antimicrobial stewardship (AMS) in the secondary healthcare setting.

Context

The Code of Practice on the prevention and control of infections and related guidance applies to all providers of healthcare and adult social care under the Health and Social Care Act 2008.[7] The Code sets out the 10 criteria against which a registered provider will be judged on how it complies with the registration requirement for cleanliness and infection control. Antimicrobial resistance and stewardship has been strengthened within the updated document and it also provides a range of information to support providers in complying with the regulations.

The law states that the Code must be taken into account by the Care Quality Commission (CQC) when it makes decisions about registration against the cleanliness and infection control requirements. The regulations also state that providers must have regard to the Code when deciding how they will comply with the registration requirements. So by following the Code, registered providers will be able to show that they meet the requirement set out in the regulations.

This toolkit will help healthcare providers assess whether they meet Criterion 9 of the Health and Social Care Act 2008: Code of Practice on the prevention and control of infections and related guidance.[7]

Guidance on meeting this criterion states: 'Procedures should be in place to ensure prudent prescribing and antimicrobial stewardship. There should be an ongoing programme of audit, revision and update. In healthcare this is usually monitored by the antimicrobial management team or local prescribing advisors'.[7]

Current evidence clearly demonstrates that the inappropriate use of broad-spectrum antimicrobials is associated with the selection of AMR bacteria. This includes extended-spectrum beta-lactamase (ESBL)-producing Gram-negative bacteria,[11,12] Methicillin resistant *Staphylococcus aureus* (MRSA)[13,14,15,16] and the induction of *Clostridium difficile* infection

[11] Livermore DM. Has the era of untreatable infections arrived? J Antimicrob Chemother. 2009;64(Suppl 1):29-36
[12] Hawkey, P., Jones, A. The Changing Epidemiology of Resistance. J Antimicrob Chemother. 2009; 64:Suppl 1:i3–10
[13] Lucet JC, Chevret S, Durand-Zaleski I, Chastang C, Regnier B. Prevalence and risk factors for carriage of methicillin-resistant *Staphylococcus aureus* at admission to the intensive care unit: results of a multicenter study. Arch Intern Med 2003;163:181-8
[14] Tacconelli E, De Angelis, Cataldo MA, et al. Does antibiotic exposure increase the risk of methicillin-resistant *Staphylococcus aureus* (MRSA) isolation? A systematic review and meta-analysis. J Antimicrob Chemother. 2008; 61(1): 26-38
[15] Dancer SJ. The effect of antibiotics on meticillin-resistant *Staphylococcus aureus*. J Antimicrob Chemother. 2008; 61:246-253
[16] Liebowitz LD and Blunt MC. Modification in prescribing practices for third generation cephalosporins and ciprofloxacin is associated with a reduction in meticillin- resistant *Staphylococcus aureus* bacteraemia rate. J.Hosp Inf 2008; 69:328-336

(CDI)[3,7,17,18,19] and can cause long-lasting harmful changes to the body's protective microbial flora.[20,21]

Broad-spectrum antibiotics (including cephalosporins, fluoroquinolones, co-amoxiclav, piperacillin-tazobactam, carbapenems and clindamycin) have been most associated with CDI, but all antibiotics should be avoided unless there are clear clinical indications for their use. Antibiotics should be used for the shortest duration possible that gives an appropriate clinical outcome. They should also be managed within a multifactorial programme (including infection prevention and control precautions) aimed at reducing healthcare-associated infections (HCAI) and improving antimicrobial use.[6,7]

A stong and robust antimicrobial stewardship programme is seen as a key component in the reduction of some HCAIs in support of patient safety. The draft NICE guideline on antimicrobial stewardship recommends that organisations should establish an antimicrobial stewardship programme taking account of the resources needed to support good antimicrobial stewardship across all care settings.[6]

There are a number of reports which highlight the failure to embed stewardship programmes into local practice. These include a National Audit Office report, published in 2009, which suggested that one-third of Trusts in England did not have a robust strategy to review antimicrobial prescriptions automatically within a defined period.[22] A separate national survey of antimicrobial stewardship activites by the English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR) revealed that although a large majority (87.9%) of Trusts reported reviewing the Start Smart Then Focus (SSTF) document formally or informally; only 48% of Trusts report implementing a SSTF action plan after a review. In addition, whilst 79% of Acute Trusts collate data on at least one of the recommended audits in SSTF, there is a low uptake of audits that can be correlated to patient outcomes (eg time to first dose in severe sepsis, post prescription review and documentation at 48 hours).[4]

Like any change and improvement activity, especially those linked to patient safety, the success of an antimicrobial stewardship program is dependent on the support of hospital management and senior clinical staff. **It is no longer the responsibility of specialists alone to champion the stewardship efforts within an organisation**. Ultimately the Trust Board, managers and staff are all responsible for establishing, maintaining and supporting a co-ordinated approach to antimicrobial stewardship.[7]

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[17] Wistrom, J., S. R. Norrby, E. B. Myhre, S. Eriksson, G. Granstrom, L. Lagergren, G. Englund, C. E. Nord, and B. Svenungsson. 2001. Frequency of antibiotic-associated diarrhoea in 2462 antibiotic-treated hospitalized patients: a prospective study. J. Antimicrob. Chemother. 47:43-50

[18] Freeman J, Bauer MP, Baines SD, Corver J, Fawley WN, Goorhuis B, Kuijper EJ, Wilcox MH The changing epidemiology of *Clostridium difficile* infections. Clin. Microbiol. Rev. 2010. 23:529–549.

[19] Nelson RL, Kelsey P, Leeman H, Meardon N, Patel H, Paul K, Rees R, Taylor B, Wood E, Malakun R. Antibiotic treatment for *Clostridium difficile*-associated diarrhea in adults. Cochrane Database of Systematic Reviews 2011, Issue 9. Art. No.: CD004610. DOI: 10.1002/14651858.CD004610.pub4

Blaser M. Antibiotic overuse: Stop the killing of beneficial bacteria. Nature. 2011 476: 393-394

[21] Hviid A, Svanström H, Frisch M Antibiotic use and inflammatory bowel diseases in childhood Gut. 2011 Jan;60(1):49-54

[22] National Audit Office. Reducing Healthcare Infections in Hospitals in England. June 2009

Antimicrobial Stewardship Programme

Current guidance and published evidence recommends an antimicrobial stewardship programme should include the following: [1,2,3,6,7,23,24,25,26,27,28,29,30,31]

- an assessment of the Trust's antimicrobial stewardship activities
- an antimicrobial stewardship management team/committee
- a ward-focused antimicrobial team
- evidence-based antimicrobial prescribing guidelines
- quality assurance measures/audits and feedback
- education and training

An assessment of the Trust's Antimicrobial Stewardship Activities

Trusts should demonstrate that there has been an assessment of the organisation's antimicrobial stewardship activities against the Start Smart Then Focus AMS toolkit as well as developing an action plan in order to provide an assurance to the Trust Board of safe, effective and appropriate antimicrobial prescribing (Table 1).

Table 1: It is recommended that as a minimum, providers should develop an action plan and monitor adherence to Start Smart Then Focus principles regularly in all clinical areas (at least annually). In particular monitoring:

- evidence of documenting indication and duration (or review date) on the drug chart
- evidence of antimicrobial stewardship review of antibiotics at 48-72 hours after initiation and documentation of the antimicrobial prescribing decision (one of five options) on the drug chart (or in the clinical notes – see Figure 1)
- the time between the onset of sepsis related hypotension and administration of appropriate antibiotics – this may be part of 'Surviving Sepsis' related audits

[23] Dellit TH, Owens RC, McGowan JE et al. Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America Guidelines for Developing an Institutional Program to Enhance Antimicrobial Stewardship. Clin Infect Dis. 2007;44:159-77.
[24] Cooke J. Alexander K. Charani E et al. Antimicrobial stewardship: an evidence-based, antimicrobial self-assessment toolkit (ASAT) for acute hospitals. J Antimicrob Chemother. 2010;65(12):2669-73
Available at: http://www.researchdirectorate.org.uk/uhsm/asat/asat.asp
[25] Thern J, Strauss R, Steib-Bauert M et al. Selection of hospital antimicrobial prescribing quality indicators: a consensus among German antibiotic stewardship (ABS) networkers. Infection, 2014;42(2): 351-362
[26] Center for Disease Control and Prevention (CDC); Checklist for Core Elements of Hospital Antibiotic Stewardship Programs. Available at: http://www.cdc.gov/getsmart/healthcare/pdfs/checklist.pdf , (10 Aug 2014, date last accessed).
[27] Buyle FM, Metz-Gercek S, Mechtler R et al. Development and validation of potential structure indicators for evaluating antimicrobial stewardship programmes in European hospitals. European journal of clinical microbiology & infectious diseases, 2013; 32(9): 1161-1170.
[28] Dumartin C, Rogues AM, Amade´o B et al. Antibiotic usage in south-western French hospitals: trends and association with antibiotic stewardship measures. J Antimicrob Chemother 2011; 66: 1631–7.
[29] Bruce J, MacKenzie FM, Cookson B et al. Antibiotic stewardship and consumption: findings from a pan-European hospital study. J Antimicrob Chemother 2009; 64: 853–60
[30] Australian Commission on Safety and Quality in Health Care. 2011. Antimicrobial stewardship in Australian hospitals. Available at: http://www.safetyandquality.gov.au/publications/antimicrobial-stewardship/ (10 Aug 2014, date last accessed).
[31] Society for Healthcare Epidemiology of America, and Infectious Diseases Society of America. "Policy Statement on Antimicrobial Stewardship by the Society for Healthcare Epidemiology of America (SHEA), the Infectious Diseases Society of America (IDSA), and the Pediatric Infectious Diseases Society (PIDS)." Policy Statement 33.4 (2012): 322-327.

within the Trust
- adherence with local guidance on the choice of antibiotic therapy (or documented reason for non-compliance)
- antimicrobial resistance and consumption trends

The use of a self-assessment tool such as the antimicrobial self-assessment toolkit (ASAT) may be a useful additional resource to enable such an appraisal.[24] There are also a number of published quality indicators and check-lists that may be useful.[25-29] While the individual elements in these tools and checklists may be helpful in improving antibiotic use, not all elements may be feasible in all hospitals.

An Antimicrobial Stewardship Management Team/Committee

It is recommended that a multidisciplinary management team/committee be set up to develop and implement the organisation's antimicrobial stewardship programme for all adults and children admitted to hospital.[6,7]

This multidisciplinary group may have different names (for example the antimicrobial/antibiotic stewardship committee/group or management team). The name of the management committee is less important than the core functions of the group, which are described below. The suggested minimum core membership should include: a consultant microbiologist/infectious diseases specialist, an antimicrobial pharmacist, an acute care physician, a surgeon, a senior member of the pharmacy management team, an anaesthetist, a paediatrician, a senior nurse and primary care representation (to ensure a whole healthcare economy approach). The aim is to ensure a multidisciplinary approach and improve engagement across the organisation.[32]

The management team/committee should report antimicrobial stewardship activities to the Trust Board via the organisation's Director of Infection Prevention and Control (DIPC)/Infection Control Committee and/or the Drugs and Therapeutic Committee (or equivalent).

The key roles of the AMS management team/committee are to:
- ensure that evidence-based local antimicrobial guidelines are in place and reviewed regularly or when new evidence is published
- ensure regular auditing of the guidelines, antimicrobial stewardship practice and quality assurance measures
- report a regular formal review of the organisation's retrospective antibiotic consumption data (especially highlighting the use of broad-spectrum antibiotics such as cephalosporins, co-amoxiclav, piperacillin-tazobactam, fluoroquinolones and carbapenems). PHE and ESPAUR measure antimicrobial consumption as Defined Daily Doses (DDD) per 100 admissions. The presentation of DDD per admissions rather than bed-days reflects hospital activity for admissions rather than those who are in hospital only. This

[32] Cortoos PJ, De Witte K, Peetermans WE et al. Opposing expectations and suboptimal use of a local antibiotic hospital guideline: a qualitative study. J Antimicrob Chemother 2008; 62(1): 189-195.

measurement would allow comparison with national data and consistent benchmarking between Trusts
- identify actions to address non-compliance with local guidelines, general antimicrobial stewardship issues and other prescribing issues

A ward-focused antimicrobial team

A ward-focused antimicrobial team is recommended in addition to the AMS management team/committee. This should include the antimicrobial pharmacist and consultant microbiologist/infectious diseases specialist that report to the AMS management team/committee. The ward-focused team would be expected to review prescriptions at ward level as part of multi-disciplinary antimicrobial stewardship ward rounds.

Evidence-based antimicrobial prescribing guidelines

It is recommended that each organisation draw up a local antimicrobial stewardship policy and develop local antimicrobial guidelines based on national guidance (for example from the British National Formulary, NICE or Public Health England).

These local guidelines should be evidence-based, relevant to the local healthcare setting and take into account local antibiotic resistance patterns. They should cover diagnosis and treatment of common infections and prophylaxis of infection. Prescribers should adhere to these guidelines and compliance should be monitored and supported by senior clinicians and pharmacists. Responsibility for guideline implementation should reside with the AMS management team/committee; Drugs and Therapeutics Committee or equivalent and the Director for Infection Prevention and Control.

The local antimicrobial stewardship policy should contain:

1. a policy statement that outlines the need for clear clinical case definitions and associated evidence of infection to minimise unnecessary prescribing of antimicrobials [33,34]
2. an emphasis of the urgent need to start treatment with effective antibiotic agents for severe sepsis or life-threatening infections [35,36,37,38]
3. a reminder for prescribers to use antibiotic agent(s) with an adequate spectrum to cover only the expected pathogens for less severe infections. To highlight that

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[33] Costello C, Metcalfe C, Lovering A, et al. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systemic review and meta-analysis. BMJ 2010; 340:c2096.
[34] Saeed K, Dryden M, Bourne S, Paget C, Proud A; Reduction in antibiotic use through procalcitonin testing in patients in the medical admission unit or intensive care unit with suspicion of infection. J Hosp Infect. 2011 Aug;78(4):289-92.
[35] Kollef MH, Sherman G, Ward S, et al: Inadequate antimicrobial treatment of infections. Chest 1999; 115:462-474
[36] Kumar A, Roberts D, Wood KE, Light B, Parrillo JE, Sharma S, Suppes R, Feinstein D, Zanotti S, Taiberg L, Gurka D, Kumar A, Cheang M. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006 Jun;34(6):1589-96.
[37] Tang CM, Macfarlane JT. Early management of younger adults dying of community acquired pneumonia. Resp Med 1993;87: 289-94
[38] Dellinger RP, Levy MM, Rhodes A et al. surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. Crit Care Med 2013; 41: 580–637. Available at: http://www.survivingsepsis.org/SiteCollectionDocuments/Final%2008%20SSC%20Guidelines.pdf

broad-spectrum antibiotics are sometimes not as potent in vitro as their narrower-spectrum counterparts against certain pathogens [39,40]

4. a reminder for prescribers to consider the risk of resistant pathogens such as MRSA or ESBL-producing organisms and offer alternative treatment regimens accordingly or encourage prescribers to seek expert advice [41,42,43]
5. a description of the importance of confirming the allergy status of recommended antibiotic agents in patients as there may be a need to offer alternative treatment choices for those who are allergic.[44] In line with NICE guidance on drug allergy,[45] patients with a history of such allergies should be assessed, and the allergy label removed where it is not correct, in order to improve patient outcomes
6. an outline for prescribers to take appropriate specimens for culture and sensitivity testing prior to commencing antibiotic treatment. However they should not delay starting treatment in patients with severe sepsis or life-threatening infections [38]
7. a recommendation for intravenous (IV) administration only to patients who are severely ill, unable to tolerate oral treatment, or where oral therapy would not provide adequate coverage or tissue penetration
8. an outline for prescribers to review microbiology results daily and to de-escalate to pathogen-directed narrow-spectrum treatment promptly where appropriate [46,47]
9. a recommendation for prescribers to document the next review date or stop date and switch to the oral route of administration promptly in accordance with local IV-to-oral switch guidance [48]

Antimicrobial prescribing guidelines should be guided by evidence and local susceptibility data (eg by area team where available).[4] Guidelines should include the following:

1. clinical diagnosis - to include: case definition, evidence of infection, severity assessment and relevant microbiology investigations
2. recommendations for non-antimicrobial treatment (eg fluid resuscitation or surgery)

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[39] EUCAST. MIC distributions. http://www.eucast.org/mic_distributions/.
[40] HPA Antimicrobial Resistance and Prescribing in England, Wales and Northern Ireland, 2008 http://www.hpa.org.uk/web/HPAwebFile/HPAweb_C/1216798080469
[41] Safdar N, Maki DG. The commonality of risk factors for nosocomial colonization and infection with antimicrobial-resistant Staphylococcus aureus, enterococcus, gram-negative bacilli, Clostridium difficile, and Candida. Ann Intern Med. 2002 Jun 4;136(11):834-44.
[42] Owens, R.C., Donskey, C.J., Gaynes, R.P. et al. (2008) Antimicrobial-associated risk factors for Clostridium difficile infection. Clin Infect Dis. 46(Suppl 1), S19-S31
[43] Vernaz N, Sax H, Pittet D, Bonnabry P, Schrenzel J, Harbarth S. Temporal effects of antibiotic use and hand rub consumption on the incidence of MRSA and Clostridium difficile. J Antimicrob Chemother. 2008 vol. 62(3) pp. 601-607
[44] Charneski L, Deshpande G, Smith SW. Impact of an antimicrobial allergy label in the medical record on clinical outcomes in hospitalized patients. Pharmacother. 2011;31(8):742-7
[45] NICE Clinical Guideline183. Drug allergy: diagnosis and management of drug allergy in adults, children and young people. http://www.nice.org.uk/guidance/cg183
[46] Alvarez-Lerma, F Modification of empiric antibiotic treatment in patients with pneumonia acquired in the intensive care unit: ICU-Acquired Pneumonia Study Group. Intensive Care Med 1996;22,387-394
[47] Alvarez-Lerma F, Alvarez B, Luque P, Ruiz F, Dominguez-Roldan JM, Quintana E, Sanz-Rodriguez C; ADANN Study Group. Empiric broad-spectrum antibiotic therapy of nosocomial pneumonia in the intensive care unit: a prospective observational study. Crit Care 2006; 10:R78.
[48] Mertz D, Koller M, Haller P, Lampert ML, Plagge H, Hug B, et al Outcomes of early switching from intravenous to oral antibiotics on medical wards. J Antimicrob Chemother 2009;64:188-199

3. empirical antimicrobial treatment recommendations: Initial antimicrobial therapy prior to availability of microbiology results or if a microbiological diagnosis is not going to be possible*
4. directed antimicrobial treatment when microbiology results are known and advice to contact clinical microbiologists/infectious diseases specialists if required*
5. oral switch guidance to highlight which oral agents to switch to and when [48]
6. duration of therapy for IV and oral agents [49]
7. specific guidance for exceptions and special cases if appropriate
8. provide advice regarding monitoring and follow-up and contingency advice for treatment failure [6,48,50]
9. guidance for prophylaxis for surgery or procedures. These should also include: the aim of prophylaxis eg reduce surgical site infection, where prophylaxis is required and where it is not, distinction between risk groups eg patients colonised with multi-drug resistant organisms such as MRSA, ESBL and CRE, alternatives where penicillin or other allergy exists and recommendation of single dose surgical prophylaxis regimens as appropriate and redosing frequency when more than one dose is required [51,52,53]

*Empirical and directed treatment recommendations should specify the choice of drug(s), route of administration and dose. In addition a reminder for prescribers to adjust dosing for specific patient factors eg renal or hepatic impairment.[54]

Quality Assurance Measures/Audits and Feedback

Procedures should be in place to ensure prudent antibiotic prescribing and antimicrobial stewardship. This will necessitate an ongoing programme of audit, revision and update and should be monitored by the AMS management team/committee.

It is recommended that a multi-disciplinary quality improvement/audit programme for antimicrobial stewardship should be developed and sustained in every Acute Trust. Regular (at least annual) feedback of adherence to audits recommended within the Start Smart Then Focus toolkit should be provided to the Trust Board (as part of the annual infection control committee report), prescribers, lead clinicians, microbiologists/infectious diseases specialists, nurses, pharmacists and the DIPC (see Table 1).

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[49] Chastre J, Wolff M, Fagon JY, Chevret S, Thomas F, Wermert D, Clementi E, Gonzalez J, Jusserand D, Asfar P, Perrin D, Fieux F, Aubas S; PneumA Trial Group. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults: a randomized trial. JAMA. 2003 Nov 19;290(19):2588-98.
[50] Singh N, Rogers P, Atwood CW, Wagener MM, Yu VL.Short-course empiric antibiotic therapy for patients with pulmonary infiltrates in the intensive care unit. A proposed solution for indiscriminate antibiotic prescription. Am J Respir Crit Care Med. 2000 Aug;162(2 Pt 1):505-11.
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[52] NICE Clinical Guideline 74. Surgical Site Infection – Prevention and treatment of surgical site infection Available at: http://www.nice.org.uk/nicemedia/pdf/CG74NICEGuideline.pdf
[53] Sign 104: Antibiotic prophylaxis in surgery. www.sign.ac.uk/guidelines/fulltext/104/index.html. 2008
[54] Thomas JK, Forrest A, Bharnani SM, et al. Pharmacodynamic evaluation of factors associated with the development of bacterial resistance in acutely ill patients during therapy. Antimicrob Agents Chemother. 1998;42:521-7

The AMS management team/committee and the DIPC should review antibiotic consumption trends regularly (at least annually).

Action should be taken to investigate non-adherence to local protocols for antibiotic prescribing (based on best practice) or unexpected trends in prescribing. It is recommended that these should be documented and reported, for example in minutes of the Antimicrobial Stewardship Committee/Team meetings

Trust-wide six-monthly or annual point prevalence studies (PPS) may be used to collect data to monitor compliance with the organisation's stewardship programme, and provide assurance for the organisation around compliance with the code of practice on prevention and control or infections.

Organisations should consider the formal investigation, via an existing clinical governance framework, of cases of repeated non-compliance (without clinical justification) or inappropriate prescribing, particularly when these result in an adverse patient outcome (eg development of an HCAI, prolonged length of stay, etc.). The Medical Director or Director of Infection Prevention and Control should challenge individuals whose prescribing practice is found to be repeatedly inappropriate.

It is important for providers to monitor patient outcomes to ensure that qualitative or quantitative alterations (changing, reducing, restricting) to antimicrobial prescribing do not have unintended detrimental effects for example increased time to clinical cure, increased mortality or increased readmission rate.[55,56]

Improving antimicrobial prescribing and stewardship is dependant on strong clinical leadership. Within local Trusts, medical teams, in particular consultants should take a leadership role for antimicrobial quality improvement in their specialist areas. This would be done in collaboration with a consultant microbiologist/infectious diseases specialist and the antimicrobial pharmacist.

These initiatives should also seek to engage with junior doctors in order to develop a wider understanding of antimicrobial stewardship throughout the organisation. This is in agreement with the draft NICE antimicrobial stewardship guideline which recommends that organisations should encourage senior health professionals to promote antimicrobial stewardship within their teams, recognising the influence that senior prescribers can have on prescribing practices of colleagues.

Trusts are encouraged to benchmark antimicrobial quality assurance measures to provide an additional context to their individual data.

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Education and Training

'There should be mandatory core training in prudent antibiotic use for doctors, pharmacists and nurses in addition to an introductory session on each induction programme. Post-registration, this training should be repeated by all such staff every three years and should specifically cover those antibiotics that are linked to CDI'.[9]

Independent prescribers should use the antimicrobial prescribing and stewardship competencies (developed by the Department of Health advisory committee on antimicrobial resistance and healthcare associated infections (ARHAI) and PHE)[57,58] to help develop their practice in relation to prescribing antimicrobials.

Nurses have a significant role to play in limiting the threat posed by AMR.[56,59,60] They should be educated on the importance of avoiding missed and/or omitted doses (to maintain therapeutic levels) and ensuring that all diagnostic tests are carried out promptly. A targeted education strategy may facilitate the role that nurses also play in questioning and highlighting the duration of therapies and prescription of medications where these do not meet with established organisational guidelines. [56,57,58]

Why use the toolkit?

The NHS Standard Contract is a key enabler for commissioners to secure improvements in the quality of services for patients and to hold providers of NHS funded care to account. Each provider is required to have an HCAI reduction plan for each contract year (and to comply with its obligations under that plan) that must reflect local and national priorities relating to HCAI including AMR, set out obligations for the management and reduction of HCAI and be agreed between the provider and the commissioner.

It is recommended that organisations should use this toolkit as part of their quality improvement strategy for patient safety, enhancing stewardship in antibiotic usage, and ensuring optimal patient care and safety by reducing inappropriate prescribing. Compliance with this toolkit and auditing can be used as evidence of compliance with criterion 9 of the Code of Practice on the prevention and control of infections and incorporated into the HCAI reduction plan.

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[57] Department of Health and Public Health England. Antimicrobial prescribing and stewardship competencies. London: Department of Health. 2013. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/253094/ARHAIprescrcompetencies__2_.pdf

[58] The Royal College of Nursing: Antimicrobial resistance: RCN position on the nursing contribution http://www.rcn.org.uk/__data/assets/pdf_file/0003/590484/004681.pdf

[59] Edwards R Loveday H, Drumright L N, and Holmes A. Should nurses be more involved in antimicrobial management? J Infect Prev 2011 12: 4-5

[60] Edwards R, Drumright L N, Kiernan M, Holmes A Covering more territory to fight resistance: considering nurses role in antimicrobial stewardship. J Infect Prev 2011 12: 6-10

Start Smart

- **Do not start antibiotics in the absence of clinical evidence of bacterial infection**

If there is evidence/suspicion of bacterial infection, use local guidelines to initiate prompt effective antibiotic treatment within one hour of diagnosis (or as soon as possible) in patients with life-threatening infections such as severe sepsis.[38] Avoid inappropriate use of broad-spectrum antibiotics.[11-21]

- **For antibiotic(s) prescribed, document each of the following on the drug chart and in the clinical notes: clinical indication (including disease severity if appropriate), dose, route and duration or review date.**

Antibiotics in hospitals are often continued unnecessarily because clinicians caring for the patient do not have information indicating why the antibiotics were initially commenced and how long they were planned to be continued. This problem is compounded where primary responsibility for patient care is frequently transferred from one clinician to another. Ensuring that all antibiotic prescriptions are always accompanied by an indication and a clear duration or review date will help clinicians change or stop therapy when appropriate. In children the dose of antimicrobials should be prescribed according to the individuals weight/age - refer to local formulary or BNFc

- **Obtain cultures first where possible**

Knowing the antibiotic susceptibility of an infecting organism can help clinicians to prescribe the most appropriate antibiotic. This is useful for narrowing of broad-spectrum therapy, changing therapy to effectively treat resistant pathogens and stopping antibiotics when cultures suggest an infection is unlikely. Cultures are also important for epidemiological surveillance.
Do not delay treatment for patients with life-threatening infections eg severe sepsis.

- **Prescribe single dose antibiotics for surgical prophylaxis; where antibiotics have been shown to be effective.**

Critical to this advice is that the single dose is administered within the 60 minutes prior to surgical incision or tourniquet inflation to enable peak blood levels to be present at the start of the surgical procedure.[51] Intraoperative redosing is needed to ensure adequate serum and tissue concentrations of the antimicrobial if the duration of the procedure exceeds two half-lives of the antimicrobial or there is excessive blood loss (eg >1500 mL in adults, >25 ml/kg in children).[61] A treatment course of antibiotics may also need to be given (in addition to appropriate prophylaxis) in cases of dirty surgery or infected wounds. The appropriate use and choice of antibiotics should be discussed with infection specialists for each case (see Figure 2 - Surgical Prophylaxis Algorithm).[51,52]

[61] Bratzler DW, Dellinger EP, Olsen KM et al. (2013). Clinical practice guidelines for antimicrobial prophylaxis in surgery. Am J Health Syst Pharm 2013; 70(3): 195-283

Then Focus

- **Review the clinical diagnosis and the continuing need for antibiotics by 48-72 hours and make a clear plan of action - the 'antimicrobial prescribing decision'**

Antibiotics are generally started before a patient's full clinical picture is known. By 48-72 hours, when additional information is available, including microbiology, radiographic and clinical information, it is important for clinicians to re-evaluate why the therapy was initiated in the first place and to gather evidence on whether there should be changes to the therapy.

- **The five 'antimicrobial prescribing decision' options are Stop, Switch, Change, Continue and OPAT:**
  1. Stop antibiotics if there is no evidence of infection
  2. Switch antibiotics from IV to oral
  3. Change antibiotics – ideally to a narrower spectrum – or broader if required. Prescribers should seek expert advice when necessary
  4. Continue and document next review date or stop date for IV and oral antibiotics
  5. Outpatient Parenteral Antibiotic Therapy (OPAT).[10]

For paediatric patients in particular, the choice of oral antibiotic should account for factors potentially affecting adherence such as dosing frequency and palatability/taste of formulation. Palatable oral drugs in a sensible regimen (up to 3 times per day) should be used where possible and middle of the night dosing of oral antibiotics should be avoided whenever possible, especially following discharge.

- **It is essential that the review and subsequent decision be clearly documented in the clinical notes. The decision should also be documented clearly on the drug chart.**

Components of Best Practice for Antimicrobial Prescribing (Treatment)

Organisations should develop their own audit strategy/programme and action plan.[7] Each of the criteria below should be audited at least annually however there may be a need to monitor some aspects more frequently.

It is recommended that as a minimum, providers should develop an action plan and monitor adherence to Start Smart Then Focus principles regularly in all clinical areas (at least annually). In particular monitoring:

- evidence of documenting indication and duration (or review date) on drug chart
- evidence of antimicrobial stewardship review of antibiotics at 48-72 hours after initiation and documentation of the antimicrobial prescribing decision (one of five options) on the drug chart (or in the clinical notes) (Figure 1)
- the time between the onset of sepsis related hypotension and administration of appropriate antibiotics – this may be part of 'Surviving Sepsis' related audits within the Trust
- adherence with local guidance on the choice of antimicrobial therapy (or documented reason for non-compliance)
- antimicrobial resistance and consumption trends

Several components of best practice can be audited as part of the Trust-wide six-monthly or annual point prevalence studies (PPS) or integrated into existing audit programmes established locally.*

* The tables below along with sample audit tools are available in Annex 1: Resource Materials - examples of audit tools, review stickers and drug charts

Table 2: Components of Best Practice for Antimicrobial Prescribing (Treatment)

Criteria	Description of audit	Rationale for audit
1. Treatment of infection emergencies	Audit the treatment of severe sepsis and septic shock against clinical standards. This should include an audit of the time from the onset of severe sepsis to the administration of the first dose of antibiotic therapy[62]	A delay in starting adequate antibiotic therapy in severe infection is associated with increased morbidity and mortality

[62] The UK Sepsis Trust. Clinical toolkits for professionals. http://sepsistrust.org/info-for-professionals/clinical-toolkits/

Criteria	Description of audit	Rationale for audit
2.Communication of the decision to prescribe antimicrobials	Audit the documentation of the decision to start antimicrobial therapy along with the indication or provisional diagnosis in the clinical notes and on the drug chart. This should include the clear identification of the prescriber and their contact details	Communication between healthcare teams is vital to ensure safe and effective patient care. This is mandated by the Royal Colleges. The requirement to document prescribing decisions will discourage antimicrobial prescribing where evidence of infection is lacking
3. Microbiology culture and sensitivities (MC&S)	Audit the appropriateness of specimens (for specific infections) obtained for MC&S. This should conform to local guidelines	The availability of appropriate cultures and sensitivities will facilitate the prompt de-escalation of broad-spectrum agents or the tailoring of therapy in cases of treatment failure
4. Antimicrobial consumption	Audit the consumption of antimicrobial agents (or de-escalation audit)	The unnecessary continuation of antimicrobials is associated with HCAIs and contributes to the development of AMR
5. Choice of antimicrobial agent(s)	Audit the choice of antimicrobial therapy. This should be according to local guidelines where available. This audit may also opt to include the dose and route of administration of the antimicrobials prescribed	Inappropriate antimicrobial therapy is associated with HCAIs, the development of AMR and the associated risks of unnecessary drug exposure
6. Review date for prescribed antimicrobials	Audit the review of antimicrobials at 48-72 hours after initiation. This should capture the documentation of the decision to continue current therapy and subsequent specified review or stop date	An expected duration or review date should be documented on antimicrobial prescriptions. This practice will discourage open-ended prescriptions
7. Duration of IV antimicrobial therapy	Where IV antimicrobials are continued at 48-72 hours after initiation, audit the documentation for continuing treatment. Audit the relative consumption of IV and oral antimicrobials	Treatment with IV antimicrobials should not continue beyond 48-72 hours unless recommended by local guideline or consultant microbiologist/infectious diseases specialist Unnecessary continuation of IV treatment increases the risk of line infection

Criteria	Description of audit	Rationale for audit
8. IV-to-oral antimicrobial switch	Audit compliance with local IV to oral switch OR Audit the relative consumption of IV and oral antimicrobials	Treatment with IV antimicrobials should be switched to oral therapy within 24 hours of meeting local switch criteria Unnecessary continuation of IV treatment increases the risk of line infection
9. Total duration of antimicrobial therapy	Audit antimicrobial consumption	Treatment with antimicrobials should not continue beyond 7 days (IV plus oral) unless recommended by a local guideline or consultant microbiologist/infectious diseases specialist Prolonged antibiotic therapy is associated with HCAIs, the development of AMR and other consequences of prolonged drug exposure

Components of Best Practice for Antimicrobial Prescribing (peri-operative prophylaxis)

Annual audit of local surgical prophylaxis practice to include:*

* The tables below along with sample audit tools are available in Annex 1: Resource Materials - examples of audit tools, review stickers and drug charts

Table 3: Components of Best Practice for Antimicrobial Prescribing (peri-operative prophylaxis)

Criteria	Description of audit	Rationale for audit
1. Need for antimicrobial prophylaxis	Audit the indication for antimicrobial prophylaxis. Practice should conform to local guidelines	For certain clean procedures, evidence suggests a lack of benefit of antimicrobials The clinical indication should comply with *NICE 74: Surgical site infection: Prevention and treatment of surgical site infection*[52]
2. Choice of antimicrobial agent(s) for perio-operative prophylaxis	Audit the choice of antimicrobial therapy. This should be according to local guidelines where available	Antimicrobial prophylaxis should ensure adequate coverage of expected pathogens according to surgical site. Whenever possible the prophylaxis should avoid cephalosporins, clindamycin and fluoroquinolones Where necessary, appropriate alternatives should be prescribed for patients with penicillin/ beta-lactam allergy, or those colonised with resistant organisms eg MRSA The choice of antimicrobial agent(s) should be prescribed according to local guidelines.
3. Timing of antimicrobial prophylaxis	Audit the time between the administration of antimicrobial prophylaxis and skin incision	Antimicrobial prophylaxis should be administered within 60-minutes prior to incision (or tourniquet) or according to local guidelines[52]. The lowest surgical site infection rates associated with optimal timing of pre-incision administration of antimicrobials

Criteria	Description of audit	Rationale for audit
4.Repeat doses of antimicrobial prophylaxis	Audit cases of multiple or post-operative antimicrobial prophylaxis	Single dose is indicated for majority of procedures and should be implemented unless there is clear evidence that multiple or post-operative dosing improves outcomes. Reason for antimicrobial administration beyond one dose should be documented and/or comply with criteria below agreed criteria
5. MRSA positive patients	Audit MRSA decolonization practice (normally collected by IPC teams)	Decolonisation therapy is recommended prior to surgery and antibiotic prophylaxis should include cover for MRSA

Appendix 1

See separate document: Resource Materials - Examples of audit tools, review stickers and drug charts

Appendix 2 - Other relevant toolkits and resources

PHE does not necessarily endorse the examples of antimicrobial stewardship in this section.

European Antibiotic Awareness Day: 2014 resources:
https://www.gov.uk/government/collections/european-antibiotic-awareness-day-resources

Prescribing competencies:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/253094/ARHAIprescrcompetencies__2_.pdf

Start Smart Then Focus Prescribers checklist:
https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/366944/Secondary_care_prescribers_checklist.pdf

Antimicrobial Self-Assessment Toolkit:
http://imperial-asat.herokuapp.com/

Sepsis clinical toolkit and audit tools:
http://www.collemergencymed.ac.uk/Shop-Floor/Clinical%20Standards/Sepsis
http://sepsistrust.org/info-for-professionals/clinical-toolkits/

TARGET Antimicrobial prescribing toolkit for Primary Care:
http://www.rcgp.org.uk/clinical-and-research/target-antibiotics-toolkit.aspx

Appendix 3: List of ESPAUR SSTF implementation subgroup members

Dr Diane Ashiru-Oredope	Chair of ESPAUR SSTF implementation subgroup; PHE Pharmacist lead for AMRS and HCAI
Dr Gavin Barlow	Consultant in Infection, Hull & East Yorkshire Hospitals NHS Trust
Mr Brian Brown	National Pharmacy Manager, Care Quality Commission.
Dr Emma Budd	ESPAUR secretariat, PHE AMRS & HCAI programme
Dr Druin Burch	Consultant, Oxford University Hospitals. Representing the Royal College of Physicians
Dr Teh-Li Chin	Microbiology Consultant, North Bristol NHS Trust
Dr Oliver Dyar	Junior Doctor representative
Ms Rose Gallagher	Professional Lead - Infection Prevention & Control, Royal College of Nursing
Mr Mark Gilchrist	Consultant pharmacist for infection, Imperial College Healthcare NHS Trust. Representing UK Clinical Pharmacy Association
Mr Kieran Hand	Consultant Pharmacist – anti-infectives, University Hospital Southampton. Representing the DH Advisory Committee on Antimicrobial Resistance & Healthcare Associated infections (ARHAI)
Dr James Hatcher	Infectious Diseases/Medical Microbiology registrar, Imperial College London Healthcare NHS Trust
Mr Philip Howard	Consultant Pharmacist – Antimicrobials, Leeds Teaching Hospitals NHS Trust. Representing the Royal Pharmaceutical Society
Mr David Ladenheim	Lead SSTF editorial group. Antimicrobial Pharmacist, East & North Herts NHS Trust
Prof Heather Loveday	President, Infection Prevention Society
Prof Alasdair Macgowan	Professor of Antimicrobial Therapeutics, University of Bristol
Ms Kate Morrow	National Patient Safety Lead, NHS England
Dr Bharat Patel	PHE, AMRS & HCAI medical microbiologist
Dr Sanjay Patel	Consultant in Paediatric infectious diseases and immunology, Southampton Children's Hospital. Representing the Royal College of Paediatrics and Child Health.
Ms Laura Whitney	Consultant Pharmacist – Antimicrobials, St. George's Healthcare NHS Trust.
Prof Tony Young	Consultant Urological Surgeon, Southend University Hospital. Representing the Royal College of Surgeons