



Messaggi chiave per Dirigenti/amministratori ospedalieri

Funzioni

- Le vostre funzioni relative al miglioramento dell'uso degli antibiotici includono [31,42,56,71,75]:
 - istituire un team multidisciplinare per il programma di stewardship antibiotica nel vostro ospedale. Questo team dovrebbe comprendere specialisti di malattie infettive, microbiologi e farmacisti e dovrebbe ricevere appositi fondi e risorse;
 - sostenere l'attuazione di linee guida in materia di uso di antibiotici e di misure di prevenzione e controllo delle infezioni;
 - mettere in atto attività di training e formazione mirate che:
 - ottimizzino la gestione diagnostica e terapeutica dei pazienti;
 - assicurino che le raccomandazioni sulla stewardship antibiotica vengano seguite;
 - affrontino i fattori comportamentali alla base dell'uso improprio degli antibiotici;
 - migliorino la prevenzione e il controllo delle infezioni correlate all'assistenza e la diffusione di batteri antibiotico-resistenti;
 - promuovere la collaborazione tra medici prescrittori e responsabili del team di stewardship antibiotica per la conduzione di audit proattivi e i feedback;
 - stabilire indicatori qualitativi e quantitativi di processo e di esito del programma di stewardship antibiotica;
 - garantire che gli antibiotici elencati nel prontuario farmaceutico ospedaliero siano sempre disponibili;
 - assicurare che l'uso prudente degli antibiotici e la prevenzione della resistenza agli antibiotici costituiscano "aree di azione prioritarie" nel piano annuale dell'ospedale.

Cose che dovrete sapere

2. I programmi di stewardship antibiotica, insieme alle pratiche di prevenzione e controllo delle infezioni, possono aumentare la sicurezza dei pazienti e la qualità dell'assistenza oltre a ridurre i costi ospedalieri in tutti i servizi, migliorando il modo in cui gli antibiotici vengono utilizzati nonché diminuendo le infezioni da C. difficile e altri eventi avversi [19,42].

Esempio

L'attuazione di programmi di stewardship antibiotica ha portato a [46]:

- una riduzione del 20 % del consumo di antibiotici;
- una riduzione dell'incidenza delle infezioni correlate all'assistenza;
- una riduzione della durata delle degenze ospedaliere e
- una riduzione del 33 % dei costi per gli antibiotici.

- Specialisti di malattie infettive, microbiologi e farmacisti sono i principali responsabili del team di stewardship antibiotica [56,76].
- Molti medici prescrittori e altri professionisti sanitari ritengono che la loro formazione relativa all'uso appropriato degli antibiotici sia insufficiente. Chiedono linee guida locali in materia di antibiotici, formazione specifica e un team di stewardship antibiotica [25,27].
- I medici sono responsabili delle prescrizioni e devono essere pienamente coinvolti nel processo decisionale condiviso con il team di stewardship antibiotica [42].
- Per avere successo, i team di stewardship antibiotica necessitano del sostegno attivo di altri professionisti fondamentali negli ospedali, come gli esperti della prevenzione e del controllo delle infezioni, i medici del pronto soccorso, gli epidemiologi ospedalieri, gli infermieri e il personale preposto ai sistemi informatici [42,77].
- Migliorare l'uso degli antibiotici nel pronto soccorso può contribuire a un più corretto utilizzo degli stessi in tutta l'organizzazione, in quanto il pronto soccorso è un punto di accesso comune alle strutture di degenza [77].
- Sia misure restrittive sia persuasive possono ridurre l'uso degli antibiotici [19,43,54,56]:
 - le misure restrittive includono decisioni di pre-approvazione e post-autorizzazione riguardo a specifici antibiotici;
 - le misure persuasive includono audit proattivi e feedback da parte di infettivologi, microbiologi e farmacisti.
- Linee guida in materia di antibiotici nonché sessioni e corsi di formazione periodici migliorano la gestione delle infezioni da parte dei medici [78].
- Alcune strategie strutturali possono migliorare le prescrizioni di antibiotici e gli esiti nei pazienti. Queste comprendono [54,79-81]:
 - decisioni supportate da tecnologia informatica, che colleghino indicazione clinica, dati microbiologici e dati relativi alla prescrizione, e
 - l'utilizzo di test diagnostici rapidi presso il punto di cura (*point of care*).

Cose che potete fare nel vostro ospedale o istituto

- Supportare il team multidisciplinare di stewardship antibiotica designando le figure specificamente preposte in base alla capacità di assunzione di responsabilità e alle competenze sui farmaci e stabilendo il ruolo di sostegno di altri gruppi chiave [42,71].
- Dare priorità alle politiche di stewardship antibiotica e di prevenzione e controllo delle infezioni nonché a strategie e attività che favoriscano l'uso prudente degli antibiotici e prevengano la diffusione di batteri antibiotico-resistenti [31,71].
- Fornire fondi e risorse per un programma di stewardship antibiotica (tra cui, ad esempio, retribuzioni per personale apposito, risorse informatiche, test diagnostici rapidi presso il punto di cura [31]).
- Finanziare e promuovere attività di istruzione, formazioni e riunioni sulla stewardship antibiotica e sulla resistenza agli antibiotici per tutti i professionisti sanitari (medici, specialisti di malattie infettive, farmacisti, microbiologi e personale infermieristico) [19,53,56].
- Rafforzare le attività di sorveglianza sull'uso di antibiotici e sulla resistenza [56].

16. Promuovere l'aderenza a linee guida evidence-based per la diagnosi e la gestione di infezioni comuni e per la profilassi antibiotica perioperatoria. Se queste linee guida non fossero disponibili nel vostro ospedale, allora supportarne lo sviluppo [31,54,56].
17. Promuovere l'uso della microbiologia a livello locale e la conoscenza dei pattern locali di resistenza agli antibiotici per indirizzare le linee guida e le scelte degli antibiotici per la terapia empirica [31].
18. Promuovere l'aderenza a linee guida evidence-based sulle misure di controllo delle infezioni, al fine di ridurre la trasmissione di batteri antibiotico-resistenti [82].
19. Promuovere audit proattivi e garantire che i singoli medici prescrittori ricevano feedback [54,56].
20. Promuovere la verifica *inter pares* delle prescrizioni di antibiotici e della gestione delle infezioni nonché incoraggiare la comunicazione tra i professionisti sanitari [71].

Bibliografia:

1. European Centre for Disease Prevention and Control. Antimicrobial resistance surveillance in Europe 2014. Annual Report of the European Antimicrobial Resistance Surveillance Network (EARS-Net) Stockholm: ECDC; 2015. Available from: <http://ecdc.europa.eu/en/publications/Publications/antimicrobial-resistance-europe-2014.pdf>.
2. Zasowski EJ, Claeys KC, Lagnf AM, Davis SL, Rybak MJ. Time is of the essence: the impact of delayed antibiotic therapy on patient outcomes in hospital-onset enterococcal bloodstream infections. *Clin Infect Dis*. 2016 May 15;62(10):1242-50.
3. Lemos EV, de la Hoz FP, Einarson TR, McGhan WF, Quevedo E, Castaneda C, et al. Carbapenem resistance and mortality in patients with *Acinetobacter baumannii* infection: systematic review and meta-analysis. *Clin Microbiol Infect*. 2014 May;20(5):416-23.
4. Falagas ME, Tansarli GS, Karageorgopoulos DE, Vardakas KZ. Deaths attributable to carbapenem-resistant Enterobacteriaceae infections. *Emerg Infect Dis*. 2014 Jul;20(7):1170-5.
5. Martin-Loeches I, Torres A, Rinaudo M, Terraneo S, de Rosa F, Ramirez P, et al. Resistance patterns and outcomes in intensive care unit (ICU)-acquired pneumonia. Validation of European Centre for Disease Prevention and Control (ECDC) and the Centers for Disease Control and Prevention (CDC) classification of multidrug resistant organisms. *J Infect*. 2015 Mar;70(3):213-22.
6. Marquet K, Liesenborgs A, Bergs J, Vleugels A, Claes N. Incidence and outcome of inappropriate in-hospital empiric antibiotics for severe infection: a systematic review and meta-analysis. *Crit Care*. 2015;19:63.
7. de Kraker ME, Davey PG, Grundmann H, Burden study group. Mortality and hospital stay associated with resistant *Staphylococcus aureus* and *Escherichia coli* bacteremia: estimating the burden of antibiotic resistance in Europe. *PLoS Med*. 2011 Oct;8(10):e1001104.
8. World Health Organization. Global action plan on antimicrobial resistance. Geneva: WHO; 2015. Available from: http://apps.who.int/iris/bitstream/10665/193736/1/9789241509763_eng.pdf?ua=1.
9. Poulikakos P, Falagas ME. Aminoglycoside therapy in infectious diseases. *Expert Opin Pharmacother*. 2013 Aug;14(12):1585-97.
10. Morgan DJ, Diekema DJ, Sepkowitz K, Perencevich EN. Adverse outcomes associated with Contact Precautions: a review of the literature. *Am J Infect Control*. 2009 Mar;37(2):85-93.
11. Teillant A, Gandra S, Barter D, Morgan DJ, Laxminarayan R. Potential burden of antibiotic resistance on surgery and cancer chemotherapy antibiotic prophylaxis in the USA: a literature review and modelling study. *Lancet Infect Dis*. 2015 Dec;15(12):1429-37.
12. de Kraker ME, Wolke W, Davey PG, Koller W, Berger J, Nagler J, et al. Burden of antimicrobial resistance in European hospitals: excess mortality and length of hospital stay associated with bloodstream infections due to *Escherichia coli* resistant to third-generation cephalosporins. *J Antimicrob Chemother*. 2011 Feb;66(2):398-407.
13. Nathwani D, Raman G, Sulham K, Gavaghan M, Menon V. Clinical and economic consequences of hospital-acquired resistant and multidrug-resistant *Pseudomonas aeruginosa* infections: a systematic review and meta-analysis. *Antimicrob Resist Infect Control*. 2014;3(1):32.
14. Hoxha A, Karki T, Giambi C, Montano C, Sisto A, Bella A, et al. Attributable mortality of carbapenem-resistant *Klebsiella pneumoniae* infections in a prospective matched cohort study in Italy, 2012-2013. *J Hosp Infect*. 2016 Jan;92(1):61-6.
15. Bell BG, Schellevis F, Stobberingh E, Goossens H, Pringle M. A systematic review and meta-analysis of the effects of antibiotic consumption on antibiotic resistance. *BMC Infect Dis*. 2014;14:13.
16. Carlet J, Jarlier V, Harbarth S, Voss A, Goossens H, Pittet D, et al. Ready for a world without antibiotics? The penicillin antibiotic resistance call to action. *Antimicrob Resist Infect Control*. 2012;1(1):11.
17. Agodi A, Auxilia F, Barchitta M, Brusafiero S, D'Errico MM, Montagna MT, et al. Antibiotic consumption and resistance: results of the SPIN-UTI project of the GISIO-SitI. *Epidemiol Prev*. 2015 Jul-Aug;39(4 Suppl 1):94-8.
18. Dryden M, Johnson AP, Ashiru-Oredope D, Sharland M. Using antibiotics responsibly: right drug, right time, right dose, right duration. *J Antimicrob Chemother*. 2011 Nov;66(11):2441-3.
19. Davey P, Brown E, Charani E, Fenelon L, Gould IM, Holmes A, et al. Interventions to improve antibiotic prescribing practices for hospital inpatients. *Cochrane Database Syst Rev*. 2013 (4):CD003543.
20. Slimings C, Riley TV. Antibiotics and hospital-acquired *Clostridium difficile* infection: update of systematic review and meta-analysis. *J Antimicrob Chemother*. 2014 Apr;69(4):881-91.
21. Brown KA, Khanafer N, Daneman N, Fisman DN. Meta-analysis of antibiotics and the risk of community-associated *Clostridium difficile* infection. *Antimicrob Agents Chemother*. 2013 May;57(5):2326-32.
22. Feazel LM, Malhotra A, Perencevich EN, Kaboli P, Diekema DJ, Schweizer ML. Effect of antibiotic stewardship programmes on *Clostridium difficile* incidence: a systematic review and meta-analysis. *J Antimicrob Chemother*. 2014 Jul;69(7):1748-54.
23. Asensio A, Di Bella S, Lo Vecchio A, Grau S, Hart WM, Isidoro B, et al. The impact of *Clostridium difficile* infection on resource use and costs in hospitals in Spain and Italy: a matched cohort study. *Int J Infect Dis*. 2015 Jul;36:31-8.
24. Wiegand PN, Nathwani D, Wilcox MH, Stephens J, Shelbaya A, Haider S. Clinical and economic burden of *Clostridium difficile* infection in Europe: a systematic review of healthcare-facility-acquired infection. *J Hosp Infect*. 2012 May;81(1):1-14.
25. Pulcini C, Williams F, Molinari N, Davey P, Nathwani D. Junior doctors' knowledge and perceptions of antibiotic resistance and prescribing: a survey in France and Scotland. *Clin Microbiol Infect*. 2011 Jan;17(1):80-7.
26. Rezal RS, Hassali MA, Alrasheedy AA, Saleem F, Yusof FA, Godman B. Physicians' knowledge, perceptions and behaviour towards antibiotic prescribing: a systematic review of the literature. *Expert Rev Anti Infect Ther*. 2015 May;13(5):665-80.

27. Navarro-San Francisco C, Del Toro MD, Cobo J, De Gea-Garcia JH, Vano-Galvan S, Moreno-Ramos F, et al. Knowledge and perceptions of junior and senior Spanish resident doctors about antibiotic use and resistance: results of a multicenter survey. *Enferm Infecc Microbiol Clin*. 2013 Apr;31(4):199-204.
28. Lee CR, Cho IH, Jeong BC, Lee SH. Strategies to minimize antibiotic resistance. *Int J Environ Res Public Health*. 2013 Sep;10(9):4274-305.
29. Freire-Moran L, Aronsson B, Manz C, Gyssens IC, So AD, Monnet DL, et al. Critical shortage of new antibiotics in development against multidrug-resistant bacteria-Time to react is now. *Drug Resist Updat*. 2011 Apr;14(2):118-24.
30. Livermore DM, British Society for Antimicrobial Chemotherapy Working Party on The Urgent Need: Regenerating Antibacterial Drug D, Development. Discovery research: the scientific challenge of finding new antibiotics. *J Antimicrob Chemother*. 2011 Sep;66(9):1941-4.
31. European Centre for Disease Prevention and Control. Proposals for EU guidelines on the prudent use of antimicrobials in humans. Stockholm: ECDC; 2017. Available from: TO BE DEFINED.
32. The Federal Council. Strategy on antibiotic resistance Switzerland, 2015. Available from: https://www.bundespublikationen.admin.ch/cshop_mimes_bbl/2C/2C59E545D7371EE5A7B100F51A6EBB0E.pdf.
33. World Health Organization. The evolving threat of antimicrobial resistance: options for action 2012. Geneva: WHO; 2012. Available from: http://whqlibdoc.who.int/publications/2012/9789241503181_eng.pdf.
34. Friedman ND, Temkin E, Carmeli Y. The negative impact of antibiotic resistance. *Clin Microbiol Infect*. 2016 May;22(5):416-22.
35. De Luca M, Dona D, Montagnani C, Lo Vecchio A, Romanengo M, Tagliabue C, et al. Antibiotic prescriptions and prophylaxis in Italian children. Is it time to change? Data from the ARPEC Project. *PLoS One*. 2016;11(5):e0154662.
36. Akhloufi H, Streefkerk RH, Melles DC, de Steenwinkel JE, Schurink CA, Verkooijen RP, et al. Point prevalence of appropriate antimicrobial therapy in a Dutch university hospital. *Eur J Clin Microbiol Infect Dis*. 2015 Aug;34(8):1631-7.
37. European Centre for Disease Prevention and Control. Point prevalence survey of healthcare associated infections and antimicrobial use in European acute care hospitals Stockholm: ECDC; 2013. Available from: <http://ecdc.europa.eu/en/publications/Publications/healthcare-associated-infections-antimicrobial-use-PPS.pdf>.
38. European Centre for Disease Prevention and Control. Report on point prevalence survey of antimicrobial prescribing in European hospitals, 2009 ESAC-3: hospital care subproject group. Available from: http://ecdc.europa.eu/en/activities/surveillance/ESAC-Net/publications/Documents/report_survey_antimicrobial_prescriptions_eu_hospitals_2009.pdf.
39. Guillemot D, Carbon C, Balkau B, Geslin P, Lecoœur H, Vauzelle-Kervroedan F, et al. Low dosage and long treatment duration of beta-lactam: risk factors for carriage of penicillin-resistant *Streptococcus pneumoniae*. *JAMA*. 1998 Feb 04;279(5):365-70.
40. Gorska A, Marasca G, Schröder W, Tacconelli E. Selection of antibiotic-resistant bacteria is a predictable, severe, adverse drug event of the most used antibiotics in hospitalized patients. 25th European Congress of Clinical Microbiology and Infectious Diseases (ECCMID); 25 - 28 April 2015, Copenhagen, Denmark. Available from: https://www.escmid.org/escmid_publications/escmid_elibrary/?q=election+of+antibiotic-resistant+bacteria+is+a+predictable%2C+severe%2C+adverse+drug+event+of+the+most+used+antibiotics+in+hospitalized+patients&id=2173&=0&tx_solr%5Bfilter%5D%5B0%5D=author%25AEvelina%2BTacconelli&x=0&y=0.
41. Jernberg C, Lofmark S, Edlund C, Jansson JK. Long-term impacts of antibiotic exposure on the human intestinal microbiota. *Microbiology*. 2010 Nov;156(Pt 11):3216-23.
42. Centers for Disease Control and Prevention. Core elements of hospital antibiotic stewardship programs 2016. Available from: <http://www.cdc.gov/getsmart/healthcare/implementation/core-elements.html>.
43. Kaki R, Ellingsen M, Walker S, Simor A, Palmay L, Daneman N. Impact of antimicrobial stewardship in critical care: a systematic review. *J Antimicrob Chemother*. 2011 Jun;66(6):1223-30.
44. Wagner B, Filice GA, Drekonja D, Greer N, MacDonald R, Rutks I, et al. Antimicrobial stewardship programs in inpatient hospital settings: a systematic review. *Infect Control Hosp Epidemiol*. 2014 Oct;35(10):1209-28.
45. Dellit TH, Owens RC, McGowan JE, Gerding DN, Weinstein RA, Burke JP, 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 Jan 15;44(2):159-77.
46. Karanika S, Paudel S, Grigoras C, Kalbasi A, Mylonakis E. Systematic review and meta-analysis of clinical and economic outcomes from the implementation of hospital-based antimicrobial stewardship programs. *Antimicrob Agents Chemother*. 2016 Aug 60(8):4840-52.
47. Howard P, Pulcini C, Levy Hara G, West RM, Gould IM, Harbarth S, et al. An international cross-sectional survey of antimicrobial stewardship programmes in hospitals. *J Antimicrob Chemother*. 2015 Apr;70(4):1245-55.
48. Talpaert MJ, Gopal Rao G, Cooper BS, Wade P. Impact of guidelines and enhanced antibiotic stewardship on reducing broad-spectrum antibiotic usage and its effect on incidence of *Clostridium difficile* infection. *J Antimicrob Chemother*. 2011 Sep;66(9):2168-74.
49. Oppenheimer M, Rezwan N. CQUIN audit for prescription of antibiotics for urinary tract infections in an acute medical assessment unit. *BMJ Qual Improv Rep*. 2015;4(1).
50. Roque F, Herdeiro MT, Soares S, Teixeira Rodrigues A, Breitenfeld L, Figueiras A. Educational interventions to improve prescription and dispensing of antibiotics: a systematic review. *BMC Public Health*. 2014;14:1276.
51. van den Bosch CM, Geerlings SE, Natsch S, Prins JM, Hulscher ME. Quality indicators to measure appropriate antibiotic use in hospitalized adults. *Clin Infect Dis*. 2015 Jan 15;60(2):281-91.
52. Lee CR, Lee JH, Kang LW, Jeong BC, Lee SH. Educational effectiveness, target, and content for prudent antibiotic use. *Biomed Res Int*. 2015;2015:214021.
53. Pulcini C, Gyssens IC. How to educate prescribers in antimicrobial stewardship practices. *Virulence*. 2013 Feb 15;4(2):192-202.
54. Barlam TF, Cosgrove SE, Abbo LM, MacDougall C, Schuetz AN, Septimus EJ, et al. Implementing an antibiotic stewardship program: guidelines by the Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America. *Clin Infect Dis*. 2016 May 15;62(10):e51-77.
55. Septimus EJ, Owens RC, Jr. Need and potential of antimicrobial stewardship in community hospitals. *Clin Infect Dis*. 2011 Aug;53 Suppl 1:S8-S14.

56. de With K, Allerberger F, Amann S, Apfalter P, Brodt HR, Eckmanns T, et al. Strategies to enhance rational use of antibiotics in hospital: a guideline by the German Society for Infectious Diseases. *Infection*. 2016 Jun;44(3):395-439.
57. Schuts EC, Hulscher ME, Mouton JW, Verduin CM, Stuart JW, Overdiek HW, et al. Current evidence on hospital antimicrobial stewardship objectives: a systematic review and meta-analysis. *Lancet Infect Dis*. 2016 Mar 2.
58. Charbonneau P, Parienti JJ, Thibon P, Ramakers M, Daubin C, du Cheyron D, et al. Fluoroquinolone use and methicillin-resistant *Staphylococcus aureus* isolation rates in hospitalized patients: a quasi experimental study. *Clin Infect Dis*. 2006 Mar 15;42(6):778-84.
59. Amadeo B, Dumartin C, Parneix P, Fourrier-Reglat A, Rogues AM. Relationship between antibiotic consumption and antibiotic policy: an adjusted analysis in the French healthcare system. *J Antimicrob Chemother*. 2011 Feb;66(2):434-42.
60. Nachtigall I, Tafelski S, Deja M, Halle E, Grebe MC, Tamarkin A, et al. Long-term effect of computer-assisted decision support for antibiotic treatment in critically ill patients: a prospective 'before/after' cohort study. *BMJ Open*. 2014;4(12):e005370.
61. Peto Z, Benko R, Matuz M, Csullog E, Molnar A, Hajdu E. Results of a local antibiotic management program on antibiotic use in a tertiary intensive care unit in Hungary. *Infection*. 2008 Dec;36(6):560-4.
62. Viale P, Tumietto F, Giannella M, Bartoletti M, Tedeschi S, Ambretti S, et al. Impact of a hospital-wide multifaceted programme for reducing carbapenem-resistant Enterobacteriaceae infections in a large teaching hospital in northern Italy. *Clin Microbiol Infect*. 2015 Mar;21(3):242-7.
63. Bruins M, Oord H, Bloembergen P, Wolfhagen M, Casparie A, Degener J, et al. Lack of effect of shorter turnaround time of microbiological procedures on clinical outcomes: a randomised controlled trial among hospitalised patients in the Netherlands. *Eur J Clin Microbiol Infect Dis*. 2005 May;24(5):305-13.
64. Dik JW, Hendrix R, Lo-Ten-Foe JR, Wiltink KR, Panday PN, van Gemert-Pijnen LE, et al. Automatic day-2 intervention by a multidisciplinary antimicrobial stewardship-team leads to multiple positive effects. *Front Microbiol*. 2015;6:546.
65. Dik JW, Hendrix R, Friedrich AW, Luttjeboer J, Panday PN, Wiltink KR, et al. Cost-minimization model of a multidisciplinary antibiotic stewardship team based on a successful implementation on a urology ward of an academic hospital. *PLoS One*. 2015;10(5):e0126106.
66. Nitsch-Osuch A, Kuchar E, Zycinska K, Gyrczuk E, Miskiewicz K, Korzeniewski K. Implementation of hospital's antibiotic policy decreases antimicrobial use in the general pediatric ward. *Adv Exp Med Biol*. 2015;857:67-74.
67. Cisneros JM, Neth O, Gil-Navarro MV, Lepe JA, Jimenez-Parrilla F, Cordero E, et al. Global impact of an educational antimicrobial stewardship programme on prescribing practice in a tertiary hospital centre. *Clin Microbiol Infect*. 2014 Jan;20(1):82-8.
68. Nilholm H, Holmstrand L, Ahl J, Mansson F, Odenholt I, Tham J, et al. An audit-based, infectious disease specialist-guided antimicrobial stewardship program profoundly reduced antibiotic use without negatively affecting patient outcomes. *Open Forum Infect Dis*. 2015 Apr;2(2):ofv042.
69. Public Health England. Antibiotic Guardian. Available from: <http://antibioticguardian.com/>.
70. Public Health England. Start smart then focus 2011 [updated 2015]. Available from: <https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus>.
71. The National Institute for Health and Care Excellence. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. NICE guidelines [NG15] August 2015. Available from: <https://www.nice.org.uk/guidance/ng15>.
72. Bretonniere C, Leone M, Milesi C, Allaouchiche B, Armand-Lefevre L, Baldesi O, et al. Strategies to reduce curative antibiotic therapy in intensive care units (adult and paediatric). *Intensive Care Med*. 2015 Jul;41(7):1181-96.
73. European Centre for Disease Prevention and Control. Systematic review and evidence-based guidance on perioperative antibiotic prophylaxis. Stockholm: ECDC; 2013. Available from: <http://ecdc.europa.eu/en/publications/Publications/Perioperative%20antibiotic%20prophylaxis%20-%20June%202013.pdf>.
74. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving Sepsis Campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013 Feb;39(2):165-228.
75. Meeker D, Linder JA, Fox CR, Friedberg MW, Persell SD, Goldstein NJ, et al. Effect of behavioral interventions on inappropriate antibiotic prescribing among primary care practices: a randomized clinical trial. *JAMA*. 2016 Feb 09;315(6):562-70.
76. Wickens HJ, Farrell S, Ashiru-Oredope DA, Jacklin A, Holmes A, Antimicrobial Stewardship Group of Department of Health Advisory Committee on Antimicrobial Resistance Health Care Associated Infections. The increasing role of pharmacists in antimicrobial stewardship in English hospitals. *J Antimicrob Chemother*. 2013 Nov;68(11):2675-81.
77. May L, Cosgrove S, L'Archeveque M, Talan DA, Payne P, Jordan J, et al. A call to action for antimicrobial stewardship in the emergency department: approaches and strategies. *Ann Emerg Med*. 2013 Jul;62(1):69-77 e2.
78. Westphal JF, Jehl F, Javelot H, Nonnenmacher C. Enhanced physician adherence to antibiotic use guidelines through increased availability of guidelines at the time of drug ordering in hospital setting. *Pharmacoepidemiol Drug Saf*. 2011 Feb;20(2):162-8.
79. Agarwal R, Schwartz DN. Procalcitonin to guide duration of antimicrobial therapy in intensive care units: a systematic review. *Clin Infect Dis*. 2011 Aug;53(4):379-87.
80. Schuetz P, Muller B, Christ-Crain M, Stolz D, Tamm M, Bouadma L, et al. Procalcitonin to initiate or discontinue antibiotics in acute respiratory tract infections. *Evid Based Child Health*. 2013 Jul;8(4):1297-371.
81. Yong MK, Buising KL, Cheng AC, Thursky KA. Improved susceptibility of Gram-negative bacteria in an intensive care unit following implementation of a computerized antibiotic decision support system. *J Antimicrob Chemother*. 2010 May;65(5):1062-9.
82. World Health Organization. Guidelines on core components of infection prevention and control programmes at the national and acute health care facility level. Geneva: WHO; 2016. Available from: <http://www.who.int/gpsc/ipc-components-guidelines/en/>.
83. Pulcini C, Botelho-Nevers E, Dyar OJ, Harbarth S. The impact of infectious disease specialists on antibiotic prescribing in hospitals. *Clin Microbiol Infect*. 2014 Oct;20(10):963-72.
84. Cook E, Marchaim D, Kaye KS. Building a successful infection prevention program: key components, processes, and economics. *Infect Dis Clin North Am*. 2011 Mar;25(1):1-19.
85. European Centre for Disease Prevention and Control. Core competencies for infection control and hospital hygiene professionals in the European Union. Stockholm: ECDC; 2013. Available from: <http://www.ecdc.europa.eu/en/publications/publications/infection-control-core-competencies.pdf>.

86. Tacconelli E, Cataldo MA, Dancer SJ, De Angelis G, Falcone M, Frank U, et al. ESCMID guidelines for the management of the infection control measures to reduce transmission of multidrug-resistant Gram-negative bacteria in hospitalized patients. *Clin Microbiol Infect.* 2014 Jan;20 Suppl 1:1-55.
87. Wilson AP, Livermore DM, Otter JA, Warren RE, Jenks P, Enoch DA, et al. Prevention and control of multi-drug-resistant Gram-negative bacteria: recommendations from a Joint Working Party. *J Hosp Infect.* 2016 Jan;92 Suppl 1:S1-44.
88. Spyridopoulou K PM, Sypsa V, Goukos D, Miriagou V, Markogiannakis A, Karapanou A, Flevari P, Gainaru G, Koutsi K, Meletis J, Daikos G.L. Successful control of carbapenemase-producing Klebsiella pneumoniae (CP-Kp) transmission in a haematology unit: The pivotal role of active surveillance. 25th European Congress of Clinical Microbiology and Infectious Diseases; Copenhagen, Denmark, 25-28 April 2015. e-poster EP0432015.
89. Ducloux G, Fabry J, Nicolle L, World Health Organization. Department of Communicable Disease S, Response. Prevention of hospital-acquired infections : a practical guide. Geneva: WHO; 2002. Available from: <http://www.who.int/csr/resources/publications/whocdscsreph200212.pdf>.
90. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med.* 2013 Feb;41(2):580-637.
91. Pugh R, Grant C, Cooke RP, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. *Cochrane Database Syst Rev.* 2015 (8):CD007577.
92. Shrayteh ZM, Rahal MK, Malaeb DN. Practice of switch from intravenous to oral antibiotics. *Springerplus.* 2014;3:717.
93. Vouloumanou EK, Rafailidis PI, Kazantzi MS, Athanasiou S, Falagas ME. Early switch to oral versus intravenous antimicrobial treatment for hospitalized patients with acute pyelonephritis: a systematic review of randomized controlled trials. *Curr Med Res Opin.* 2008 Dec;24(12):3423-34.
94. Gilchrist M, Wade P, Ashiru-Oredope D, Howard P, Sneddon J, Whitney L, et al. Antimicrobial stewardship from policy to practice: experiences from UK antimicrobial pharmacists. *Infectious diseases and therapy.* 2015 Sep;4(Suppl 1):51-64.
95. Ashiru-Oredope D, Budd EL, Bhattacharya A, Din N, McNulty CA, Micallef C, et al. Implementation of antimicrobial stewardship interventions recommended by national toolkits in primary and secondary healthcare sectors in England: TARGET and Start Smart Then Focus. *J Antimicrob Chemother.* 2016 May;71(5):1408-14.
96. Edwards R, Drumright L, Kiernan M, Holmes A. Covering more territory to fight resistance: considering nurses' role in antimicrobial stewardship. *J Infect Prev.* 2011 Jan;12(1):6-10.
97. Gillespie E, Rodrigues A, Wright L, Williams N, Stuart RL. Improving antibiotic stewardship by involving nurses. *Am J Infect Control.* 2013 Apr;41(4):365-7.
98. Avdic E, Carroll KC. The role of the microbiology laboratory in antimicrobial stewardship programs. *Infect Dis Clin North Am.* 2014 Jun;28(2):215-35.
99. Baron EJ, Miller JM, Weinstein MP, Richter SS, Gilligan PH, Thomson RB, Jr., et al. Executive summary: a guide to utilization of the microbiology laboratory for diagnosis of infectious diseases: 2013 recommendations by the Infectious Diseases Society of America (IDSA) and the American Society for Microbiology (ASM)(a). *Clin Infect Dis.* 2013 Aug;57(4):485-8.
100. Buehler SS, Madison B, Snyder SR, Derzon JH, Cornish NE, Saubolle MA, et al. Effectiveness of practices to increase timeliness of providing targeted therapy for inpatients with bloodstream infections: a laboratory medicine best practices systematic review and meta-analysis. *Clin Microbiol Rev.* 2016 Jan;29(1):59-103.
101. Bailey C, Tully M, Cooke J. Perspectives of clinical microbiologists on antimicrobial stewardship programmes within NHS trusts in England. *Antimicrob Resist Infect Control.* 2015;4:47.
102. Shallcross LJ, Freemantle N, Nisar S, Ray D. A cross-sectional study of blood cultures and antibiotic use in patients admitted from the Emergency Department: missed opportunities for antimicrobial stewardship. *BMC Infect Dis.* 2016;16(1):166.
103. Gupta K, Hooton TM, Naber KG, Wullt B, Colgan R, Miller LG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: A 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis.* 2011 Mar 01;52(5):e103-20.
104. Stevens DL, Bisno AL, Chambers HF, Dellinger EP, Goldstein EJ, Gorbach SL, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. *Clin Infect Dis.* 2014 Jul 15;59(2):e10-52.
105. Garnacho-Montero J, Dimopoulos G, Poulakou G, Akova M, Cisneros JM, De Waele J, et al. Task force on management and prevention of Acinetobacter baumannii infections in the ICU. *Intensive Care Med.* 2015 Dec;41(12):2057-75.
106. Tabah A, Cotta MO, Garnacho-Montero J, Schouten J, Roberts JA, Lipman J, et al. A systematic review of the definitions, determinants, and clinical outcomes of antimicrobial de-escalation in the intensive care unit. *Clin Infect Dis.* 2016 Apr 15;62(8):1009-17.
107. Ista E, van der Hoven B, Kornelisse RF, van der Starre C, Vos MC, Boersma E, et al. Effectiveness of insertion and maintenance bundles to prevent central-line-associated bloodstream infections in critically ill patients of all ages: a systematic review and meta-analysis. *Lancet Infect Dis.* 2016 Jun;16(6):724-34.
108. Rello J, Afonso E, Lisboa T, Ricart M, Balsera B, Rovira A, et al. A care bundle approach for prevention of ventilator-associated pneumonia. *Clin Microbiol Infect.* 2013 Apr;19(4):363-9.
109. Dyar OJ, Pagani L, Pulcini C. Strategies and challenges of antimicrobial stewardship in long-term care facilities. *Clin Microbiol Infect.* 2015 Jan;21(1):10-9.
110. Fleming A, Browne J, Byrne S. The effect of interventions to reduce potentially inappropriate antibiotic prescribing in long-term care facilities: a systematic review of randomised controlled trials. *Drugs Aging.* 2013 Jun;30(6):401-8.
111. Center for Disease Control and Prevention. The core elements of antibiotic stewardship for nursing homes. Atlanta, GA: US Department of Health and Human Services, CDC. 2015. Available from: <http://www.cdc.gov/longtermcare/index.html>.