General key messages for healthcare professionals in hospitals and other healthcare settings

What is the problem?

1. Antibiotic resistance threatens the health and safety of patients in all healthcare settings in Europe [1].

Note: With the word "antibiotics", ECDC means antibacterial agents or antibacterials. However, the key messages proposed for antibiotics could be extended to other antimicrobial agents based on the specific needs of countries and of hospitals and other healthcare settings.

2. The emergence of bacteria resistant to multiple classes of antibiotics is particularly concerning. Such multidrug-resistant bacteria are a real and constant threat to clinical practice in all healthcare settings in Europe [1].

3. Infections with multidrug-resistant bacteria can be severe, fatal and costly and can directly lead to [2-11] [expert consensus]:

a) Delayed access to effective antibiotic therapy for individual patients, causing treatment failures, longer illnesses, prolonged stays in hospital and increased morbidity and mortality;

b) More adverse events, because alternative antibiotic therapies, that are more toxic, must often be used;

c) Fewer effective antibiotic treatments for immunosuppressed patients and those undergoing surgical operations;

d) Reduced quality of patient stay due to anxiety because of the need for rigorous infection control measures;

e) Higher direct and indirect hospital costs.

Examples:
- Patients with bloodstream infections have a threefold higher mortality rate, prolonged hospital stays, and higher costs if their infection is due to third-generation cephalosporin-resistant Escherichia coli, compared with third-generation cephalosporin-susceptible isolates [12].
- Patients have a 24% increased risk of mortality with any antibiotic-resistant Pseudomonas aeruginosa infection [13].
- Patients are up to three times more likely to die if their infections is caused by carbapenem-resistant Klebsiella pneumoniae, compared with carbapenem-susceptible isolates [14].

4. Misusing antibiotics increases the risk of infections with multidrug-resistant bacteria [15].

Example:
Gram-negative bacteria, such as Escherichia coli, Klebsiella spp., Pseudomonas aeruginosa, and Acinetobacter spp., are becoming resistant to most available antibiotics [16,17].

5. Antibiotics are misused when they are prescribed unnecessarily (i.e. antibiotic treatment is not clinically needed) or when they are prescribed inappropriately, i.e. one of the following [18]:

a) Delayed administration of antibiotics in critically ill patients;

b) The spectrum of antibiotic therapy is either too narrow or too broad;

c) The dose of antibiotic is either too low or too high;

d) The duration of antibiotic therapy is either too short or too long;

e) Antibiotic therapy is not reviewed after 48-72 hours, or the choice of antibiotic is not streamlined when microbiological culture data become available.

6. Misusing antibiotics increases the incidence of Clostridium difficile infections [19-22].

Example:
In European hospitals, Clostridium difficile infections can lead to up to a 42% increase in mortality, 19 extra days of hospital stay, and more than EUR 14,000 of additional costs per patient [23,24].

7. Many prescribers do not know antibiotic resistance prevalence rates in their local setting [25,26], and recognise lacks in their training regarding antibiotic use [27]. Availability of guidelines, consultation with infectious diseases specialist, and trainings represent the most helpful interventions to promote better use of antibiotics [25,27].

8. Only a few antibiotics in the research and development pipeline may be effective against existing multidrug-resistant bacteria [28-30].

9. Losing effective options for the treatment and prevention of infections is a global health security threat [31].

How is our use of antibiotics contributing to the problem

10. Misuse of antibiotics accelerates the emergence and dissemination of antibiotic resistance [8,31-34].

11. Antibiotics are given to many hospital inpatients [35,36].

12. Up to a half of all antibiotic use in European hospitals is unnecessary or inappropriate [6,37,38].

13. Antibiotic resistance is more likely to develop and spread when [39] [expert consensus]:

• Broad-spectrum antibiotics are used;

• Long durations of antibiotics are used;

• Too low doses of antibiotics are used.

Example:
Cephalosporins, carbapenems, fluoroquinolones and anti-anaerobe antibiotics have a high risk of selecting for multidrug-resistant Gram-negative bacteria [40].

14. Antibiotics have long-term effects on the development and persistence of antibiotic resistance in the microbiota. This resistance may be transferred to other bacteria [41].

15. Antibiotics are often prescribed to patients in hospitals without explaining the importance of prudent antibiotic use [expert consensus].

Why hospitals should be promoting antibiotic stewardship?

16. Promoting prudent antibiotic use is both a patient safety and a public health priority [31,42].

Example:
Increasingly, many European countries have national guidance on antimicrobial stewardship programmes for hospital prescribers. The ECDC directory (link) contains online resources for developing guidelines.

17. Antimicrobial management initiatives that promote prudent antibiotic use are called antibiotic stewardship programmes [19,42-45].

18. Antibiotic stewardship programmes, can contribute to [42,45,46] [expert consensus]:

a) Optimising how infections are treated;

b) Increasing infection cure rates and reduce treatment failures;

c) Reducing adverse events from antibiotic use; and

d) Preventing and reducing antibiotic resistance, together with infection prevention and control measures.

Examples:
In a recent survey of hospitals that had implemented an antibiotic stewardship programme [47]:

• *96% hospitals reported reduced inappropriate prescribing;*

• *86% reported reduced use of broad-spectrum antibiotics;*

• *80% reported reduced expenditures;*

• *71% reported reduced healthcare-associated infections;*

• *65% reported reduced length of stay or mortality;*

• *58% reported reductions in antibiotic resistance.*

Note: Some examples refer to antimicrobial stewardship programmes. The objectives of antimicrobial and antibiotic stewardship programmes, including the appropriate indication, selection, dosing, route of administration, and duration of antimicrobial therapy, are the same.

19. Antibiotic stewardship programmes can successfully reduce Clostridium difficile infection rates [19,22,43,44,48].

Example:
The incidence of Clostridium difficile infections decreased in the medical and surgical wards of an acute general hospital in the United Kingdom in response to revised empirical antibiotic treatment guidelines for common infections and restrictive measures for fluoroquinolone and cephalosporin usage [48].

20. Antibiotic stewardship programmes can reduce patient care costs [42,45,46].

Example:
In a pooled analysis of antibiotic stewardship programmes, total consumption fell (by 19% hospital-wide and by 40% in intensive care units), overall antibiotic costs were reduced (by about one third), and the hospital length of stay shortened (by 9%). These improvements did not cause any increase in adverse patient outcomes [46].

How do antibiotic stewardship programmes work?

21. Antibiotic stewardship programmes consist of multifaceted actions, such as [19,42,43,44,48-57]:

a) Leadership commitment: ensuring the necessary resources in terms of staff, technology and budget are available.

b) Appointing leaders that are responsible for the overall programme and for antibiotic use.

c) Hospital-based teams, which include infectious disease specialists, clinical pharmacists and microbiologists, providing support to prescribers;

d) Proactive auditing of antibiotic prescriptions with feedback to team members;

e) Training and education for medical, pharmacy, laboratory, nursing, and non-clinical staff, as well as patients and their families;

f) Using evidence-based antibiotic guidelines and policies;

g) Using restrictive measures for antibiotic prescriptions (e.g., pre-approval and post-authorization requirements for specific antibiotics);

h) Monitoring antibiotic resistance and use, and making this information available to prescribers.

Examples of antibiotic stewardship strategies, actions and outcomes in European countries include:

22. France - Restricting use of fluoroquinolones reduced consumption of this class of antibiotics and decreased the rate of meticillin-resistant Staphylococcus aureus in a teaching hospital [58].

23. France – Using information technology support for antibiotic prescriptions decreased antibiotic consumption in many hospitals [59].

24. Germany - Implementing a computerised decision support system led to higher adherence to locally adapted guidelines, increased antibiotic-free days and reduced mortality over a five-year period in five intensive care units [60].

25. Hungary - Infectious disease specialist consultation in a surgical intensive care unit, together with a restricted prescribing policy, led to lower use of all antibiotics and a marked reduction in use of broad-spectrum antibiotics [61].

26. Italy – A four-year infection control programme decreased the incidence of infections and colonisation caused by carbapenem-resistant bacteria in a teaching hospital. The programme included antibiotic stewardship measures targeting carbapenem use [62].

27. Netherlands – Implementing rapid processing of microbiology tests increased the proportion of patients receiving appropriate treatment within the first 48 hours in a teaching hospital [63].

28. Netherlands - Case audits for the reassessment of antibiotic use after 48 hours reduced antibiotic consumption and length of stay in a urology ward of an academic hospital, and also had a positive direct return on investment [64,65].

29. Poland - Developing guidelines for antibiotic prescriptions and pre-authorisation approval for restricted antibiotics decreased total antibiotic consumption in a general paediatric ward [66].

30. Spain – After only one year, education on guidelines combined with regular feedback led to a 26% improvement in the rate of appropriate treatments, and a 42% reduction of antibiotic consumption at a tertiary teaching hospital [67].

31. Sweden – Twice weekly audit and feedback in an internal medicine department led to an absolute 27% reduction of antibiotic use , especially of broad-spectrum antibiotics (cephalosporins and fluoroquinolones), as well as shorter antibiotic treatment durations and earlier switching to oral therapy [68].