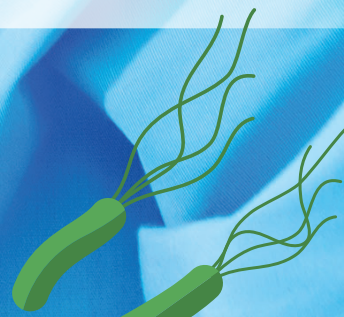




Tackling AMR in Europe's healthcare facilities:

Best practice to prevent the development
and spread of drug-resistant bacteria



ABBREVIATIONS USED IN THIS REPORT

AMR	Antimicrobial Resistance
API	Active Pharmaceutical Ingredient
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EU	European Union
GMP	Good Manufacturing Practice
HCAI	Healthcare-Associated Infection
IPC	Infection Prevention and Control
MDRO	Multi-Drug Resistant Organism
MRSA	Methicillin-Resistant <i>Staphylococcus Aureus</i>
OECD	Organisation for Economic Co-operation and Development
SOP	Standard Operating Procedure
WASH	Water, Sanitation and Hygiene
WHO	World Health Organization

INTRODUCTION

Antibiotics are vital medicines in the treatment of bacterial infections, but their effectiveness is under threat by the development and spread of drug-resistant bacteria. Described by England's Chief Medical Officer as a "catastrophic threat", antimicrobial resistance (AMR) is estimated to cause 700,000 deaths per year globally.¹²

In the EU, AMR is annually responsible for an estimated 33,000 deaths and more than €1.5bn in healthcare costs and productivity losses.^{3,4} If no effective action is undertaken, AMR will increasingly damage populations' health and place further burden on already strained healthcare budgets, particularly in Southern Europe.⁵

In June 2017 the European Commission adopted the EU One Health Action Plan against AMR to make the EU a "best practice region". This plan supports Member States to deliver effective, innovative, and sustainable responses to AMR, as well as reinforcing the research agenda for AMR and promoting global action.⁶

Healthcare facilities are considered hotspots for the development and spread of drug-resistant bacteria. According to a study published in *The Lancet Infectious Diseases* journal, approximately

75% of infections with drug-resistant bacteria in the EU/EEA are associated with healthcare.⁷

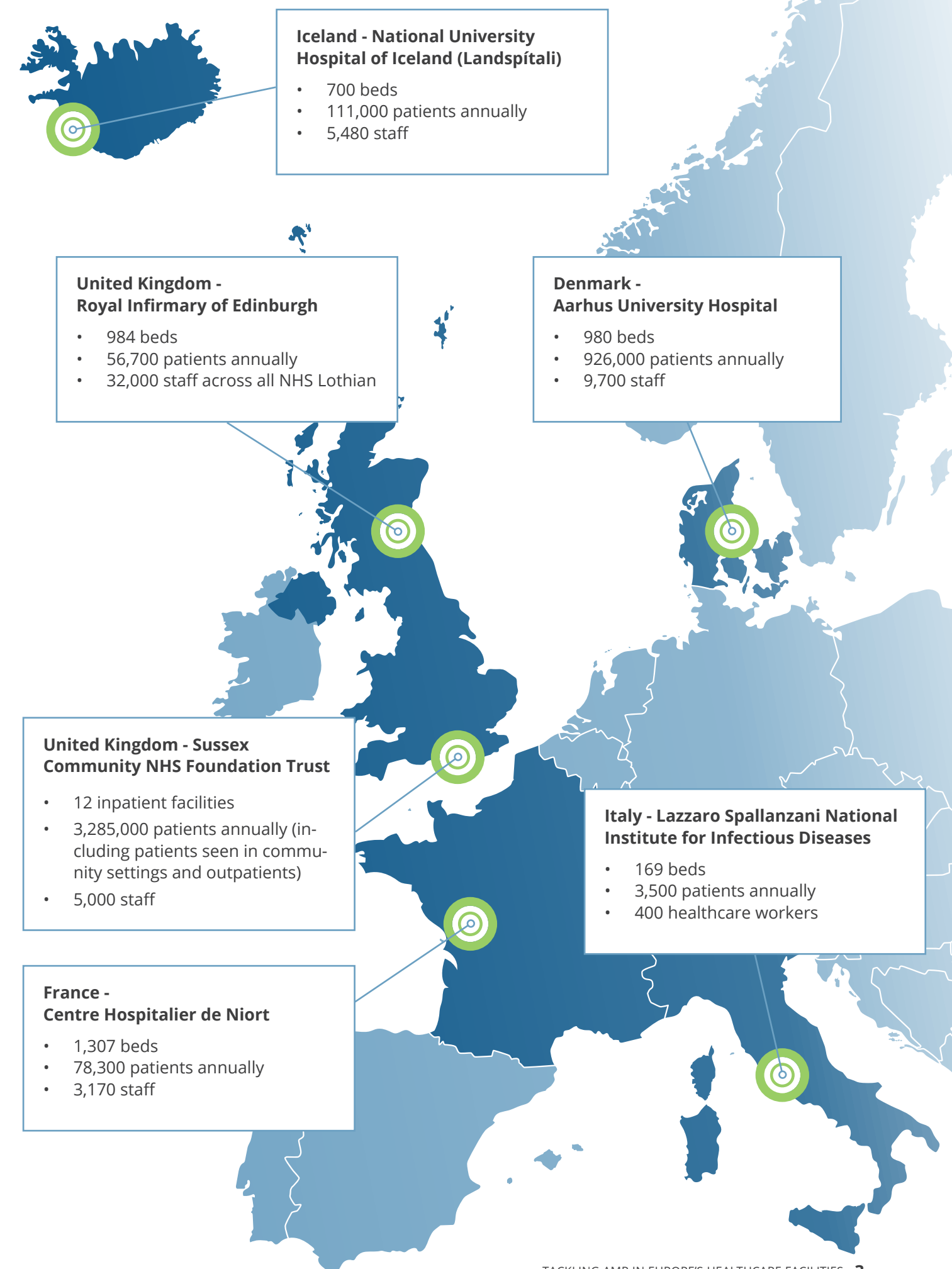
In 2018, the European Centre for Disease Prevention and Control (ECDC) identified multidrug-resistant bacteria as a leading cause of the estimated 8.9 million annual healthcare-associated infections (HCAIs) in both hospitals (one in 15 patients) and long-term care facilities (one in 26 patients) in the EU/EEA.⁸

Recognising this challenge, Health Care Without Harm (HCWH) Europe conducted a survey to identify best practice for tackling AMR in healthcare facilities across Europe. The aim of this survey, the first of this kind at the EU level, was to produce guidelines for hospitals and health systems, as well as to inform stakeholders about initiatives on the ground.

The survey was completed in 2019 by six healthcare facilities: Aarhus University Hospital (Denmark), the Centre Hospitalier de Niort (France), the Lazzaro Spallanzani National Institute for Infectious Diseases (Italy), National University Hospital of Iceland (Iceland), the Royal Infirmary of Edinburgh (UK), and Sussex Community NHS Foundation Trust (UK).

This report assesses the survey results, highlights best practice reported by respondents, and makes recommendations in five areas:

1. Antibiotic stewardship
2. Infection prevention and control
3. Wastewater treatment
4. Procurement practices
5. Training and information



1. ANTIBIOTIC STEWARDSHIP

Antimicrobial resistance is a natural process, but the misuse and overuse of antibiotics is dangerously accelerating its development. Whilst only 10-20% of all antibiotics are used in hospitals, the intensity of use is much higher than in the community. In addition, hospitals are usually where last-resort antibiotics, such as carbapenems and polymyxins, are used.⁹

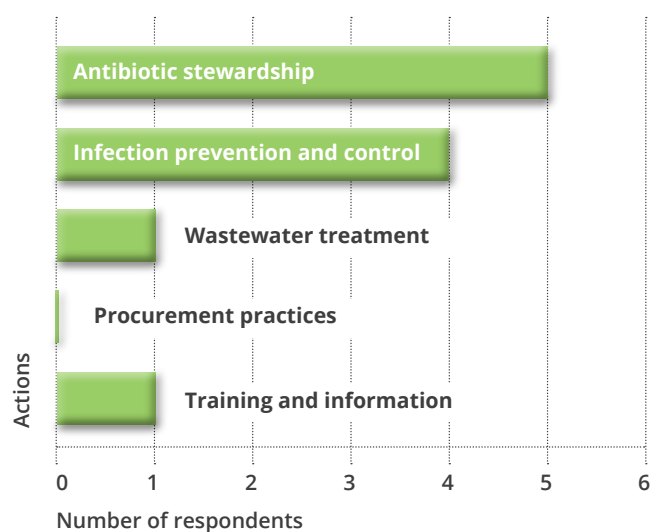
In Europe, one in three patients admitted in acute care hospitals receives at least one antimicrobial agent, primarily to treat infections.¹⁰ According to the Organisation for Economic Co-operation and Development (OECD), up to 50% of all antimicrobial consumption in human healthcare may be inappropriate, but this may reach 90% in some healthcare services.¹¹

Antimicrobial stewardship is “an organisational or healthcare system-wide approach to promoting and monitoring judicious use of antimicrobials to preserve their future effectiveness”.¹² It is recognised as a key aspect for improving the appropriate use of antimicrobial agents and curbing inadequate consumption.¹³

The European Commission recommends that antimicrobial stewardship teams are ideally composed of an infectious disease specialist (or a clinician with expertise on infection diagnosis, prevention, and treatment), as well as a hospital pharmacist and a clinical microbiologist.¹²

Survey respondents demonstrated a high level of awareness on the importance of improving antibiotic prescription and use in healthcare facilities. The majority identified antibiotic stewardship when asked which main actions were taken within their hospitals to tackle AMR.

What are the main actions taken at your hospital to address the threat posed by AMR?



As one of the biggest consumers of antibiotics in Europe, in 2008 the French National Authority for Health (Haute Autorité de Santé) published guidelines on the proper use of antibiotics and effective antibiotic strategies to prevent the development of bacterial resistance.¹⁴

In the Centre Hospitalier de Niort, antimicrobial stewardship activities are common practice; infectious disease physicians, for example, are responsible for identifying the best treatments for patients infected with drug-resistant bacteria. Additionally, prescriptions for broad-spectrum antibioticsⁱ have to undergo strong pharmaceutical control.

In early 2019 the UK government launched a new five-year national action plan to tackle AMR with a 15% reduction target for antimicrobial use in humans by 2024. The plan notably seeks to strengthen stewardship programmes to reduce inadequate prescribing and ensure timely treatment to avoid serious infections and further complications such as sepsis.¹⁵

The Royal Infirmary of Edinburgh has developed antimicrobial prescribing guidelines that are available electronically on the hospital's intranet as well as on a mobile app. The guidelines include senior reviewing by 24 hours and focusing antibiotic treatment when results are available by 72 hours to encourage prudent prescribing of antimicrobials, improve patient outcomes, and reduce the development of drug-resistant bacteria.

ANTIBIOTIC STEWARDSHIP RECOMMENDATIONS:

- Involve infectious disease specialists in decision-making processes for antibiotic prescriptions for drug-resistant infections
- Make prescriptions of broad-spectrum antibiotics conditional to strong pharmaceutical control to safeguard their effectiveness in the treatment of severe infections
- Make the best use of technology (e.g. apps, e-learning modules, intranet) to facilitate easy access and dissemination of antimicrobial prescribing guidelines
- Undertake regular reviews of clinical antibiotic prescriptions to reduce inadequate or inappropriate antibiotic consumption

ⁱ Broad-spectrum antibiotics inhibit a wide range of bacteria compared to narrow-spectrum antibiotics that are only effective against certain groups of bacteria.

2. INFECTION PREVENTION AND CONTROL

Infection prevention and control (IPC) is designed to reduce the spread of bacteria, including drug-resistant ones, within healthcare facilities and the wider community. It therefore helps prevent infections that would otherwise require further treatment.¹⁶

Water, sanitation and hygiene (WASH) in healthcare facilities are the cornerstone of IPC.¹⁷ According to the World Health Organization (WHO), the implementation of WASH measures could reduce the demand for antibiotics and therefore curb their overuse in specific categories by as much as 60% in low and middle-income countries.¹⁸

Whilst basic measures such as contact precautions, hand washing, and proper cleaning can play a significant role in preventing the spread of bacteria between patients – they are often neglected. As the spread of AMR is often unnoticed, each patient should be treated as if they are carrying drug-resistant bacteria.¹⁹

At the EU level, the Council has recently called to strengthen IPC measures in healthcare facilities to reduce the inadequate use of antibiotics and the associated risk of developing AMR. It notably recommended investment in hygiene measures and prevention actions such as biosecurity, rapid access to diagnostic tools, and vaccinations.²⁰

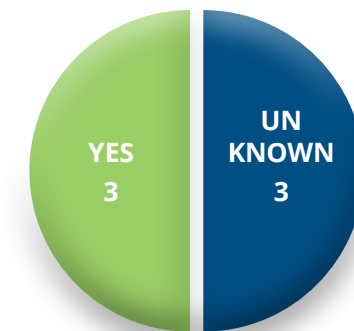
Survey respondents indicated that they pay close attention to IPC measures and maintain a good level of cooperation between antimicrobial pharmacists and IPC teams when dealing with HCAs such as Methicillin-Resistant *Staphylococcus Aureus* (MRSA).

The Lazzaro Spallanzani National Institute for Infectious Diseases is a regional referral centre for the surveillance of HCAs. The institute strictly adheres to isolation precautions, HCAI prevention bundles,ⁱⁱ and standard operating procedures (SOPs) to safeguard the environmental hygiene of isolation rooms for patients with Multi-Drug Resistant Organisms (MDROs).

Because it is challenging to assess the implementation of IPC measures in healthcare facilities, our survey enquired whether hospitals are taking steps to improve sanitation infrastructure to prevent the spread of drug-resistant bacteria. The results were mixed, however, as most respondents were unaware of potential projects in the pipeline.

ⁱⁱ Prevention bundles are evidence-based practices that, when performed collectively, improve prevention effectiveness and patient outcomes.

Does your hospital take measures to improve sanitation infrastructure to prevent the spread of resistant bacteria?



The National University Hospital of Iceland (Landspítali) indicated that improved sanitation was considered when refurbishing and that new buildings only feature single-occupancy patient rooms to control and prevent HCAs. Sussex Community NHS Foundation Trust's IPC policy prohibits the use of aerators on taps because they can hold and promote the spread of airborne bacteria.

INFECTION PREVENTION AND CONTROL RECOMMENDATIONS:

- Encourage continued cooperation between IPC teams and antimicrobial pharmacists to prevent HCAs
- Develop and implement HCAI prevention bundles to improve prevention effectiveness and patient outcomes
- Develop SOPs to ensure environmental hygiene of isolation rooms for MDRO patients
- Prioritise single-occupancy patient rooms when designing new healthcare facilities despite short-term costs to alleviate the long-term AMR burden

3. WASTEWATER TREATMENT

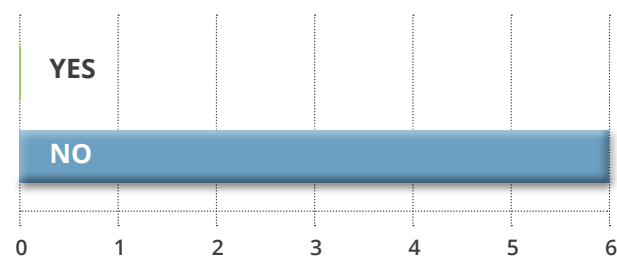
Healthcare facilities are contributing to the development and spread of AMR; drug-resistant bacteria not only leave hospitals via patients, but they can also spread through wastewater systems. In addition, antimicrobials excreted by patients via sewage systems also exert a continuous selective pressure on drug-resistant bacteria.²¹

It is estimated that 30%-90% of orally administered pharmaceuticals are excreted into wastewater as active substances in the faeces and urine of patients. Wastewater treatment plants vary in their capacity to remove these active substances, meaning that they can be discharged into the aquatic environment as a result.²²

In the EU, just 10% of medicinal products in urban effluent come from hospitals (approximately), as antibiotics are widely used outside healthcare facilities.²³ Hospital wastewater may therefore not be the largest contributor to overall resistance prevalence. There is evidence, however, that hospital effluents have an important impact on the prevalence of drug-resistant bacteria for specific antimicrobials such as ciprofloxacin, sulphonamide, and tetracycline.²²

None of the survey respondents have onsite wastewater treatment plants at their healthcare facilities. Though treating wastewater at the hospital level may have a limited effect on the environment, there is interest in reducing upstream discharges of antimicrobials that contribute to high levels of resistance in hospital effluents.

Is there a wastewater treatment plant in your hospital equipped to filter infectious bacteria?



Aarhus University Hospital is the only respondent active in this field. In collaboration with the Danish Technological Institute, the hospital has recently been testing if peracetic acid can neutralise ciprofloxacin-resistant bacteria in untreated wastewater, with positive results. It is also measuring the AMR concentration in its wastewater to determine need for action.

WASTEWATER TREATMENT RECOMMENDATIONS:

- Measure the concentration of AMR in hospital wastewater compared to local municipal wastewater to determine the need for action
- Participate in pilot projects aiming to reduce upstream discharge of antimicrobials that contribute to high levels of resistance in hospital effluents

4. PROCUREMENT PRACTICES

The majority of antibiotics are produced in developing countries that may have weaker environmental standards and regulatory systems than those in force in the EU. China currently produces 80%-90% of antibiotic active pharmaceutical ingredients (APIs) globally while India is the leading producer of finished dose products.²⁴

In 2017, UN Environment identified growing AMR linked to discharge of drugs and particular chemicals into the environment as “one of the most worrying health threats today”. It also acknowledged that the release of antimicrobial compounds from pharmaceutical facilities into the environment is driving the emergence of drug-resistant bacteria.²⁵

Partly due to manufacturing pollution, India has already become the epicentre of a drug-resistance crisis causing the death of more than 56,000 new-borns annually.²⁶ Exposure to environmental sources of antimicrobial drugs in India is also placing vulnerable populations at a higher risk for community-acquired AMR.²⁷

In the EU, the discharge of pharmaceutical production into the environment has been considered negligible, but the amount of APIs released from manufacturing plants is largely unknown as there is no systematic monitoring of manufacturing emissions at EU level, despite observations of possible downstream pollution from manufacturing plants.²⁸

The EU also shares a part of the responsibility for global pollution as the majority of antibiotics on the EU market are produced in countries where large-scale environmental pollution occurs.²⁴ Its role in this pollution is not yet sufficiently addressed - the EU Good Manufacturing Practice (GMP)ⁱⁱⁱ does not even feature environmental aspects.²⁹

ⁱⁱⁱ The EU Good Manufacturing Practice (GMP) is the set of required standards for production of pharmaceuticals intended for the EU market.

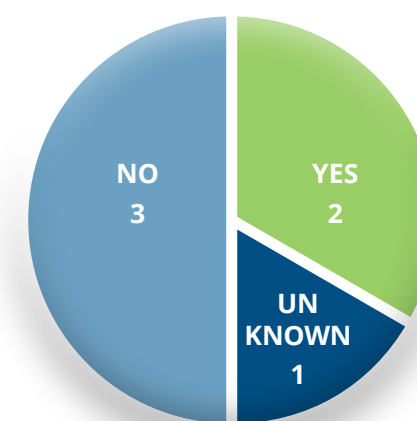
The EU cannot turn a blind eye to this issue, not least because drug-resistant bacteria emerging in developing countries are spreading around the world through trade and travel. It is estimated, for instance, that more than 70% of tourists who travel to India come back with drug-resistant bacteria in their guts.³⁰

As a major purchaser of pharmaceuticals, the European healthcare sector holds economic and ethical influence that if mobilised can transform the system. Through sustainable procurement practices, healthcare facilities can leverage their purchasing power to address the issue of pollution from pharmaceutical manufacturing.

The EU Public Procurement Directive lays the legal groundwork for public authorities to set environmental and social criteria in procurement. Although tenders should be identified on the basis of price or cost, contracting authorities may consider the best price-quality ratio assessed on additional criteria including environmental and/or social aspects.

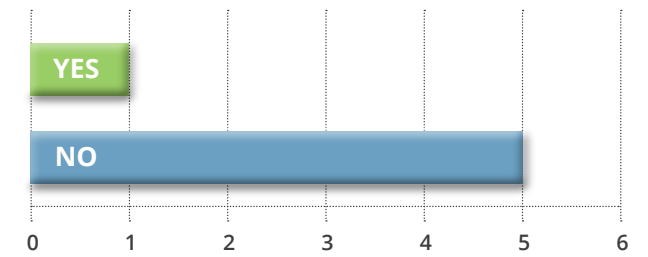
Amongst our survey respondents, awareness of manufacturing conditions is growing; enquiring about environmental policies in manufacturing sites is standard practice within at least two respondents. It can be assumed, however, that the level of engagement is dependent on country-specific practices as the responsibility for procurement may lie with third parties.

Does your hospital ask providers if they have environmental policies in place at their manufacturing sites?



The transition from information gathering to sustainable procurement practices, however, is still low among respondents. The Centre Hospitalier de Niort is so far the only surveyed hospital that evaluates the global sustainable development policy of each supplier as a standard step of its purchasing process.

Does your hospital include environmental criteria in pharmaceutical procurement decisions?



PROCUREMENT PRACTICES RECOMMENDATIONS:

- Mobilise the economic and ethical influence of the healthcare sector to transform the pharmaceutical production chain within the framework of the EU Public Procurement Directive
- Include environmental criteria in pharmaceuticals procurement to support informed decision-making when purchasing
- Raise the issue of pharmaceutical manufacturing pollution with policy makers and advocate for strengthened environmental regulations

5. TRAINING AND INFORMATION

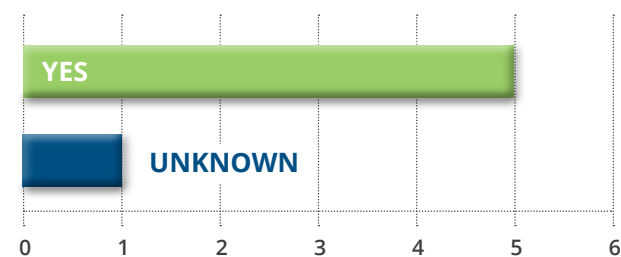
Education and awareness-raising activities targeting both the general public and healthcare professionals are vital for decreasing the ineffective use of antimicrobials. The OECD suggests that this approach is even more effective when combined with training programmes, for instance as part of continuing medical education schemes.¹¹

Training healthcare workers is integral to tackling AMR in healthcare facilities; antibiotic management requires effective teamwork, so it is important that all healthcare professionals receive continuing education around the adequate use of antimicrobials, biocides, and disinfectants that can trigger resistance, as well as patient management.³¹

The fight against AMR requires a multidisciplinary approach; whilst physicians certainly have a major role to play, so too do nurses and other healthcare practitioners in direct contact with patients. Pharmacists also can importantly educate patients about medication compliance and proper antimicrobial use.¹⁶

Most survey respondents organise training for healthcare workers, some also provide materials to raise awareness amongst patients on antibiotic use and its link with AMR. Training sessions mainly deal with antibiotic stewardship, IPC, and prescription practices.

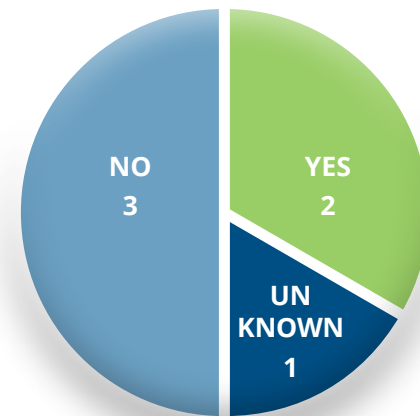
Does your hospital organise training sessions for healthcare workers on how to better deal with AMR at hospital level?



The Royal Infirmary of Edinburgh organises training sessions on antibiotics monitoring (e.g. gentamicin, vancomycin), antibiotic stewardship, infection control, and good prescription practices. In the Centre Hospitalier de Niort, physicians annually receive their Defined Daily Dose^{iv} ward profile in addition to training on prescription practices and additional precautions.

^{iv} A Defined Daily Dose is a statistical measure defined by the WHO to allow for comparisons of drug consumption at an international level.

Does your hospital provide or distribute materials to inform patients and the general public about the threat of AMR?



The Lazzaro Spallanzani National Institute for Infectious Diseases organises awareness-raising activities and distributes campaign materials during World Antibiotic Awareness Week and European Antibiotic Awareness Day. Sussex Community NHS Foundation Trust makes leaflets available for staff to print off for patients such as Public Health England's *Become an Antibiotic Guardian*.^v

TRAINING AND INFORMATION RECOMMENDATIONS:

- Develop multidisciplinary training programmes on antibiotics monitoring, good prescription practices, and infection prevention and control
- Provide prescribers annually with their Defined Daily Dose ward profile as a benchmarking and control exercise
- Organise awareness-raising activities and provide patients with information (e.g. leaflets, signs) on medication compliance and proper antimicrobial use

^v Public Health England. (2017) *Become an Antibiotic Guardian*. www.antibioticguardian.com/assets/AntibioticGuardianLeaflet_3-Fold_FINAL_.pdf

CONCLUSION

Healthcare facilities play a significant role in the development and spread of drug-resistant bacteria. Whilst delivering their mission to support the health and wellbeing of patients, the European healthcare sector is paradoxically undermining the effectiveness of the antimicrobials that underpin modern medicine.

There is a high level of awareness among survey respondents on this issue; from antibiotic stewardship programmes to training sessions on prescription practices, all healthcare facilities that were surveyed have taken a number of actions to mitigate their contribution to AMR, often supported by local guidelines or national action plans.

The survey results also indicate, however, that healthcare facilities could make better use of the wide range of tools at their disposal, notably in the areas of procurement and wastewater treatment. Tackling AMR in European hospitals is a complex challenge that requires multifaceted solutions.

Measures may also come at a financial and environmental cost – an extra hurdle for the underfunded healthcare sector. In its combat against AMR, the National University Hospital of Iceland (Landspítali) has strict isolation policies that impair rapid patient flow, and the hospital performs expensive susceptibility testing, whilst the Centre Hospitalier de Niort reported an increased consumption of plastic aprons.

This highlights the need for more public funding to support ambitious measures and foster research for sustainable solutions. These short-term burdens need to be overcome to prevent heavy long-term costs for healthcare systems. AMR already costs more than €1.5bn every year in healthcare costs and productivity losses in the EU.⁴

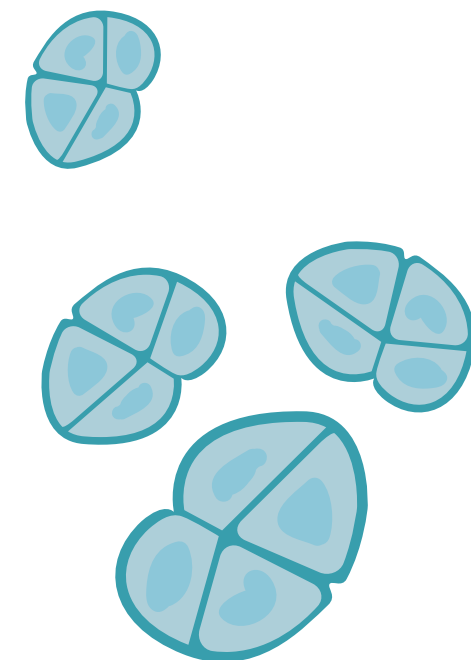
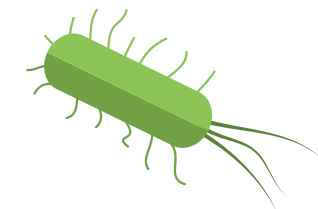
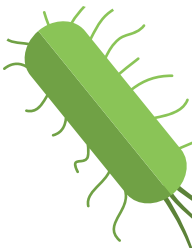
According to the OECD, three out of four deaths from drug-resistant infections could be averted by annual spending of \$2 USD per person on simple measures such as hand washing and prudent prescription practices – such measures would produce \$4.8bn USD savings per year in OECD countries.⁵

IPC measures are particularly cost-effective since prevented infections do not need treatment. According to the WHO, hand hygiene is the single most important measure to prevent the transmission of bacteria in healthcare facilities. Yet the cost to promote hand hygiene represents less than 1% of the cost to care for patients with HCAs.³²

Many successful initiatives are taking place across Europe: the Canisius-Wilhelmina Hospital in Nijmegen, The Netherlands, for instance, reduced

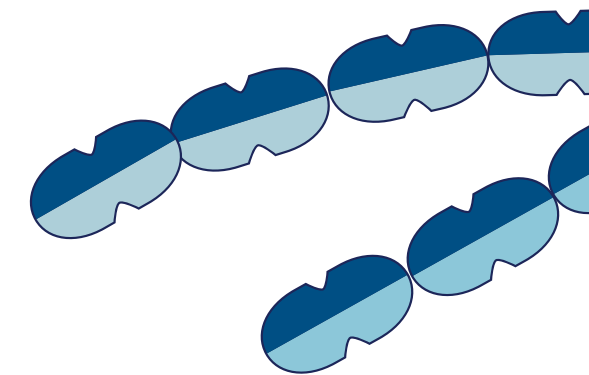
prescriptions of last-resort antibiotics by 25% and saved €40,000 in costs one year after introducing an antibiotic stewardship programme.³³

Overall, there is a need for greater sharing of best practice to allow for peer learning across Europe; this report plays a key part in this process and recommends that further similar initiatives are implemented to ensure that the healthcare sector plays a leading role in the fight against AMR.



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Health Care Without Harm (HCWH) Europe is the European arm of a global not-for-profit NGO whose mission is to transform healthcare worldwide so that it reduces its environmental footprint, becomes a community anchor for sustainability, and a leader in the global movement for environmental health and justice. HCWH's vision is that healthcare mobilises its ethical, economical, and political influence to create an ecologically sustainable, equitable, and healthy world.

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