Antimicrobial Resistance in the EU/EEA

A One Health Response

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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

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A Briefing Note
For EU/EEA countries to inform the French presidency of the EU council

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Key messages

Antimicrobial resistance remains a serious challenge for everyone, a silent pandemic that calls for a One Health response in the EU/EEA.

Misuse of antibiotics is among the main drivers underpinning the development of antimicrobial resistance (AMR). Resistance to last-line antibiotics also compromises the effectiveness of life saving medical interventions such as intensive care, cancer treatment and organ transplantation.

Overall consumption of antibiotics in humans in the European Union/European Economic Area (EU/EEA) decreased by 23% between 2011 and 2020, especially during the Coronavirus Disease 2019 (COVID-19) pandemic (between 2019 and 2020, the mean total consumption of antibiotics dropped by almost 18%). However, relative use of broad-spectrum antibiotics has increased and significant variability across countries suggests that reductions are still possible.

Efforts to reduce unnecessary use of antibiotics in food-producing animals have resulted in a 43% decrease in use between 2011 and 2020 in 25 countries with consistent reporting.

Despite reductions in antibiotic consumption in both humans and food-producing animals, AMR in bacteria from humans in the EU/EEA has increased for many antibiotic-bacterium combinations since 2011. Particularly worrisome is the rise in resistance to critically important antibiotics used to treat common healthcare-associated infections.

While recent trends have been encouraging, resistance to commonly used antibiotics in bacteria from food-producing animals remains high (>20% to 50%) or very high (>50% to 70%), and there is significant regional variation across the EU/EEA region.

Evidence that AMR can spread between animals, humans and the environment is mounting. Reducing the use of antibiotics in food-producing animals, replacing them where possible and rethinking the livestock production system in a One Health approach is essential for the future of animal and public health.

EU/EEA countries have made important strides in recent years in developing and implementing national action plans on AMR, but gaps remain. Analyses by the OECD suggest that top priorities for the EU/EEA include:

- Evaluation and monitoring of the implementation of national action plans.
- Integrated and expanded surveillance of AMR in bacteria from humans, animals and the environment.
- Investing in effective cost-saving interventions, such as antimicrobial stewardship programmes and infection prevention and control (IPC).

Plans for a new EU policy initiative to boost the implementation of the EU One Health Action Plan against AMR are a timely opportunity to:

- Continue incentivising new vaccines, treatments (including new antibiotics) and tests while maximising access to existing resources such as antibiotics with low availability.
- Target antibiotic consumption and AMR in long-term care facilities (LTCFs). A new OECD survey shows that very few countries have policies that specifically address AMR in LTCFs, with a majority of EU/EEA countries reporting they plan to include references to LTCFs in their next national action plan.
- Establish a system to share and promote the implementation of best practices to tackle AMR.
- Renew focus on international co-operation on surveillance and regulation, including with non-EU/EEA partners.

While available data suggests that there has been a reduction in antibiotic consumption in humans during the pandemic, AMR remains a serious challenge in the EU/EEA. AMR cannot be contained within borders or regions, underlining the need for concerted action throughout the EU/EEA.

Antibiotic consumption: More progress in agriculture than in the human sector

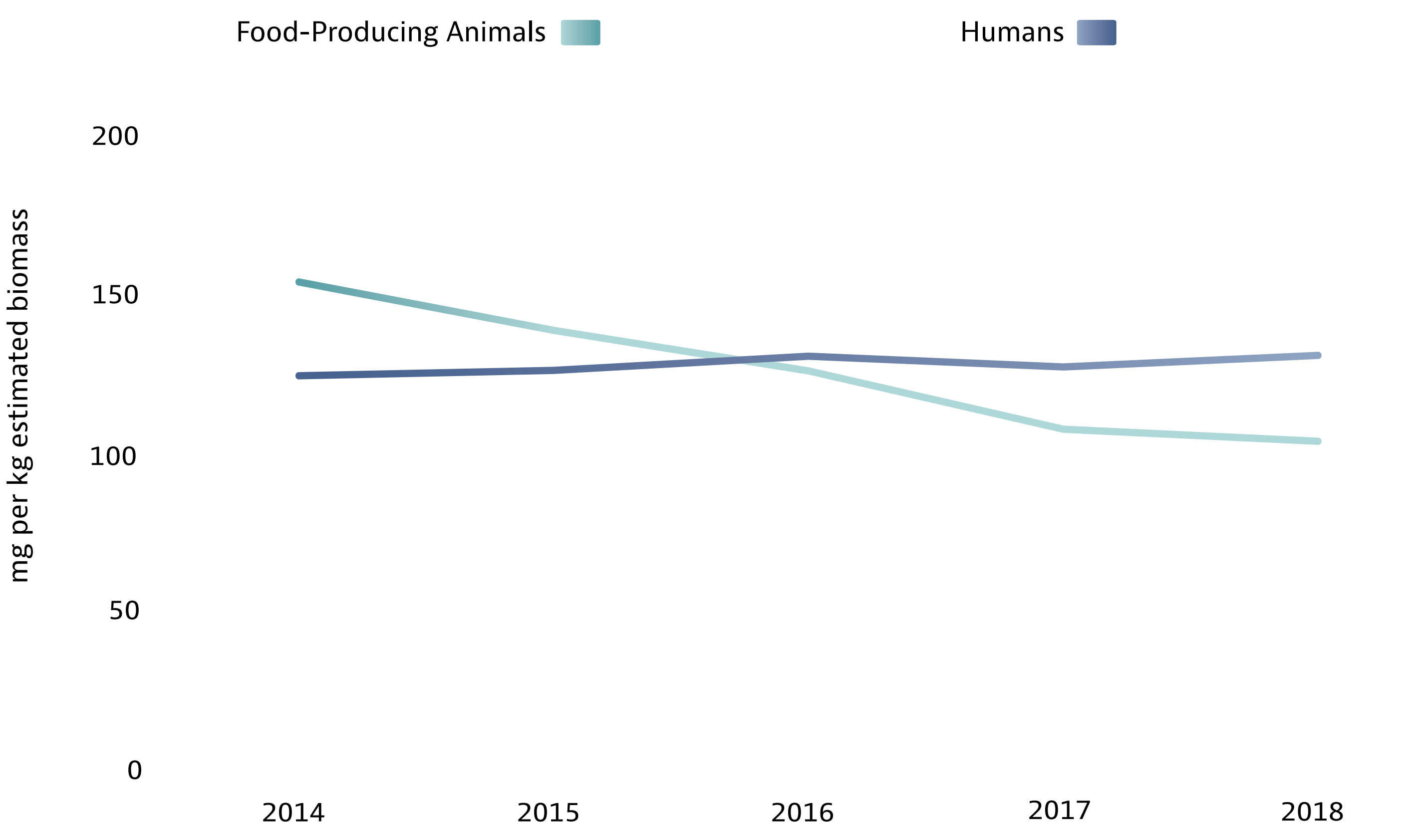
Average consumption of antibiotics in humans is now higher than in food-producing animals, after adjusting for biomass

In 2018, in 29 EU/EEA countries, 4 264 tonnes of antibiotics were used in humans corresponding to a mean antibiotic consumption of 133 mg of active substance per kg estimated biomass, whereas 6 358 tonnes of antibiotics were used in food-producing animals corresponding to a mean antibiotic consumption of 105 mg per kg estimated biomass (Figure 1). Consumption was lower in food-producing animals than in humans in 19 of 29 EU/EEA countries.

Overall antibiotic consumption per kg of estimated biomass is now higher in humans than in food-producing animals, a shift compared to previous years, which can be explained by a decrease in antibiotic use in food-producing animals since 2014. This trend suggests that the measures taken at country-level to reduce the use of antibiotics in food-producing animals have been effective.

Figure 1. Consumption of antibiotics in humans and food-producing animals, EU/EEA (population-weighted mean), 2014-2018

Population-weighted mean of the total consumption of antibiotics in humans and food-producing animals in 27 EU/EEA countries for which data were available for both humans and animals, for 2014-2018



Note: For humans: ATC J01 Antibacterials for systemic use. For food-producing animals: ATCvet QA07AA, QA07AB, QG01AA, QG01AE, QG01BA, QG01BE, QG51AA, QG51AG, QJ01, QJ51, QP51AG. Population-weighted mean of 27 EU/EEA countries for which data were available: Austria, Belgium, Bulgaria, Croatia, Cyprus, Denmark, Estonia, Finland, France, Germany, Hungary, Iceland, Ireland, Italy, Latvia, Lithuania, Luxembourg, Netherlands, Norway, Poland, Portugal, Romania, Slovak Republic, Slovenia, Spain, Sweden, United Kingdom.

Source: ECDC, EFSA, EMA (2021).

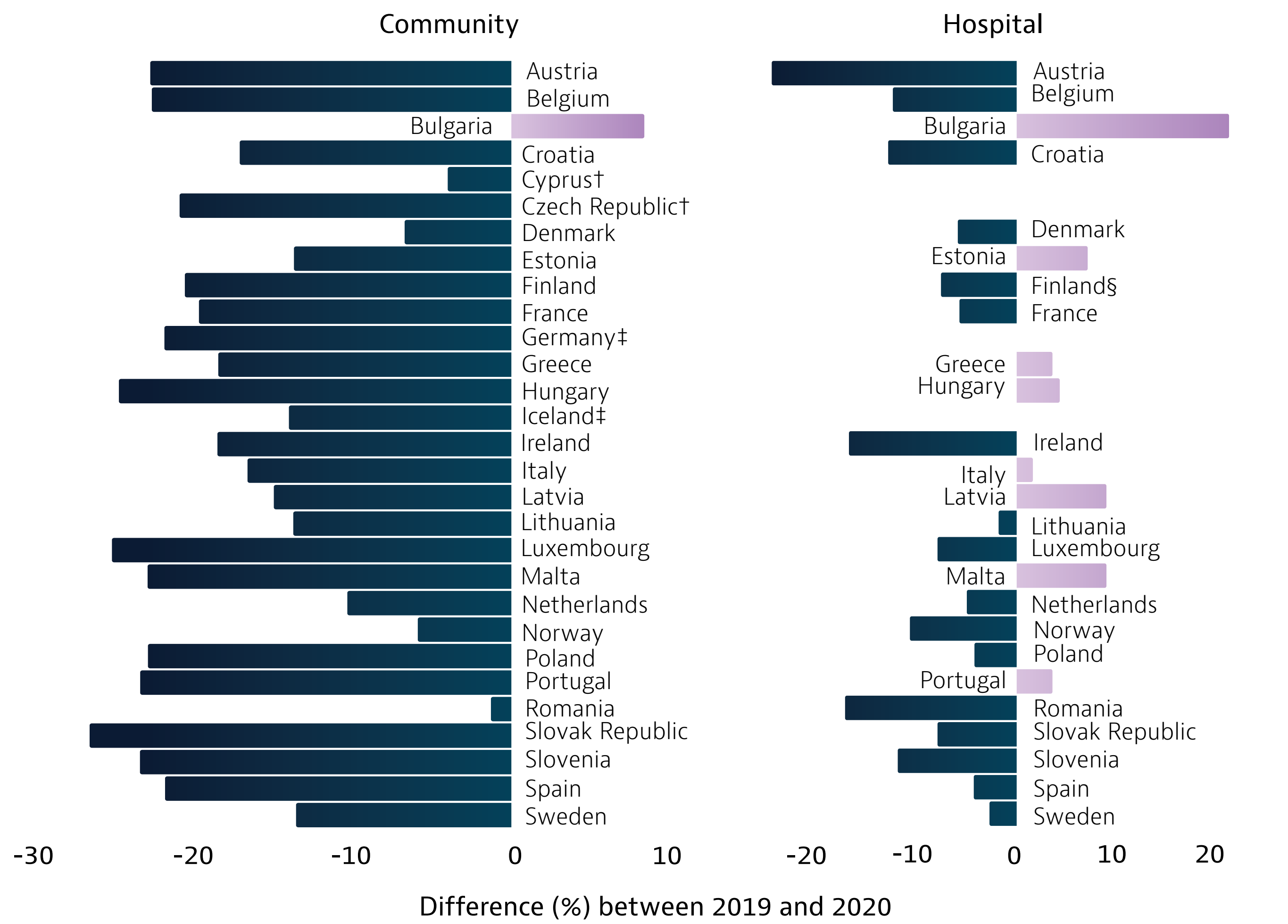
Overall antibiotic consumption in humans decreased since 2014 and data for 2020 suggest that it dropped even more during the first year of the COVID-19 pandemic

In humans, antibiotic consumption is usually expressed in defined daily doses (DDD) per 1 000 inhabitants per day. In 2020, the mean total consumption of antibiotics in humans in the EU/EEA was 16.4 DDD per 1 000 inhabitants per day, ranging from 8.5 in the Netherlands to 28.9 in Cyprus. Most antibiotic consumption in humans takes place in the community (on average 90% of all DDDs consumed, country range: 81%-94%, 25 EU/EEA countries, 2020), while the remaining takes place in the hospital sector.

During the period 2014-2020, a 23% decrease in the total consumption of antibiotics was observed for the EU/EEA overall, from 21.2 DDD per 1 000 inhabitants per day in 2014 to 16.4 DDD per 1 000 inhabitants per day in 2020.

Most of this decrease happened between 2019 and 2020. There was a decrease of total antibiotic consumption of only 1.3 DDD per 1 000 inhabitants per day between 2014 and 2019 followed by a decrease of 3.5 DDD per 1 000 inhabitants per day between 2019 and 2020, with a majority of countries reporting decreases in antibiotic consumption for both the community and the hospital sector, and generally larger decreases in the community than in the hospital sector (Figure 2). In the community, the decrease between 2019 and 2020 was proportionally larger in countries with high antibiotic consumption than in countries with low antibiotic consumption.

Figure 2. Differences in national consumption of antibiotics between 2019 and 2020 in the community and the hospital sector



Note: Differences calculated from antibiotic consumption rates expressed in DDD per 1 000 inhabitants per day; † Cyprus and the Czech Republic: total (community and hospital sector combined); ‡ Germany and Iceland: only reported data for the community; § Finland: hospital sector data include consumption in remote primary health care centres and nursing homes.

Source: ECDC (2021).

Interventions to curb the COVID-19 pandemic are likely to be behind changes in antibiotic consumption in humans observed in 2020

From March 2020 onward, all EU/EEA countries were affected by COVID-19, with sustained transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). As already shown, data for 2020 suggest that the COVID-19 pandemic has had a considerable impact on antibiotic consumption in humans in the EU/EEA. The observed reductions in consumption could be attributed to:

- Changes in infectious disease epidemiology, with particularly prominent decreases in groups of antibiotics prescribed for respiratory infections and to the youngest age groups;
- Non-pharmaceutical interventions introduced to reduce SARS-CoV-2 transmission, including restrictions on movement (such as lockdowns), physical distancing, respiratory etiquette, hand hygiene and travel restrictions, which probably had an effect on transmission and prevalence for a larger set of infectious diseases;
- Reduced use of and difficulties in accessing primary care services, due to lockdowns and reprioritisation of resources, could have led to a decrease in inappropriate prescribing for milder and self-limiting infection.

COVID-19 has put extraordinary pressure on hospitals in EU/EEA countries, with a rapidly increasing demand for intensive care beds. In parallel, the number of patients admitted for elective surgery or chronic diseases decreased in many hospitals. These changes are not reflected in the indicator 'DDD per 1 000 inhabitants per day'. In theory, if the total number of hospitalised patients decreased substantially in 2020 because of the COVID-19 pandemic, the apparent decrease in hospital antibiotic consumption expressed in 'DDD per 1 000 inhabitants per day' could actually become an increase, if expressed in 'DDD per 100 bed-days'. Thus, changes in hospital consumption between 2019 and 2020 should be interpreted with caution until further data and analyses are available. Moreover, it is still unclear whether reduced community antibiotic consumption was sustained in 2021 and what implications it may have on AMR.

Despite overall reductions, relative use of broad-spectrum antibiotics in humans increased and significant variability across countries suggests reductions are possible

The overall reductions in antibiotic consumption observed in recent years in the EU/EEA suggest that coordinated and EU-wide initiatives towards prudent use of antibiotics have had a positive impact. Yet, on average across the EU/EEA, in 2020, community consumption of broad-spectrum antibiotics was 3.5 times higher than consumption of narrow-spectrum antibiotics, which should generally be the first-line therapy.[1] Moreover, between 2011 and 2020, an increasing trend was observed in this ratio for the EU/EEA overall and for nine individual countries (Bulgaria, Croatia, Estonia, Hungary, Italy, Latvia, Lithuania, Slovak Republic, Slovenia), indicating a shift towards broad-spectrum antibiotics to treat infections in the community in these countries, whereas a decreasing trend was observed for eight countries (Austria, Belgium, Denmark, Finland, France, Germany, Ireland, Norway), indicating a shift towards narrow-spectrum antibiotics in these countries.

In the hospital sector, the proportion of broad-spectrum antibiotic consumption[2] showed an increasing trend overall for the EU/EEA between 2011 and 2020, with six countries (Bulgaria, Croatia, Denmark, Greece, Malta, Slovak Republic) showing an increasing trend and only one country (Slovenia) with a decreasing trend. Overall, in the EU/EEA, consumption of last-line antibiotics in humans, such as carbapenems and polymyxins (mainly colistin), also increased between 2011 and 2020, by 10% and 67% respectively. Last-line antibiotics are used mainly in hospitals to treat patients with confirmed or suspected serious infections and are the last line of defence against multidrug-resistant bacteria.

1 Broad-spectrum antibiotics: broad-spectrum penicillins (ATC groups J01CR, J01CD), broad-spectrum cephalosporins (J01DC, J01DD), macrolides (J01 FA) except erythromycin (J01FA01), and fluoroquinolones (J01MA); narrow-spectrum antibiotics: narrow-spectrum penicillins (J01CA, J01CE, J01CF), narrow-spectrum cephalosporins (J01DB) and erythromycin (J01FA). Consumption expressed in DDD per 1 000 inhabitants per day.

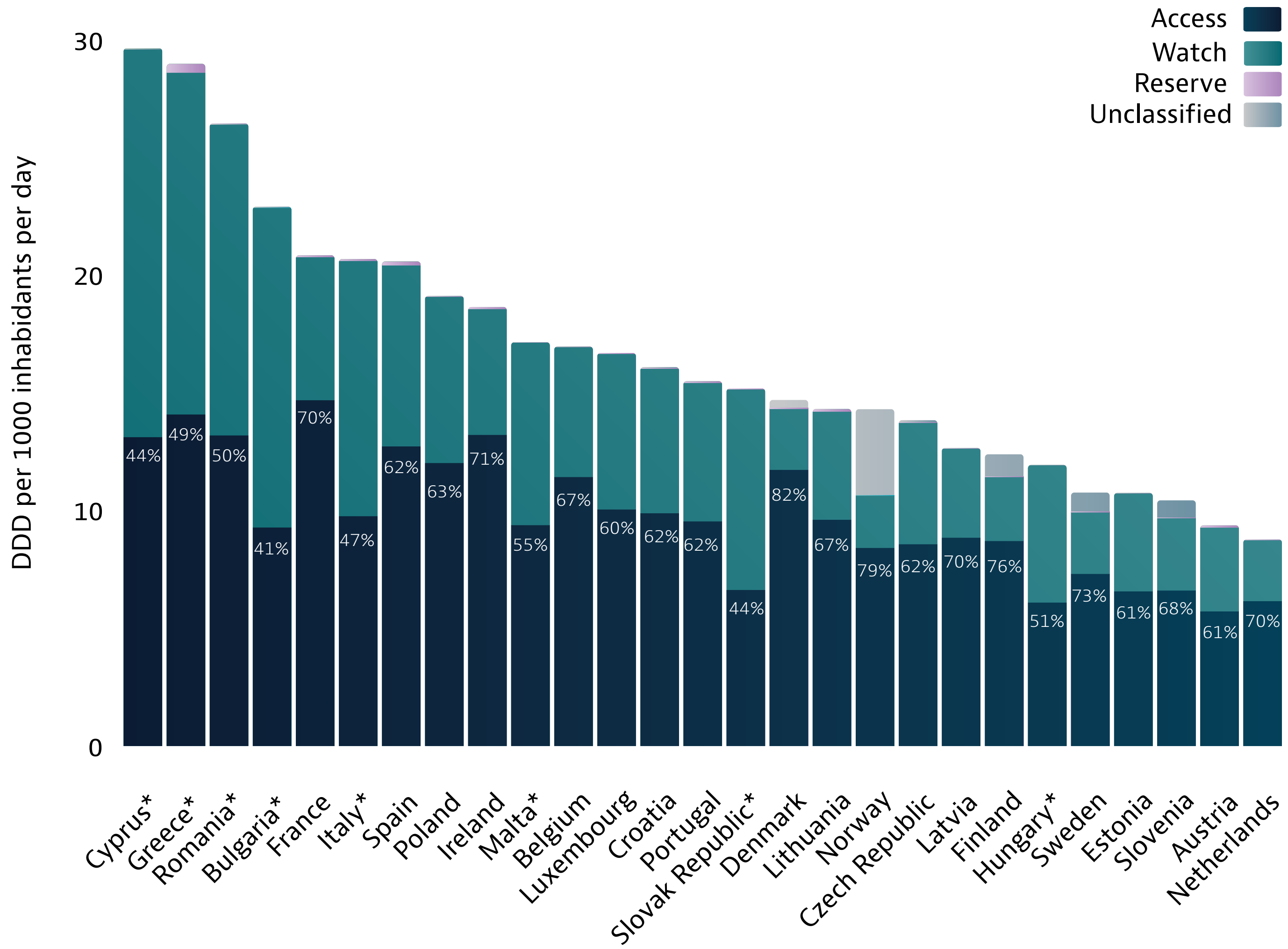
2 Proportion (%) of glycopeptides, third- and fourth-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitors, linezolid, tedizolid and daptomycin (DDD per 1 000 inhabitants per day) out of total hospital consumption of antibiotics for systemic use.

In 2017, the World Health Organization (WHO) introduced the 'Access, Watch, Reserve' or AWaRe classification as a tool for improving the use of antibiotics and has since proposed that antibiotics in the 'Access' group (mostly first-line and second-line therapies that offer the best therapeutic value, while minimising the potential for AMR) make up at least 60% of total national consumption by 2023. Yet, in 2020, consumption of antibiotics in the 'Access' group represented less than 60% of total antibiotic consumption in humans in eight EU/EEA countries (Figure 3; Bulgaria, 41%; Cyprus, 44%; Slovak Republic, 44%; Italy, 47%; Greece, 49%; Romania, 50%; Hungary, 51%; Malta, 55%).

Considerable variability in antibiotic consumption overall and in the types of antibiotics used across EU/EEA countries further suggests opportunities for significant reductions through antimicrobial stewardship initiatives in human health care and other public health investment.

Figure 3. Total antibiotic consumption in humans according to the 'Access, Watch, Reserve' classification, 2020

The WHO has set a national-level target that at least 60% of all antibiotic consumption be for 'Access' antibiotics by 2023. Consumption of 'Access' antibiotics relative to all categories shown in the bars.



Note: * Countries with less than 60% consumption of 'Access' agents (total excluding 'Unclassified'). Only countries reporting data for both the community and the hospital sector are included. AWaRe: Access, Watch and Reserve classification of antimicrobials (WHO, 2021). 'Access' antibiotics are mostly first-line and second-line therapies that offer the best therapeutic value, while minimising the potential for AMR. 'Watch' antibiotics have higher AMR potential and should be prioritised in stewardship and monitoring efforts. 'Watch' antibiotics include most of the highest priority agents in the WHO Critically Important Antimicrobials for Human Medicine. 'Reserve' antibiotics include antibiotics of last resort and should be saved for treatment of confirmed or suspected infections due to multidrug-resistant organisms. Agents included in this analysis: antibacterials for systemic use, neomycin, streptomycin, polymyxin B, kanamycin, vancomycin, colistin, rifamixin, fidaxomicin, rifamycin, rifampicin, rifamycin, rifabutin, metronidazole, tinidazole, ornidazole and secnidazole. Consumption of 'Unclassified' mainly consisted of benzathine phenoxymethylpenicillin, combinations of benzylpenicillin/procain-benzylpenicillin/benzathine benzylpenicillin and methenamine.

Source: ECDC (2022).

Sales of antibiotics for food-producing animals fell by 43% between 2011 and 2020 in 25 EU/EEA countries that consistently report data

In 2020, the average antibiotic consumption in 31 countries was 89.0 mg of active substance per kg of estimated animal biomass,[3] ranging from 2.3 mg per kg to 393.9 mg per kg (Figure 4). Between 2011 and 2020, an overall decline in sales of 43% was observed for the 25 EU/EEA countries that consistently reported since 2011, with a noticeable decrease in sales identified for some of the highest-selling countries.

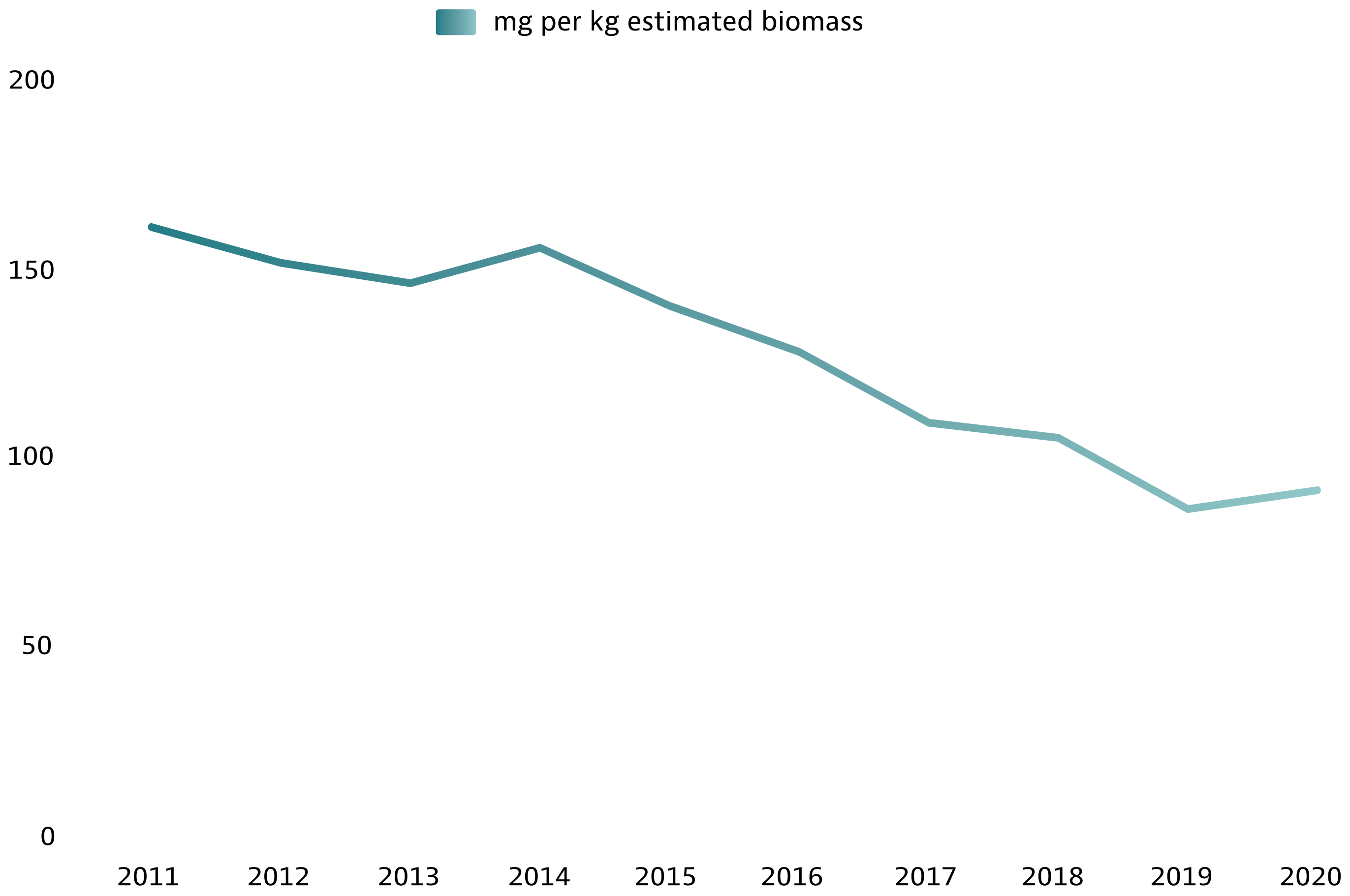
Nevertheless, differences between countries remain apparent, and for a few countries sales increased by more than 5% (between 8.6% and 79.3%) between 2011 and 2020.

These figures would suggest that efforts at both national and EU/EEA level have been successful, resulting in a continuous decrease over time in the use of antibiotics in food-producing animals in most participating European countries.

Substantial progressive reduction has also been observed for secondary indicators beyond the main indicator of overall reduction in sales, namely sales in mg per kg of 3rd- and 4th-generation cephalosporins, polymyxins and quinolones. Sales of fluoroquinolones registered more modest aggregated reductions.

Figure 4. Changes in overall aggregated sales of antibiotics for food-producing animals

Changes in average overall sales, in mg per kg estimated biomass, for 25 EU/EEA countries, 2011 to 2020



Source: EMA (2021)

3 The term 'milligrams per kilogram of estimated biomass' is used as a synonym for 'milligrams per PCU' (PCU = population correction unit), the reporting unit for animal biomass equivalents developed by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) initiative.

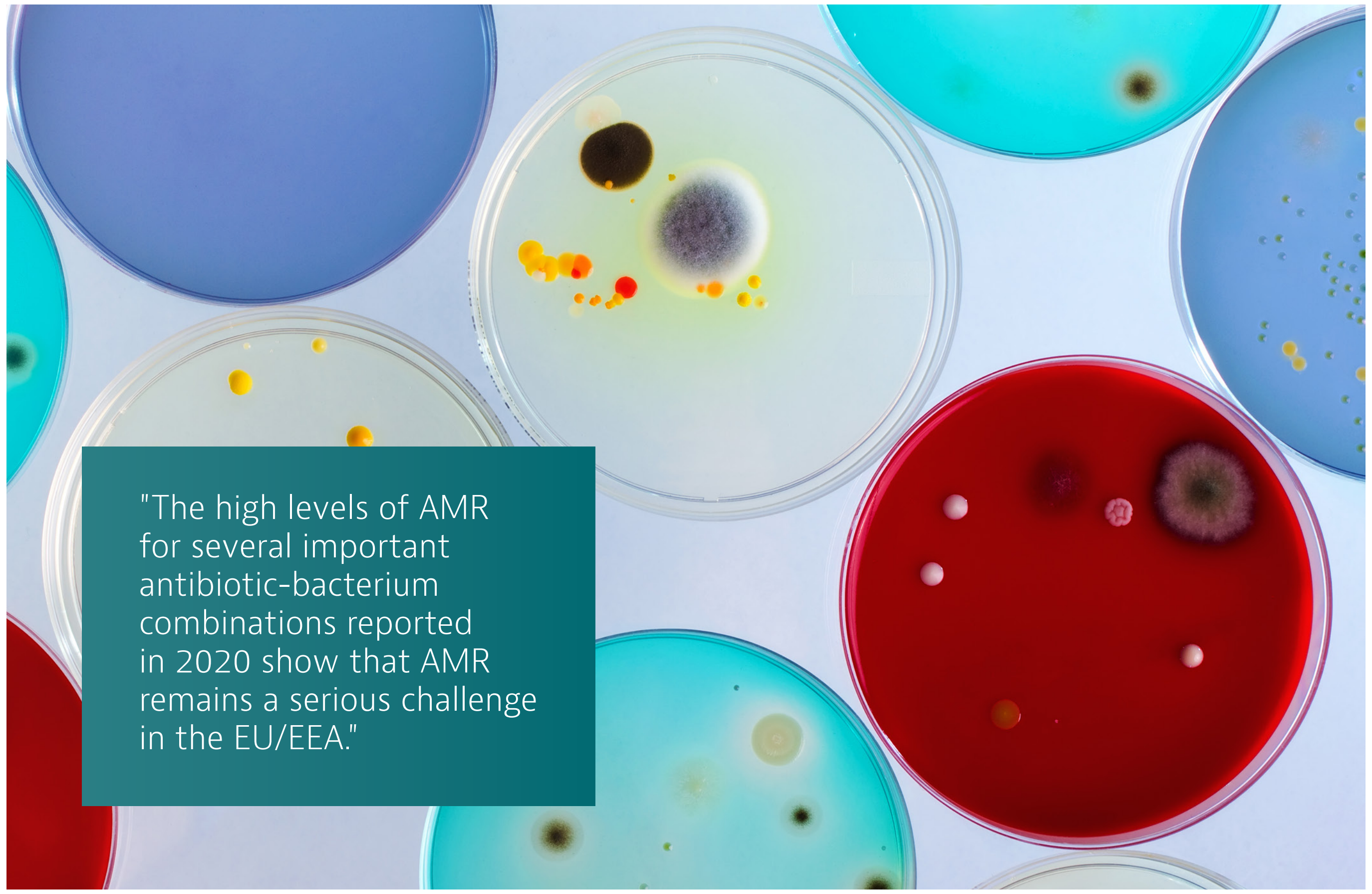
Antimicrobial resistance: a silent pandemic that is not subsiding

High levels of antimicrobial resistance in bacteria from human infections warrant a strong public health response

Between 2014 and 2020, AMR percentages in bacteria from human infections (mostly bloodstream infections) in the EU/EEA did not show large variations, with the exception of *Enterococcus faecium* for which the percentage of vancomycin resistance increased from 9% in 2014 to 17% in 2020 (Figure 5). The percentage of *Klebsiella pneumoniae* resistant to carbapenems continued to slowly increase from 8% in 2014 to 10% in 2020 while AMR percentages were slowly decreasing or generally remained stable for other bacteria.

The levels of resistance to critically important antibiotics in bacteria commonly responsible for healthcare-associated infections remains high or very high, e.g. resistance to third-generation cephalosporins in *K. pneumoniae*, and resistance to carbapenems in *Pseudomonas aeruginosa* and *Acinetobacter* species (2020 EU/EEA population-weighted mean resistance percentages of 34%, 18% and 38%, respectively).[4]

The AMR percentages in countries in the southern and eastern parts of the EU/EEA are particularly worrying. The large variability in AMR in bacteria from human infections across EU/EEA countries, e.g. resistance to vancomycin in *E. faecium* or to carbapenems in *K. pneumoniae* and *P. aeruginosa* and *Acinetobacter* spp., highlights opportunities for significant reduction in AMR through interventions to improve infection prevention and control, as well as antimicrobial stewardship practices.

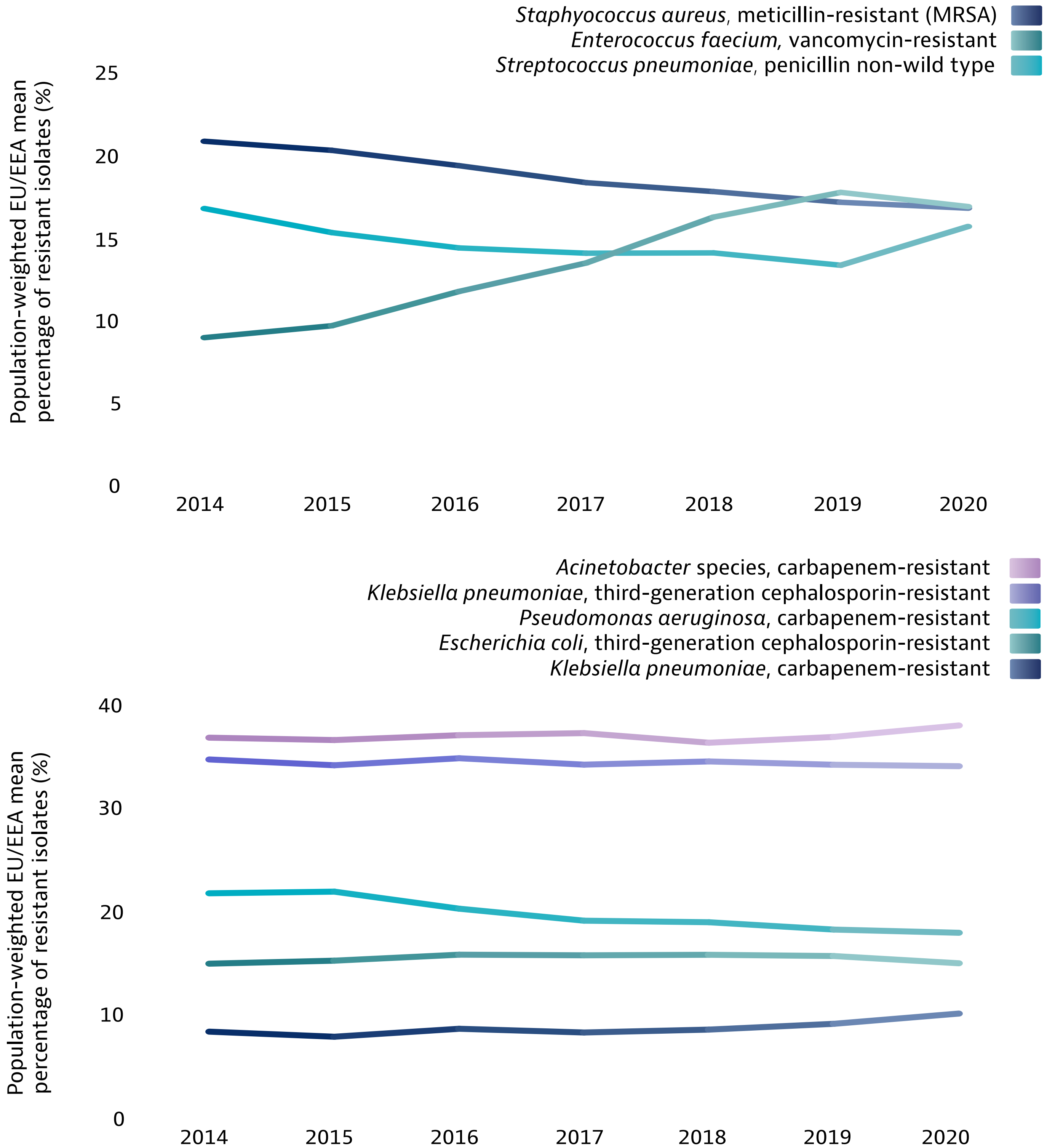


> "The high levels of AMR for several important antibiotic-bacterium combinations reported in 2020 show that AMR remains a serious challenge in the EU/EEA."

4 WHO/Europe, ECDC (2022).

Figure 5. Antimicrobial resistance remains high and only shows slow changes or remains stable in bacteria commonly responsible for healthcare-associated infections

Population-weighted mean percentage of resistant isolates among bacterial invasive isolates (mostly bloodstream infections), in 29 EU/EEA countries, 2014-2020; Top Panel – Gram-positive bacteria; Bottom Panel – Gram-negative bacteria

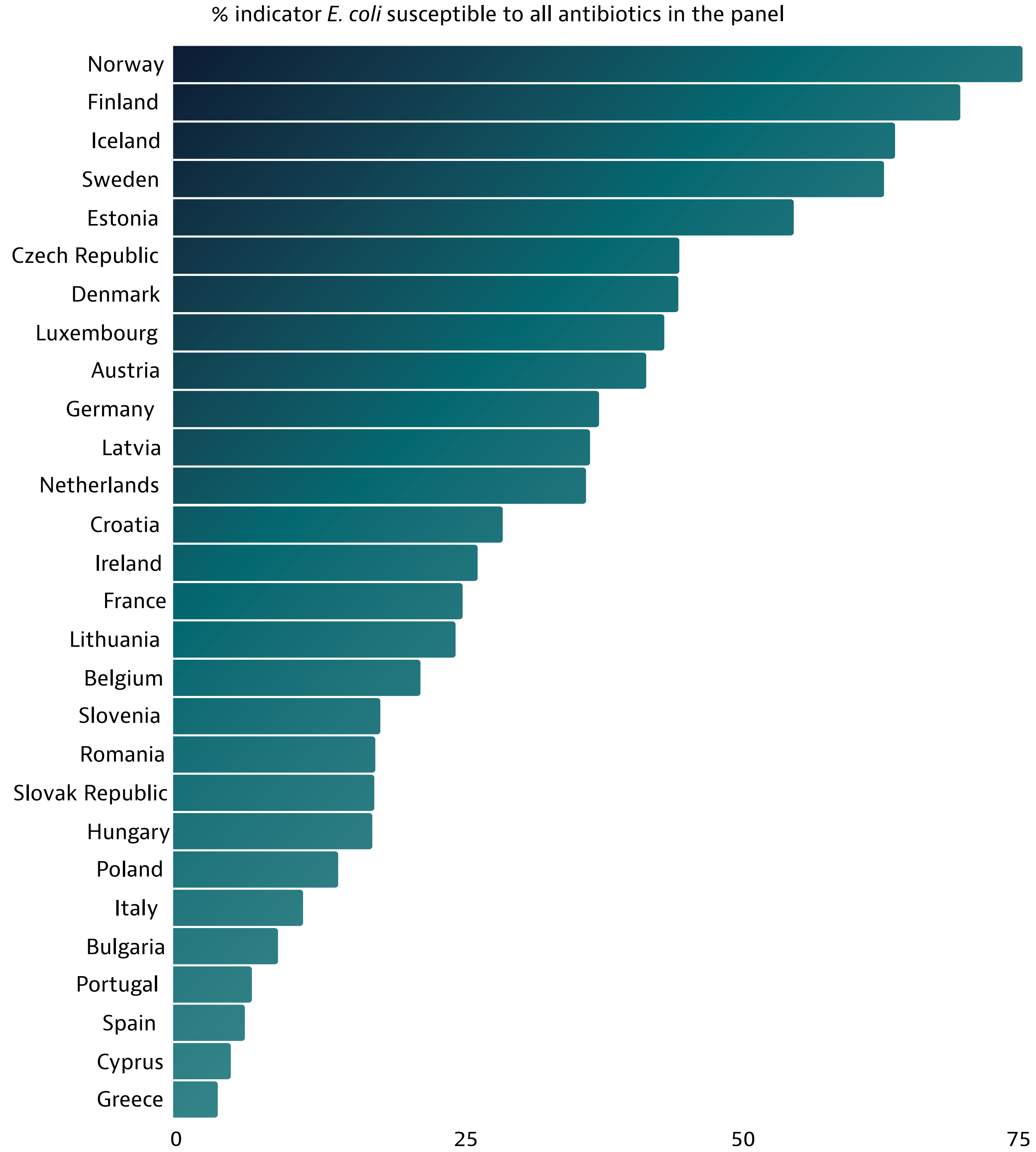


Note: Liechtenstein is not included. The term penicillin non-wild-type refers to S. pneumoniae isolates reported by local laboratories as 'susceptible, increased exposure' or resistant to penicillin.

Source: EARS-Net, ECDC (2021).

Figure 6. Increasing trends in complete susceptibility in *Escherichia coli* from food-producing animals

Complete susceptibility in indicator *E. coli* from food-producing animals, 2018



Note: Percentage of complete susceptible *E. coli*. Each value of the 'complete susceptibility indicator' for *E. coli* in food-producing animals represents a combination of two years (i.e. 2015 represents data combined from 2014 and 2015). A completely susceptible isolate is one defined as non-resistant to the antimicrobial substances that should be included in the AMR monitoring according to Commission Implementing Decision 2013/652/EU.

Source: ECDC, EFSA, EMA (2021).

Encouraging progress in tackling antimicrobial resistance in food-producing animals

While there are marked variations across reporting countries in outcome indicators for AMR in food-producing animals, recent trends have been encouraging.[5] Between 2014 and 2019, statistically significant increasing trends in the proportion of *Escherichia coli* isolates from food-producing animals susceptible to all tested antibiotics were observed in 12 countries (out of a total of 30 EU/EEA countries reporting data). The lowest percentages for this indicator were generally observed in countries in eastern and southern Europe, and the highest percentages in countries in the northern part (numbers for 2018 in Figure 6).

In addition, between 2015 and 2019 the prevalence of ESBL-/AmpC-producing *E. coli* decreased in 14 countries. Combined resistance to critically important antibiotics – fluoroquinolones and third-generation cephalosporins in *Salmonella*, and fluoroquinolones and macrolides in *Campylobacter* – remains low.

While these outcome indicators show some progress in reducing AMR in bacteria from food-producing animals in several EU/EEA countries in recent years, resistance to commonly used antibiotics remains high (>20% to 50%) or very high (>50% to 70%), and large differences across countries highlight once again the potential benefits of policy actions to tackle AMR.

Antimicrobial resistance can spread between animals, humans and the environment, fuelled in part by inappropriate antibiotic use in any of the interlinked areas

The evidence of links between antibiotic consumption and AMR in bacteria from food-producing animals and humans is mounting. With higher antibiotic consumption in humans, there is an increasing probability of detecting AMR in bacterial infections in humans (e.g. in *E. coli* bloodstream infections). It has also been shown that with higher antibiotic consumption in food-producing animals there is a consistently lower probability of detecting fully susceptible *E. coli* in these animals. For *E. coli*, both antibiotic consumption in food-producing animals and in humans are associated with AMR in isolates from food-producing animals and from humans, respectively.

5 EFSA and ECDC (2021)

The impact of the COVID-19 pandemic on antimicrobial resistance is still unclear

The COVID-19 pandemic, and the related public health interventions, probably also affected the reporting and results on bacterial invasive isolates (mostly bloodstream infections) and observed AMR percentages in the EU/EEA in 2020.

For all bacterial species under surveillance by the European Antimicrobial Resistance Surveillance Network (EARS-Net), except for *Streptococcus pneumoniae*, the number of reported bacterial invasive isolates (mostly bloodstream infections) increased at EU/EEA level in 2020 compared to 2019. This was the case for pathogens commonly responsible for healthcare-associated infections such as *Acinetobacter* spp. and *Enterococcus faecium*. Such increases, however, were not observed in all EU/EEA countries.

For *S. pneumoniae*, the number of reported invasive isolates decreased by 44%, from 15 608 in 2019 to 8 689 in 2020, with similar large decreases by 20% or more being reported in all but one EU/EEA country. This is a likely consequence of decreased health care activities in areas not directly linked to the COVID-19 response, as well as decreased circulation of pathogens in the community due to the implementation of non-pharmaceutical interventions as well as lower antibiotic consumption than in previous years in the community in the EU/EEA.

Such changes in the reported number of bacterial invasive isolates affect the resulting AMR percentages and make the observed changes in AMR percentages between 2019 and 2020 difficult to interpret. Robust surveillance systems will continue to be vital to monitor the situation, and to assess the consequences and inform public health decisions.

Antimicrobial resistance remains a serious challenge for everyone

The high levels of AMR for several important antibiotic-bacterium combinations reported in 2020 show that resistance remains a serious challenge in the EU/EEA. The European Centre for Disease Prevention and Control (ECDC) estimated that, each year, more than 670 000 infections occur in the EU/EEA due to bacteria resistant to antibiotics and that approximately 33 000 people die as a direct consequence of these infections. The OECD has estimated that the related cost to the health care systems of EU/EEA countries is around EUR 1.1 billion each year. At a global level, it has been estimated that 1.27 million deaths were attributable to bacterial AMR in 2019, with the highest burden in western sub-Saharan Africa.[6] Resistance to last-line antibiotics such as vancomycin and those in the carbapenems group remains a major issue. When these antibiotics are no longer effective, there are very limited treatment options that may not work in all situations, sometimes leading to fatal outcomes. Resistance to last-line antibiotics also compromises the effectiveness of life saving medical interventions such as intensive care, cancer treatment and organ transplantation.

Antimicrobial-resistant bacteria cannot be contained within borders, underlining the need for concerted international action.

6 Murray et al. (2022).

One Health policies to tackle antimicrobial resistance: Options for action

EU/EEA countries have made important strides in recent years in developing and implementing national action plans on antimicrobial resistance, but gaps remain

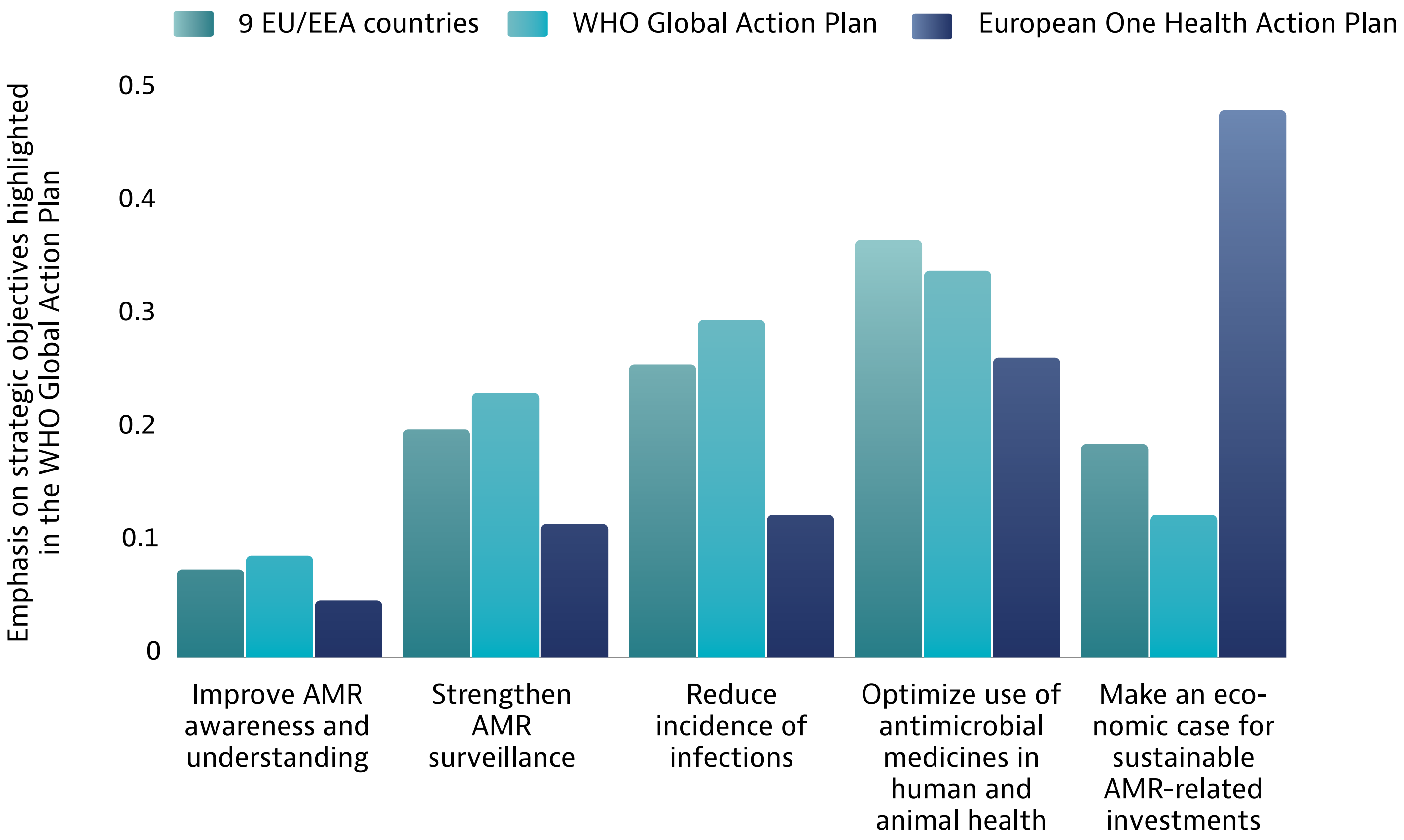
As of May 2021, 25 out of 29 EU/EEA countries had developed an action plan to tackle AMR. Despite this, only eight countries were implementing their action plans and tracking performance using a monitoring and evaluation framework. The food safety sector was actively involved in the development and implementation of national action plans in 26 out of 29 EU/EEA countries. Yet, other sectors were less involved. The food production and the environment sectors were actively contributing to the development and implementation of action plans in 21 countries. The plant health sector was actively involved only in 11 countries.

An OECD analysis of action plans from nine EU/EEA countries reveals that, consistent with the WHO Global Action Plan (WHO-GAP), national action plans emphasise policies to optimise antibiotic use in human and animal health the most, followed by policies to strengthen AMR surveillance, and IPC measures (Figure 7). A review of the content of national action plans is currently being conducted by the European Commission.

The 2017 EU action plan broadly aligns with the strategic objectives highlighted in the WHO-GAP, with an added emphasis on the economic case for investment including references to research and development, new economic models and incentives to promote more prudent use of antibiotics both in the EU and abroad. In addition to these strategic objectives, collaboration with international organisations and non-EU countries is explicitly highlighted as an integral element of the European approach to tackling AMR.

Figure 7. Comparing the content of 9 national action plans in EU/EEA countries, the European One Health Action Plan and the WHO Global Action Plan

Emphasis on each strategic objective highlighted in the WHO-GAP is measured as a function of the frequency of terms associated with that strategic objective relative to the frequency of terms linked to all of the strategic objectives.



Notes: (1) Data on the development and implementation of the 29 EU/EEA national action plans were extracted from the Tripartite AMR Country Self-Assessment Survey 2020-2021. (2) The OECD analysis compares the content of the EU One Action Plan, and national action plans from 9 EU/EEA countries against the WHO-GAP using natural language processing methods. Only EU/EEA countries that published action plans in English following the publication of the WHO-GAP in 2015 were chosen to be included in the analysis to assess the extent to which national action plans reflected the strategic objectives highlighted in the WHO-GAP. Countries included in the analysis: Denmark, Finland, France, Germany, Ireland, Malta, Norway, Slovak Republic, Sweden.

The COVID-19 pandemic demonstrates the need to strengthen investments in policies to curb antimicrobial resistance

Previous OECD analyses found that investing just EUR 1.5 per capita per year in a policy package to tackle AMR is effective and cost-saving, avoiding 27 000 deaths and saving EUR 1.4 billion each year in EU/EEA countries.[7] The policy package includes improving hygiene in health facilities, adopting antimicrobial stewardship programmes, increasing reliance on rapid diagnostic tests, delaying antibiotic prescriptions and raising public awareness.

Based on the OECD analyses and the WHO Global Action Plan, the most pressing priorities include:

- Monitoring and evaluating of the implementation of national action plans across the EU/EEA through systematic, cross-country-harmonised and multi-sectoral approaches.
- Supporting ongoing efforts to strengthen surveillance of AMR in bacteria from humans, animals and the environment, through enhanced laboratory network capacity, integration of new data sources and technologies (e.g. whole genome sequencing), and harmonsation of data collection methods across the EU/EEA (e.g. Commission Implementing Decision (EU) 2020/1729).
- Investing in effective cost-saving interventions, such as antimicrobial stewardship programmes that promote the use of forgotten older antibiotics and scale up electronic prescribing, IPC initiatives that involve education, training and feedback to healthcare workers, enhanced biosecurity and farm managment measures such as animal vaccination and improved breeding, housing and nutrition.

The European Commission is well-placed to support EU/EEA countries in tackling AMR

Plans for a new EU policy initiative to boost the implementation of the EU One Health Action Plan against AMR are a timely opportunity to address the gaps identified by the OECD and for:

- Promoting innovative economic models and incentives for new antibiotics, diagnostics and vaccines, and maximising the use of existing resources, including forgotten older antibiotics and antibiotics with low availability. A renewed emphasis on joint procurement and stockpiling will open new avenues to help ensure adequate and uninterrupted access to antibiotics. Harmonising and modernising product information for "older" antibacterials supports the appropriate use.
- Going beyond acute care settings and the community in actions to tackle AMR, for instance including also LTCFs, where prevalence of antibiotic use among LTCF residents was 5% on average across participating EU/EEA countries in 2016.
- Establishing a system to share and promote the implementation of best practices to tackle AMR across all relevant sectors, building on the success of this model in tackling chronic diseases. Best practices identified and evaluated by EU/EEA countries are adapted and implemented in other countries with the support of the European Commission and partner intergovernmental organisations.
- Renewing the focus on international co-operation, thus promoting the use of EU standards to tackle AMR, limiting disruptions in antimicrobial stewardship in low- and middle-income countries as many ountries re allocated resources to tackling the COVID-19 pandemic, and fostering multi-sectoral collaborations with non-EU/EEA partners.
- Helping EU/EEA countries achieve the antibiotic consumption reduction targets set out under the European Green deal and to be implemented under the Common Agricultural Policy, calling for a reduction in sales of antimicrobials in food-producing animals and in aquaculture by 50% by 2030 (compared to the 2018 values).

A One Health approach to tackling the threat of AMR from antibiotic use in food-producing animals

Successful strategies to reduce antibiotic use in food-producing animals follow an integrated, multifaceted approach which takes into account the local livestock production system and involves all relevant stakeholders – from governments to farmers. A detailed analysis of options was published by EMA and EFSA in 2017 (RONAFA opinion). The newly applicable EU Regulation 2019/6 on veterinary medicinal products provides a range of concrete measures to limit the use of antimicrobials in animals in a One Health perspective. These measures will be instrumental in achieving the EU Farm to Fork Strategy objective of reducing overall EU sales of antimicrobials for farmed animals and in aquaculture by 50% by 2030. The measures include:

- A mandatory data collection on the volume of sales of veterinary antimicrobials and on the use of antimicrobials by animal species – moving beyond sales data for antibiotics.
- An extension of the ban on the use of antibiotics for growth promotion and yield increase to the use of antimicrobial medicinal products.
- A ban on the preventive use of antibiotics in groups of animals, and restrictions on the use of antimicrobials in groups of animals ahead of an expected disease outbreak (metaphylaxis).
- A ban on the use in animals of antimicrobials designated in the EU as reserved for the treatment of certain conditions in humans.

Crucially, bans on use of antimicrobials for growth promotion and on use of antimicrobials designated as reserved for human use, also apply to producers outside the EU seeking to export to the EU food-producing animals or food produced from animals to the EU.

There are also alternatives to antimicrobials that have been shown to improve animal health and thereby reduce infection and disease occurrence and thus the need to use antimicrobials, including vaccines, probiotics, prebiotics, bacteriophages and organic acids. However, reducing the use of antimicrobials and finding alternatives is not enough.

7 OECD (2018).

Spotlight on antimicrobial resistance in long-term care facilities: A unique challenge

Antimicrobial resistance is an especially significant challenge in the context of long-term care facilities…

Long-term care facilities (LTCFs) provide care for extended periods to older people who frequently require antibiotics to treat and prevent infections, a leading cause of morbidity and mortality among older residents of LTCFs.

OECD analyses suggest that up to 75% of antibiotic prescriptions in LTCFs are inappropriate regarding the need for therapy, and the duration and choice of therapy. Moreover, between 54% and 96% of antibiotic prescriptions in LTCFs are given without laboratory or diagnostic testing.

Inappropriate use of antibiotics is associated with high rates of multidrug-resistant organisms that are identified in LTCFs, and may exacerbate the threat of AMR, both in LTCFs and in the community.

…Yet, very few countries have policies that specifically address antimicrobial resistance in long-term care facilities

Out of 26 EU/EEA countries that responded to a recent OECD survey, only eleven reported having national action plans on AMR that specifically mention LTCFs, and 16 countries reported having legislation, policies and/or programmes aimed at addressing antibacterial resistance in LTCFs (Figure 8). Only six countries reported having a process for auditing the quality of care provided in LTCFs which includes indicators related to antibacterial resistance antimicrobial stewardship and IPC).

Only eight EU/EEA countries reported having guidelines, protocols or requirements for the adoption of written guidelines for appropriate antibiotic use in LTCFs at either national, subnational or institutional level, and only two countries reported having those guidelines for residents with cognitive impairments or advanced dementia.

A majority, 17 EU/EEA countries, reported having guidelines, protocols or requirements for the adoption of IPC programmes or protocols in LTCFs at either national, subnational or institutional level, but only eight countries had guidelines, protocols or requirements for the adoption of a budget dedicated to IPC in LTCFs.

Despite the key role that surveillance plays in determining AMR rates, guiding the development of lists of antibiotics that should be preserved, and benchmarking, auditing and goal setting, few EU/EEA countries reported having guidelines, protocols or requirements for the adoption of surveillance of antibiotic consumption (seven countries) and AMR (six countries) in LTCFs.

Policy actions to tackle antimicrobial resistance should specifically target long-term care facilities

Countries recognise that addressing AMR and inappropriate antibiotic use in LTCFs should receive a special focus in future national action plans in their efforts to tackle AMR, with 20 EU/EEA countries reporting they plan to include references to long-term care in their next national action plan.

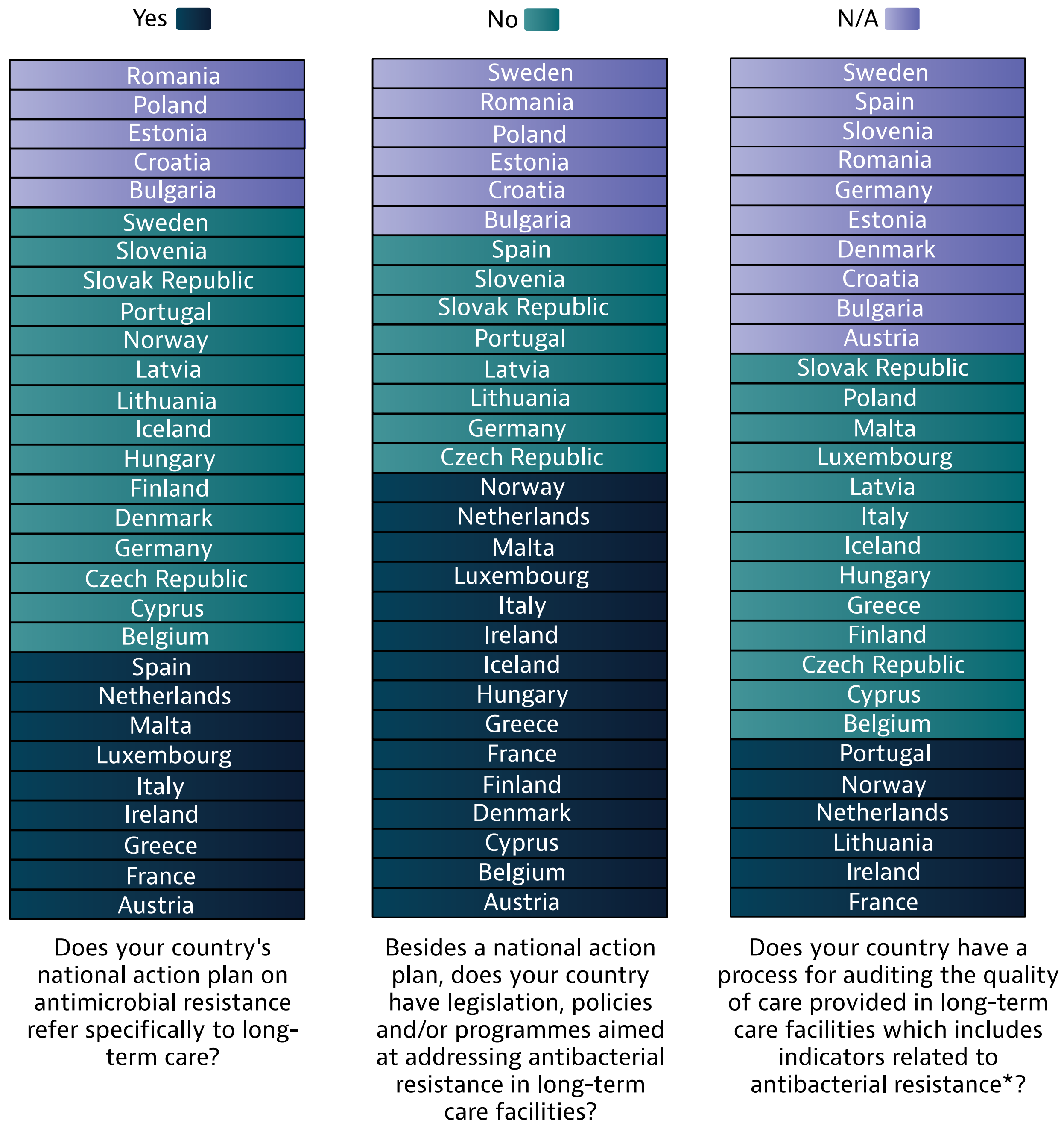
The European Commission can support EU/EEA countries in their efforts to tackle AMR and inappropriate antibiotic use in LTCFs, by specifically making reference to LTFCs in its new policy initiative to strengthen the implementation of the EU One Health Action Plan. Priorities include:

- Highlighting the need for routine surveillance systems that can collect and report data on antibiotic use and AMR in LTCFs. Routine surveillance is needed not only to design policies that are fit for LTCFs, but also to monitor and evaluate their impact.
- Promoting the design, implementation and effective use of antimicrobial stewardship programmes that are fit for LTCFs, including more integration with general practitioners, better feedback on antibiotic use and AMR profiles, more regular training and a dedicated budget.
- Incentivising adoption and compliance with IPC programmes that are tailored to LTCFs, emphasising the need for dedicated budgets, IPC committees, and procedures for surveillance and auditing of IPC policies and procedures in LTCFs.

Impact of COVID-19 on national action plans to tackle AMR

Eighteen EU/EEA countries reported that the COVID-19 pandemic had led to delays in developing, approving or operationalising the national action plan on AMR, and four countries highlighted reporting delays in surveillance of antibiotic consumption in LTCFs. On the other hand, 13 countries reported that the pandemic led to more interest and emphasis on IPC practices in LTCFs (e.g. hand hygiene), and six countries reported increased uptake of influenza vaccinations in LTCFs.

Figure 8. Few countries have policies that specifically address antimicrobial resistance in long-term care facilities



Note: *Such as indicators related to antimicrobial stewardship and/or infection prevention and control in long-term care facilities.

Source: OECD analysis of Survey on Antibacterial Resistance in Long-Term Care Facilities (2022).

The global threat of AMR can only be tackled by increased coordination in the EU/EEA, and worldwide, to develop new treatments and tests while using the existing therapies wisely and responsibly, both in the treatment of humans and animals

International co-operation needed on development of new antibiotics and on ensuring effective treatments

Converging international regulatory requirements for approval of new antibiotics

The European Medicines Agency (EMA) develops and maintains a comprehensive set of guidance documents[8] for developers of antimicrobial medicines. The EMA has teamed up with partner agencies from Japan and the United States to identify regulatory approaches for the evaluation of new antibacterial agents to be approved for human use. This work started in 2016 and, to date, the following achievements have been reached:

- The agencies aligned their data requirements for certain aspects of the clinical development of new antibiotics in order to stimulate the development of new treatments.
- They agreed to align how clinical trials should be designed to study the effects of new antibiotics in certain indications, such as uncomplicated gonorrhoea or uncomplicated urinary tract infections.
- They committed to working together to explore how to better streamline paediatric development of new antibacterial agents.

The Innovation Task Force (ITF), a platform for early dialogue with EMA, is available to developers of medicines for the treatment or prevention of life threatening infections to help strengthen the drug development pipeline for these products. The platform facilitates greater interaction between developers and the EU regulator, streamlining and optimising drug developments and, as such, fostering their accelerated availability to the patients in need.

Enabling the development and authorisation of alternatives to antibiotics as veterinary medicinal products[9] and taking measures to ensure the on-going availability of authorised veterinary antibiotics, are also key priorities.

Antimicrobial resistance is a global challenge needing international collaboration

EU/EEA countries, as well as the European Commission, are actively involved in many global initiatives to co-ordinate policy actions to tackle AMR, whether these are on promoting prudent use of antibiotics, preventing the spread of infections or promoting research and development (R&D) for new treatments and new medical technology. The list of initiatives in which the EU or EU/EEA countries participate in is too long to be summarised in a few lines.

Among some notable examples, the EU participates in actions carried forward by the G7 and the G20 such as the global AMR R&D Hub, which was launched following a call from G20 Leaders. Similarly, the EU is also actively involved in work carried out by the Transatlantic Task Force on Antimicrobial Resistance (TATFAR). Finally, the EU participates in other global activities such as those co-ordinated by the Tripartite and United Nations Environment Programme (UNEP) Joint Secretariat on AMR, the Codex Alimentarius Commission and other United Nations fora.

8 https://www.ema.europa.eu/en/human-regulatory/research-development/scientific-guidelines/clinical-efficacy-safety/clinical-efficacy-safety-anti-infectives-systemic-use

9 alternatives to antimicrobials as veterinary medicinal products. https://www.ema.europa.eu/en/promoting-authorisation-alternatives-antimicrobial-veterinary-medicinal-products-eu

Planned EU actions and legislation on the use of antibiotics

Under Regulation (EU) 2019/6 on veterinary medicines, the European Commission is to adopt an implementing act establishing a list of antimicrobials that will be reserved for the treatment of certain infections in humans, in order to help preserve their effectiveness, and thus that will be forbidden for use in veterinary medicine. The European Commission also intends to adopt a complementary implementing act establishing a list of antimicrobials which use outside the terms of their marketing authorisation will be banned or restricted, in order to help preserve public health and animal health from the risk of AMR.

Ensuring available effective treatments for humans and animals while limiting AMR

The Antimicrobial Advice Ad Hoc Expert Group (AMEG) of EMA has categorised antibiotics based on the potential consequences to public health of increased AMR when used in animals, and the need for their use in veterinary medicine (Figure 9). The categorisation is intended as a tool to support decision-making by veterinarians on which antibiotic to use, and how to administer it. For antibiotics in all categories, unnecessary use, overly long treatment periods, and under-dosing should be avoided, and group treatment should be restricted to situations where individual treatment is not feasible.

The EMA also aims to harmonise and modernise the product information for longstanding antibiotics to support appropriate use.

Figure 9. Categories of antimicrobials for use in animals based on the risk to public health

(Category A) Avoid

Antibiotics in this category are not authorized as veterinary medicine in the EU. They should not be used in food-producing animals, but may be given to companion animals under exceptional circumstances.

(Category B) Restrict

Antibiotics in this category are critically important in human medicine and use in animals should be restricted to mitigate the risk to public health. They should be considered only when there are no antibiotics in Categories C or D that could be clinically effective. Use should be based on antimicrobial susceptibility testing, whenever possible.

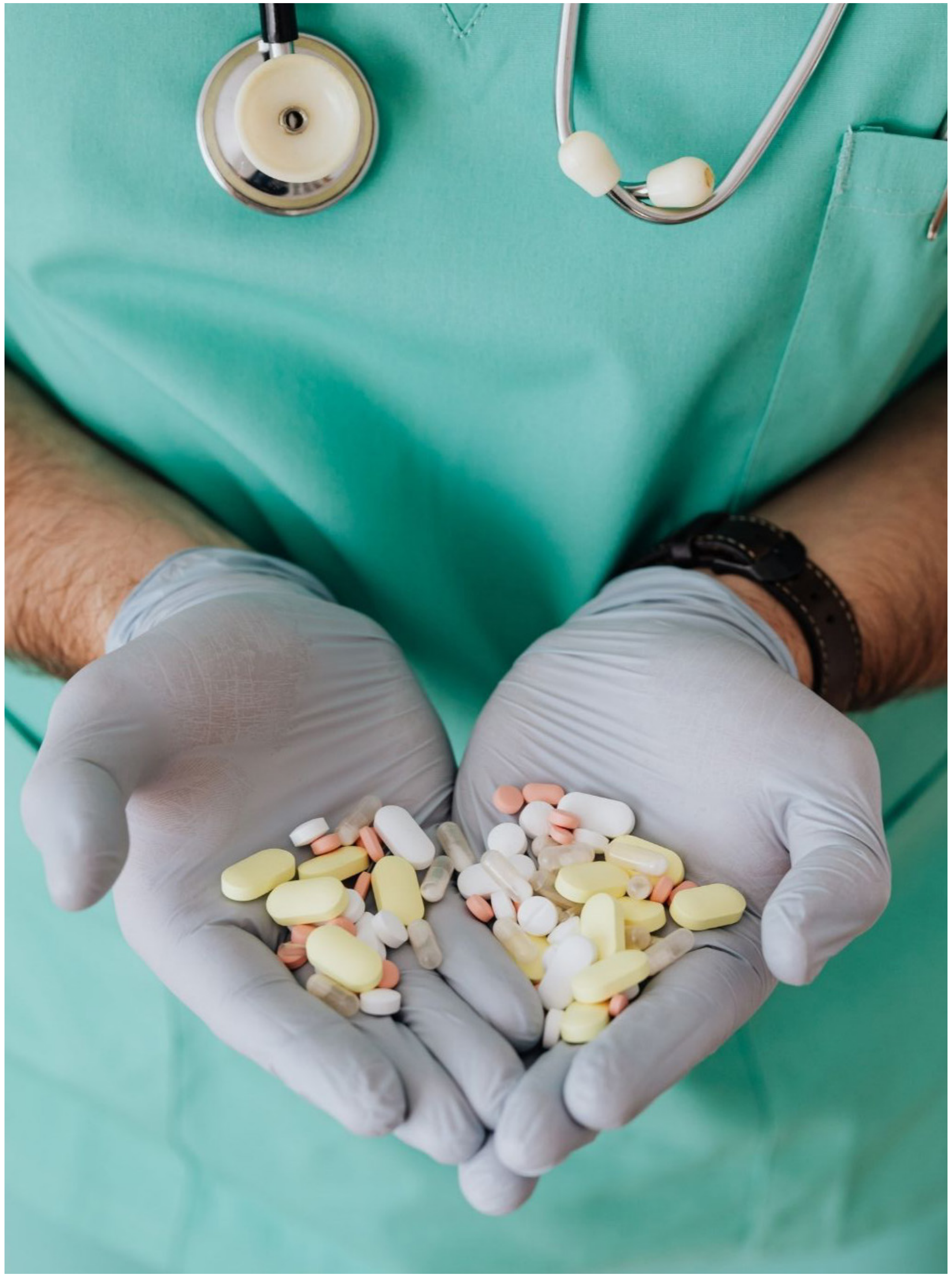
(Category C) Caution

For antibiotics in this category, there are alternatives in human medicines. They should be considered only when there are no antibiotics in Category D that could be clinically effective.

(Category D) Prudence

Antibiotics in this category should be used as first line treatments, whenever possible. As always, they should be used prudently, only when medically needed.

Source: AMEG, EMA.



Disclaimers

The present publication presents time series which end before and time series which end after the United Kingdom's withdrawal from the European Union on 1 February 2020. Whenever possible, the "European Union" aggregate presented here excludes the UK. When this is not possible, this is clearly indicated in the text (e.g. in Figure 1).

Note by Turkey: The information in this document with reference to "Cyprus" relates to the southern part of the Island. There is no single authority representing both Turkish and Greek Cypriot people on the Island. Turkey recognises the Turkish Republic of Northern Cyprus (TRNC). Until a lasting and equitable solution is found within the context of the United Nations, Turkey shall preserve its position concerning the "Cyprus issue".

Note by all the European Union Member States of the OECD and the European Union: The Republic of Cyprus is recognised by all members of the United Nations with the exception of Turkey. The information in this document relates to the area under the effective control of the Government of the Republic of Cyprus.

Image credits

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efsa European Food Safety Authority
EMA EUROPEAN MEDICINES AGENCY

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