Antimicrobial Resistance

Tackling the Burden in the European Union

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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

Briefing note
for EU/EEA countries

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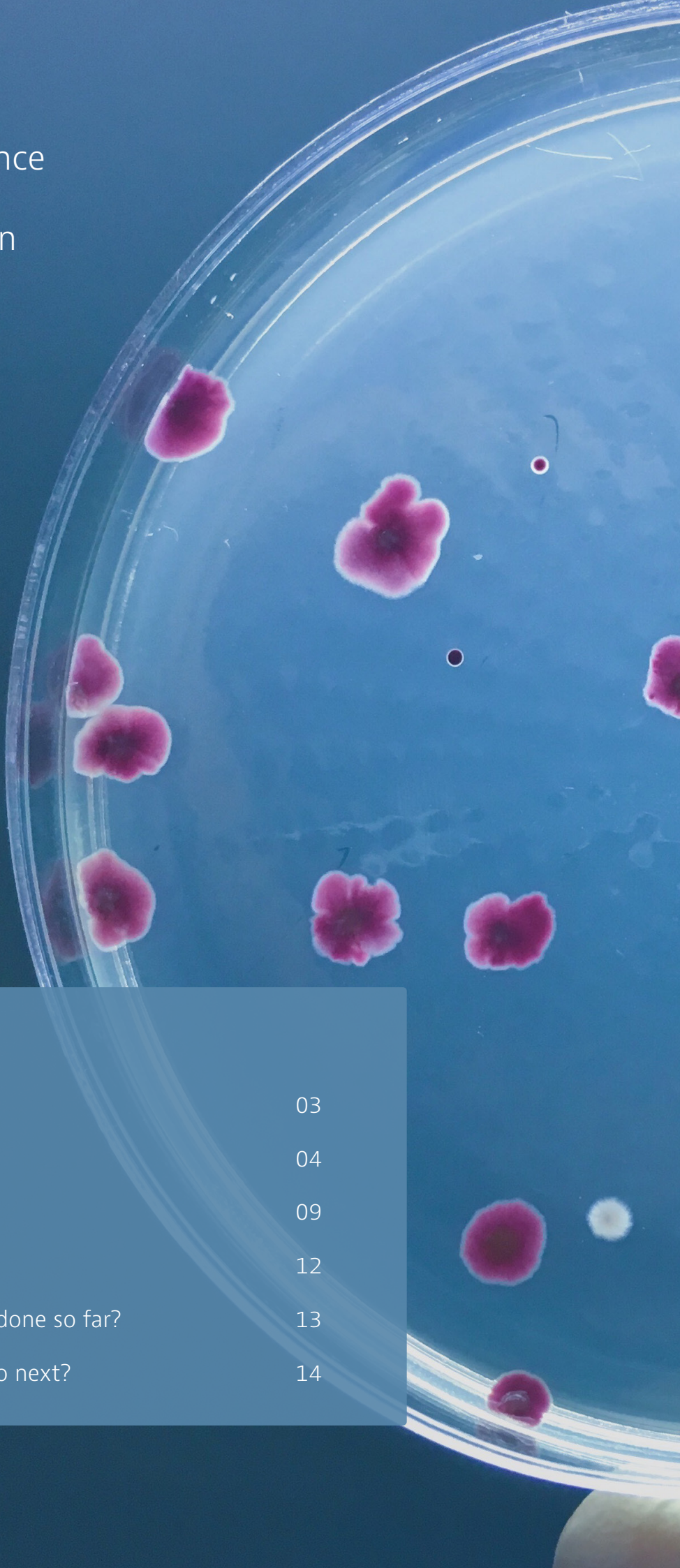
Antimicrobial Resistance Tackling the Burden in the European Union



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Key messages

AMR is a major public health concern…

Antimicrobial resistance (AMR) – the ability of microorganisms to resist antimicrobials – is the leading infectious health issue across EU/EEA countries and one of the major causes of concern in public health.

Misuse of antibiotics and insufficient infection prevention and control in hospitals are main drivers underpinning the development of AMR. The high variability in the frequency and pattern of antibiotic use across EU/EEA countries suggests that there are margins for improvement of prescribing practices. Conversely, enhanced hygiene and a higher level of resources for hospital infection prevention and control are both associated with lower AMR rates.

If no effective action is put in place, AMR to second-line antibiotics will be 72% higher in 2030 compared to 2005 in the EU/EEA. In the same period, AMR to last-line treatments will more than double.

Each year, AMR is responsible for about 33 000 deaths and costs about 1.1 billion Euros to the health care systems of EU/EEA countries.

Only a minority of EU/EEA countries have identified specific funding sources to implement national action plans to tackle AMR and have defined a monitoring and evaluation process. Investments in public health actions to tackle AMR are still insufficient.

… but it can be tackled at low cost

Promoting better hygiene in health care services, ending the over-prescription of antibiotics, rapid testing for patients to determine whether they have bacterial or viral infections, delayed antibiotic prescriptions and mass media campaigns, are all effective and cost-effective interventions to tackle AMR.

Investing in these policies would save thousands of lives and money in the long run. Many interventions to promote prudent use of antibiotics and enhance hygiene in hospitals only cost 0.15 to 1.3 Euros per capita per year in many EU/EEA countries.

Investing 1.5 Euros per capita per year in a comprehensive package of mixed public health interventions would avoid about 27 000 deaths per year in EU/EEA countries.

In addition to saving lives, such a public health package could pay for itself within just one year and end up saving about 1.4 billion Euros[1] per year in EU/EEA countries.

[1] Including savings resulting from hygiene-enhancing interventions in health care sector, associated with a reduction in infections from bacteria susceptible to antimicrobials.

Use of antibiotics

There is a high variability of antibiotic consumption across EU/EEA countries

In the community (i.e. outside of hospitals), the EU/EEA population-weighted mean consumption of antibiotics in 2017 was 18.9 defined daily doses (DDDs) per 1 000 inhabitants per day, ranging from 8.9 in the Netherlands to 32.1 in Greece (figure 1). The EU/EEA average consumption of broad-spectrum antibiotics was 10.1 DDDs per 1 000 inhabitants per day, ranging from 0.9 in Norway to 23.3 in Greece.

In acute care hospitals, the EU/EEA mean prevalence of patients receiving at least one antibiotic on a given day in 2016-2017 was 30.7% and varied from 14.9% in Hungary to 55.1% in Greece (figure 2). Of these, the EU/EEA mean proportion of patients receiving at least one broad-spectrum antibiotic on a given day was 45.9%, ranging from less than 30% in Lithuania, Iceland and Estonia to 74.7% in Bulgaria.

Along the clinical treatment guidelines, as much as possible, the use of narrow-spectrum antibiotics (i.e. those effective against only a specific group of bacteria) should be preferred in medical practice over the use of broad-spectrum antibiotics, as the latter is more likely to promote the development of AMR in a broader group of bacteria.

Figure 1. Consumption of antibiotics* in the community, EU/EEA†, 2017

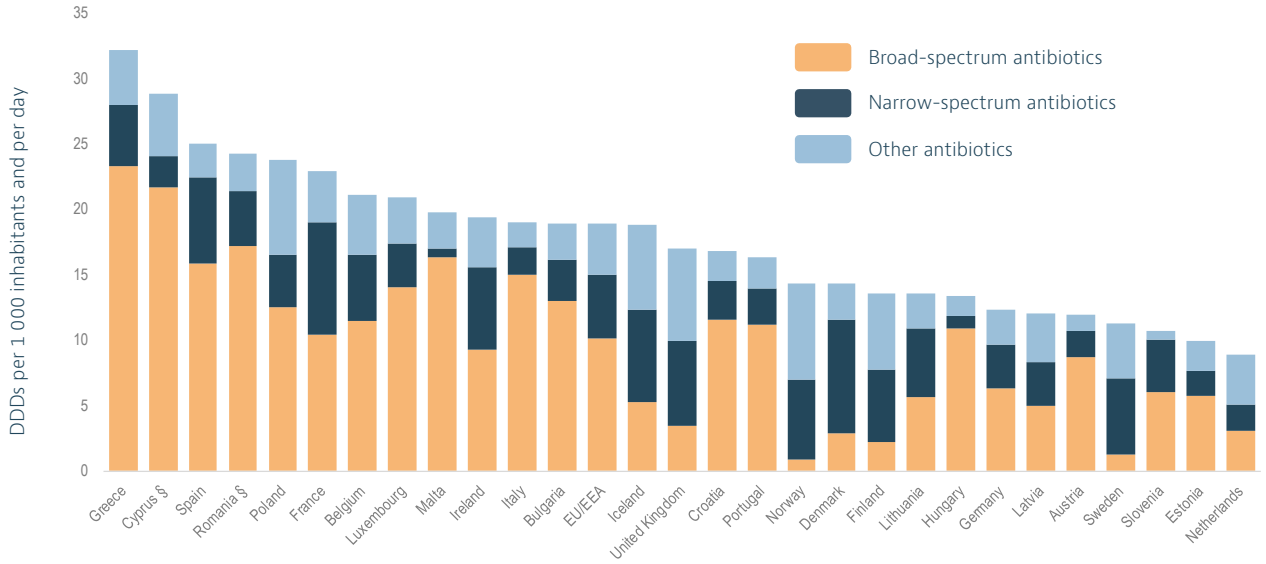


Figure 2. Prevalence of use of antibiotics* in acute care hospitals, EU/EEA†, 2016-2017

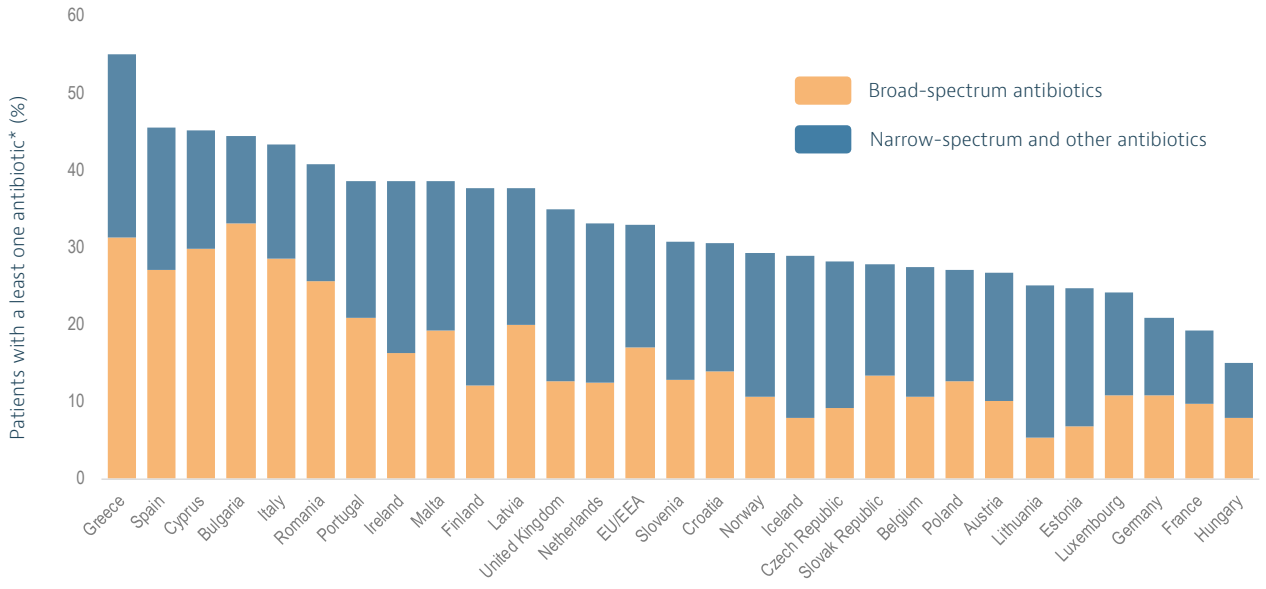


Figure 1.

Note: *Antibiotics: Antibacterials for systemic use (ATC group J01) // † 28 EU/EEA countries. The Czech Republic and the Slovak Republic did not report data for 2017 to ECDC. // § Cyprus and Romania provided total care data, i.e. including the hospital sector. On average, 90% of total care data correspond to consumption in the community. // DDD: defined daily dose. For calculating the number of DDDs, the 2019 ATC/DDD index was applied (https://www.whocc.no/) // EU/EEA: EU/EEA population-weighted mean consumption. // Broad-spectrum antibiotics: broad-spectrum penicillins, broad-spectrum cephalosporins, broad-spectrum macrolides (except erythromycin) and fluoroquinolones; narrow-spectrum antibiotics: narrow-spectrum penicillins, narrow-spectrum cephalosporins and erythromycin (https://doi.org/10.2903/j.efsa.2017.5017). **Source:** ECDC (2019). European Surveillance of Antimicrobial Consumption Network (ESAC-Net), data for 2017. https://ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database.

Figure 2.

Note: *Antibiotics: Antibacterials for systemic use (ATC group J01) // † 28 EU/EEA countries. Denmark and Sweden did not report data to ECDC. // Broad-spectrum antibiotics: defined as in the ECDC point prevalence survey as patients receiving at least one broad-spectrum antibiotic (as defined in the ECDC point prevalence survey in European acute care hospitals, i.e. piperacillin and beta-lactamase inhibitor, third- and fourth-generation cephalosporins, monobactams, carbapenems, fluoroquinolones, glycopeptides, polymyxins, daptomycin and oxazolidinones (linezolid and tedizolid)). **Source:** ECDC (2019). ECDC point prevalence survey of health care-associated infections and antimicrobial use in European acute care hospitals, 2016-2017. Plachouras D, et al. Euro Surveill. 2018 Nov; 23(46) (https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.23.46.1800393).

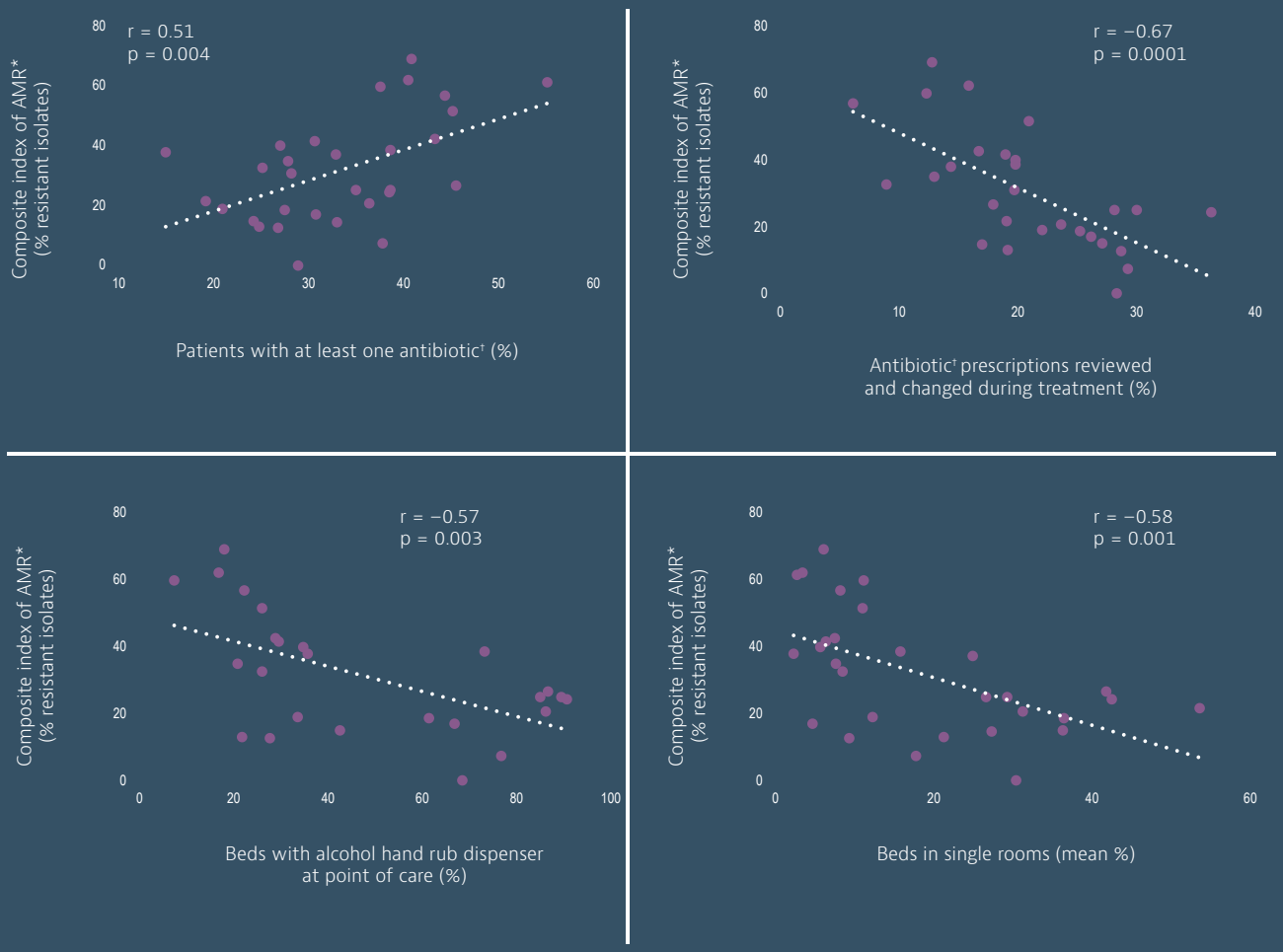
AMR is related to antibiotic use, antibiotic stewardship as well as infection prevention and control practices

A recent point prevalence survey in European acute care hospitals confirmed that antibiotic use is positively associated with AMR (figure 3). Conversely, antibiotic stewardship activities, such as reviewing and changing prescriptions when necessary, are negatively associated with AMR.

In addition, having more resources for hospital hygiene (infection prevention and control) is negatively associated with AMR.

For example, the percentage of hospital beds with alcohol hand rub dispensers at point of care, the percentage of beds in single rooms (for isolating patients with bacteria with AMR), and the percentage of hospitals with at least 0.4 full time-equivalent infection prevention and control nurse for 250 beds (r= −0.35, p=0.04, data not shown) are all negatively associated with AMR.

Figure 3. Associations between a composite index of AMR* and various determinants of AMR in European acute care hospitals (each dot represents a country)



Note: *Composite index of AMR: percentage of isolates resistant to first-level antimicrobial resistance markers in healt care-associated infections, i.e. *S. aureus* resistant to meticillin (MRSA), *E. faecium* and *E. faecalis* resistant to vancomycin, Enterobacteriaceae resistant to third-generation cephalosporins, and *P. aeruginosa* and *A. baumannii* resistant to carbapenems.

† Antibacterials for systemic use (ATC J01).

r, Spearman's correlation coefficient; p, p-value.

Source: ECDC (2019). ECDC point prevalence survey of health care-associated infections and antimicrobial use in European acute care hospitals, 2016-2017 (preliminary results).

AMR will increase if no effective action is put in place

Rising proportions of AMR will become a growing concern unless governments embrace a more robust response to the threat.

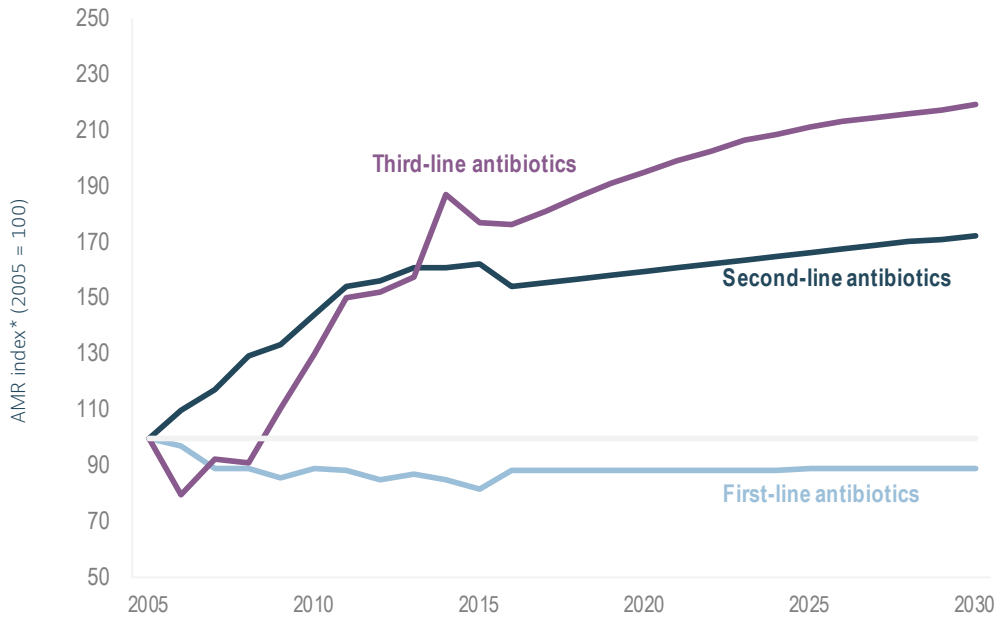
AMR proportions have been increasing across the EU/EEA between 2005 and 2015 and, currently, close to one in five infections in the EU/EEA is due to antibiotic-resistant bacteria. In some countries, like Romania and Greece, about 40% of infections are due to antibiotic-resistant bacteria.

OECD projections suggest that AMR will keep growing in the EU/EEA, from about 17% of infections with AMR in 2015 to 19% in 2030. While average AMR growth seems to be slowing down, there are serious causes for concern.

Across the EU/EEA, resistance to second-line and third-line antibiotics, which represent our back-up line of defence to treat patients with bacterial infections, is expected to grow respectively by 72% and more than double by 2030, compared to 2005 (figure 4).

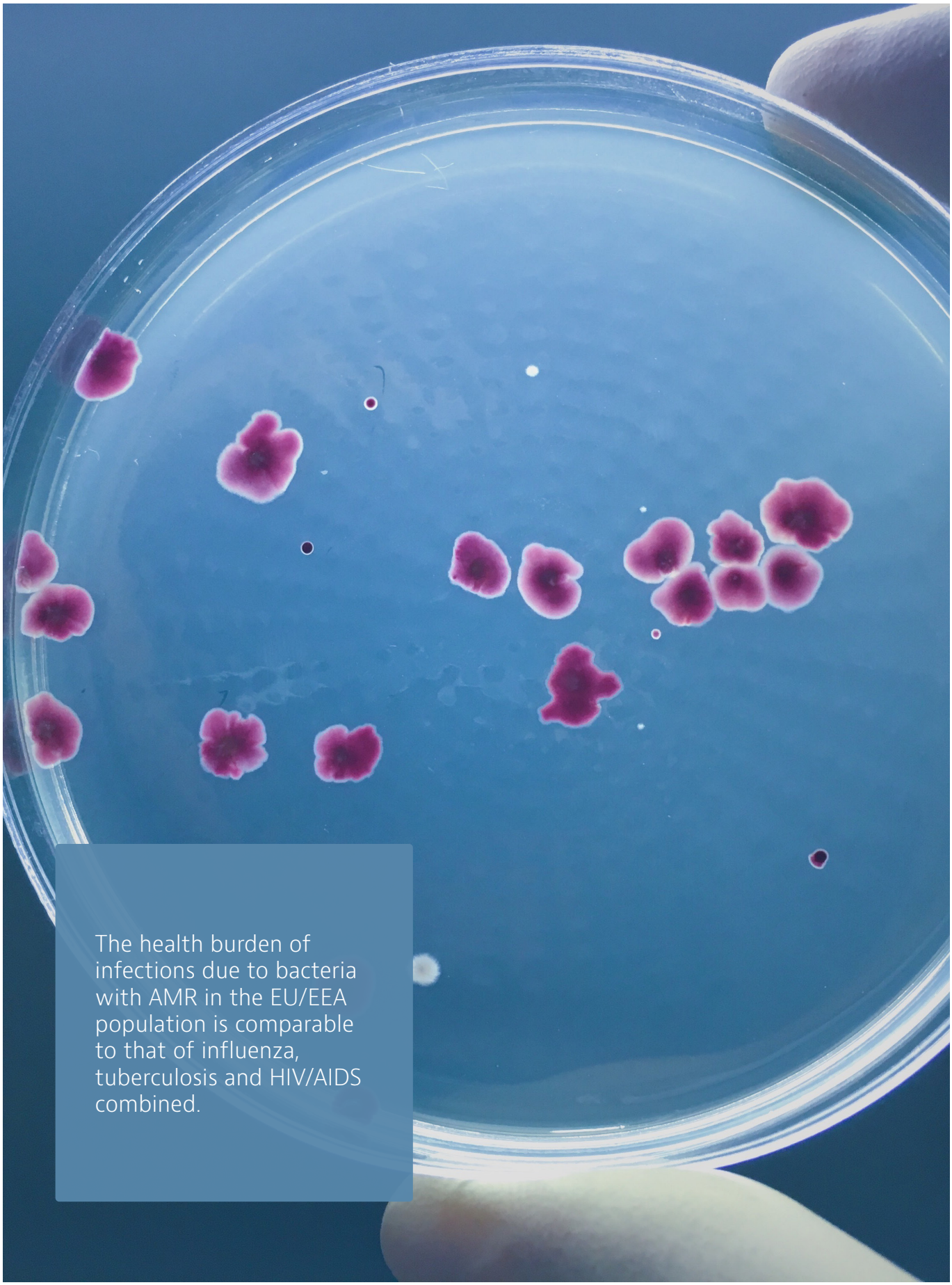
AMR proportions for these lines of antibiotics are forecast to grow more steeply in EU/EEA countries than in OECD and G20 countries. The growing AMR to the second-line and third-line antibiotics is an extremely worrying scenario, as it means that we – de facto – are exhausting our antibiotics armoury.

Figure 4. AMR to second-line and third-line antibiotics will grow the most in EU/EEA countries



Note: *Data were normalised to average antimicrobial resistance in 2005 (equal to 100) for each treatment line (e.g. a value of 172 for resistance to second-line treatments in 2015 in EU/EEA countries means that resistance to second-line treatments is 72% higher than it was in 2005 in EU/EEA countries). In the OECD report, AMR to first-line treatments was defined as the average of the percentages of penicillin-resistant *S. pneumoniae* and MRSA. AMR to second-line treatments was defined as the average of the percentages of *E. coli* and *K. pneumoniae* isolates resistant to third-generation cephalosporins and of *E. coli* isolates resistant to fluoroquinolones. AMR to third-line treatments was defined as the percentage of *K. pneumoniae* isolates resistant to carbapenems.

Source: OECD. Stemming the Superbug Tide: Just a Few Dollars More; 2018. Available at: oe.cd/amr-2018.



The health burden of infections due to bacteria with AMR in the EU/EEA population is comparable to that of influenza, tuberculosis and HIV/AIDS combined.

Impact on health

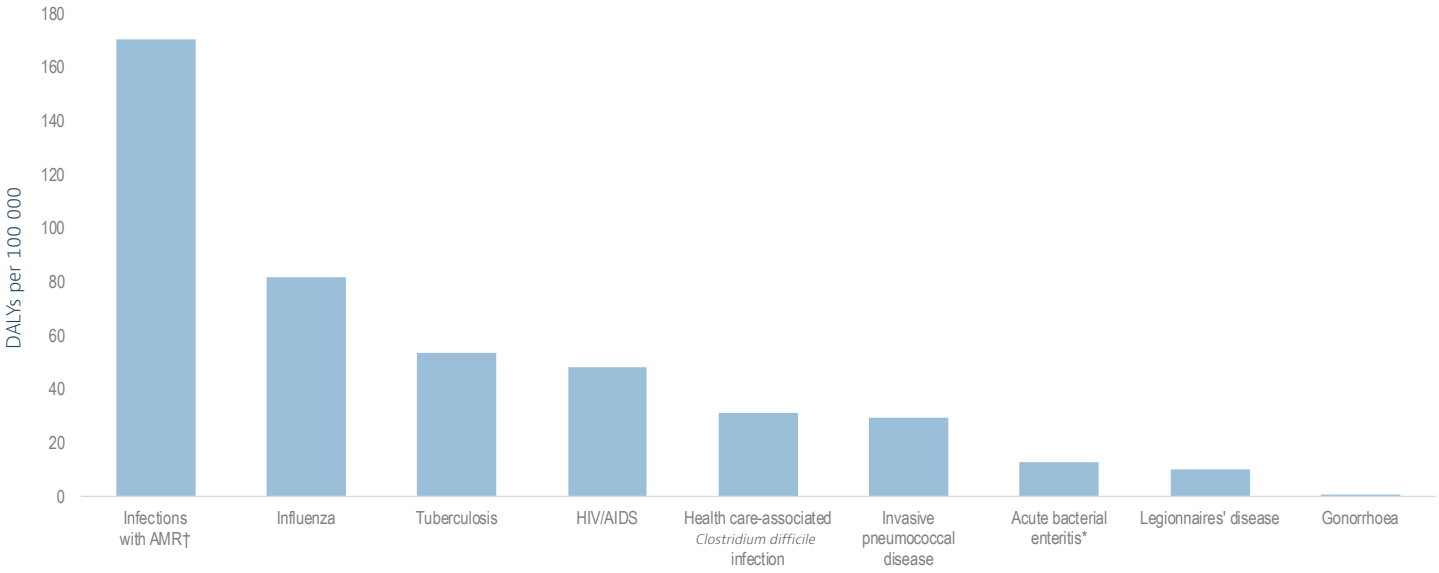
AMR has a significant detrimental effect on the health of EU/EEA citizens

The health burden of infections due to bacteria with AMR in the EU/EEA population is comparable to that of influenza, tuberculosis and HIV/AIDS combined (figure 5), and nearly 40% of the health burden of AMR is caused by infections with bacteria resistant to last-line antibiotics such as carbapenems and colistin (figure 5). This is an increase from 2007 and is worrying because these antibiotics are the last treatment option available. When last-line antibiotics are no longer effective, it is extremely difficult or, in many cases, impossible to treat infected patients.

75% of the health burden of AMR is due to health care-associated infections. Adequate infection prevention and control measures, as well as antibiotic stewardship in hospitals and other health care settings are therefore essential to reduce the burden of AMR.

Of all antibiotic-resistant bacteria studied, third-generation cephalosporin-resistant *E. coli* infections are responsible for the highest burden and more than half of these infections occurr in the community (i.e. outside of hospitals). This means that antimicrobial stewardship should not be restricted to hospital settings and that targeting primary care prescribers as well as infection prevention and control interventions in primary care are also necessary to reduce the burden of AMR.

Figure 5. Health burden of infections due to bacteria with AMR (in 2015) compared to other communicable diseases (average 2009-2013), EU/EEA



Note: Burden measured in disability-adjusted life years (DALYs) per 100 000 population, EU/EEA.

† AMR infections include: third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*, aminoglycoside- and fluoroquinolone- resistant *Acineobacter* spp., three or more antimicrobial groups-resistant *P. aeruginosa*, carbapenem- and/or colistin-resistant *E. coli, K. pneumoniae, Acinetobacter* spp. and *P. aeruginosa*; meticillin-resistant *S. aureus* (MRSA), vancomycin-resistant *E. faecalis* and *E. faecium*, penicillin-resistant, and combined penicillin and macrolide-resistant *S. pneumoniae*.

* Acute bacterial enteritis include: campylobacteriosis, salmonellosis and shigellosis.

Source: ECDC (2018). Cassini A, et al. Lancet Infect Dis. 2019 Jan;19(1):56-66 (https://www.sciencedirect.com/science/article/pii/S1473309918306054?via%3Dihub); Cassini A, et al. Euro Surveill. 2018 Apr;23(16) (https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.16.17-00454).

Each year, more than 670 000 infections due to bacteria with AMR occur in the EU/EEA

As a direct consequence, 33 000 people die of these infections. This is comparable to 100 medium-sized airplanes full of passengers crashing every year without survivors.

Between 2007 and 2015, the health burden of infections due to bacteria with AMR under study has increased in the EU/EEA:

- The number of deaths attributable to infections with *K. pneumoniae* resistant to carbapenems – a group of last-line antibiotics – **increased six-fold**. This is a worrisome trend because these bacteria can spread easily in health care settings if adequate infection prevention and control measures are not in place.
- The number of deaths attributable to infections with third-generation cephalosporin-resistant *E. coli* increased four-fold.

The contribution of various bacteria with AMR to the overall health burden varies greatly between EU/EEA countries (figure 6), thus highlighting the need for prevention and control strategies tailored to the need of each country. While there are many reasons why the situation in countries differ, the main factors that affect the burden of AMR are antibiotic use (frequency, type, dose and duration), quality of hospital care including infection prevention and control practices, and immunisation rates.

Third-generation cephalosporin-resistant *E. coli* and *K. pneumoniae*
Aminoglycoside- and fluoroquinolone-resistant *Acinetobacter spp.*
Three or more antimicrobial groups-resistant *P. aeruginosa.*

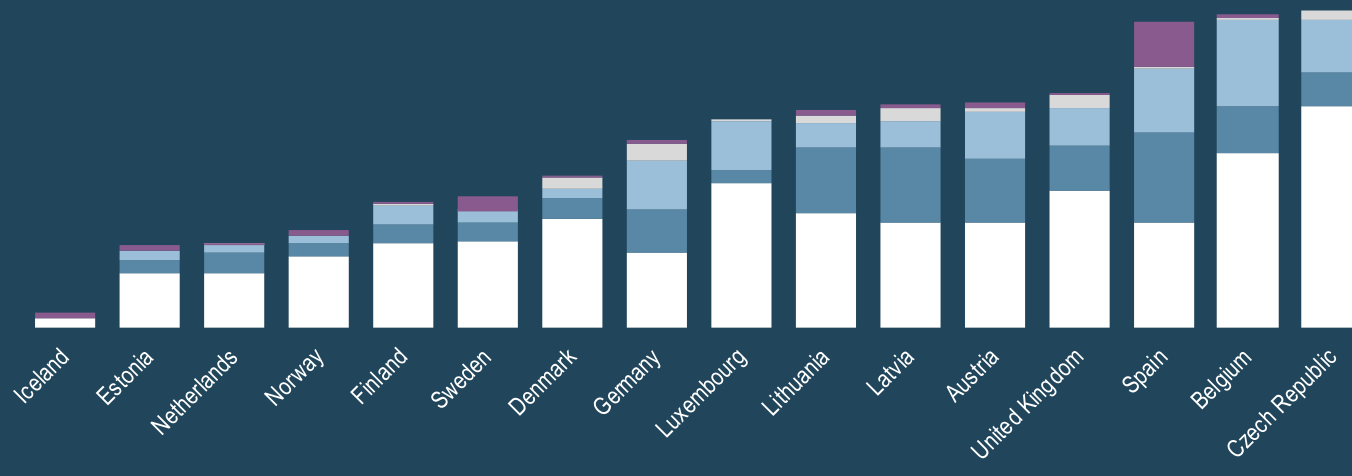
Carbapenem- and/or colistin-resistant *E. coli, K. pneumoniae, Acinetobacter* spp. and *P. aeruginosa.*

Meticilin-resistant *S. aureus* (MRSA)

Vancomycin-resistant *E. faecalis* and *E. faecium*

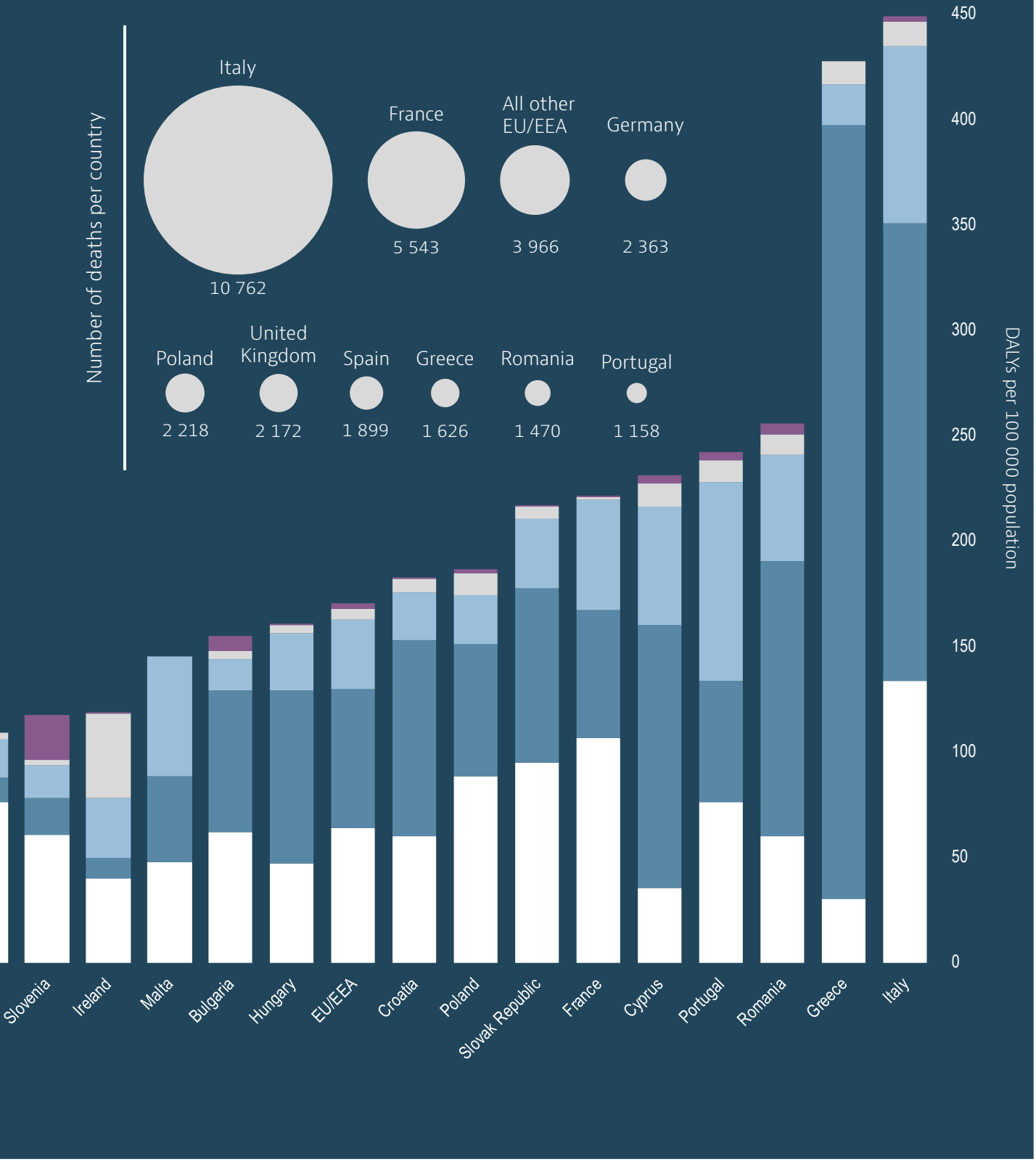
Penicilin-resistant and combined penicilin and macrolide-resistant *S. pneumoniae*

> Each year, in the EU/EEA, more than 670 000 infections occur due to bacteria with AMR.
>
> 33 000 people die as a direct consequence of these infections.



Source: ECDC (2018). Cassini A, et al. Lancet Infect Dis. 2019 Jan;19(1):56-66 (https://www.sciencedirect.com/science/article/pii/S1473099183060054?via%3Dihub).

Figure 6. Health burden of infections with antibiotic-resistant bacteria, by type of antibiotic-resistant bacteria and by country, EU/EEA, 2015



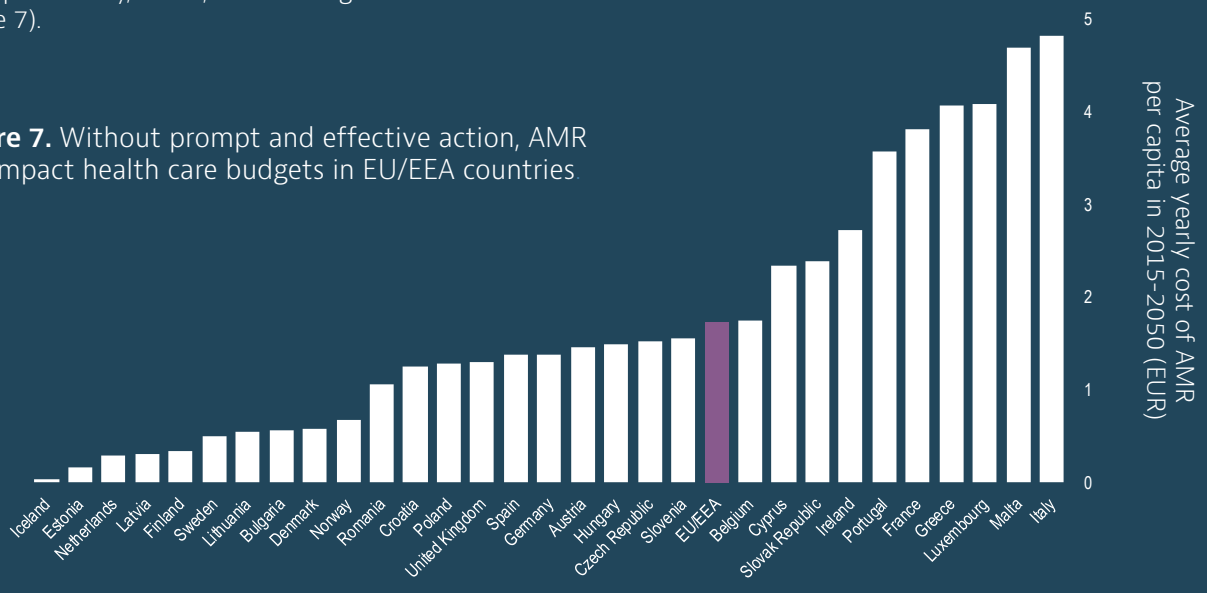
Impact on economy

AMR has a negative impact on the budget of health care systems of EU and EEA countries

If no effective action is promptly put in place, and AMR rates follow the projected trends, up to 1.1 billion Euros are expected to be spent yearly between 2015 and 2050 due to AMR across EU and EEA countries. This corresponds to about 1.8 Euros per capita per year on average, with about 4.1 - 4.8 Euros per capita in Italy, Malta, Luxembourg and Greece (figure 7).

Longer hospital stay, caused by slower recovery from infection and a higher risk of complications, will be one of the key drivers behind an increase in health care expenditure. By 2050, AMR will result in over 569 million extra hospital days annually across countries in the EU and EEA.

Figure 7. Without prompt and effective action, AMR will impact health care budgets in EU/EEA countries.



Source: OECD (2018), Stemming the Superbug Tide: Just a Few Dollars More. Available at: oe.cd/amr-2018.

> Up to 1.1 billion Euros are expected to be spent yearly between 2015 and 2050 due to AMR

What have EU/EEA countries done so far?

More efforts are needed in the fight against AMR

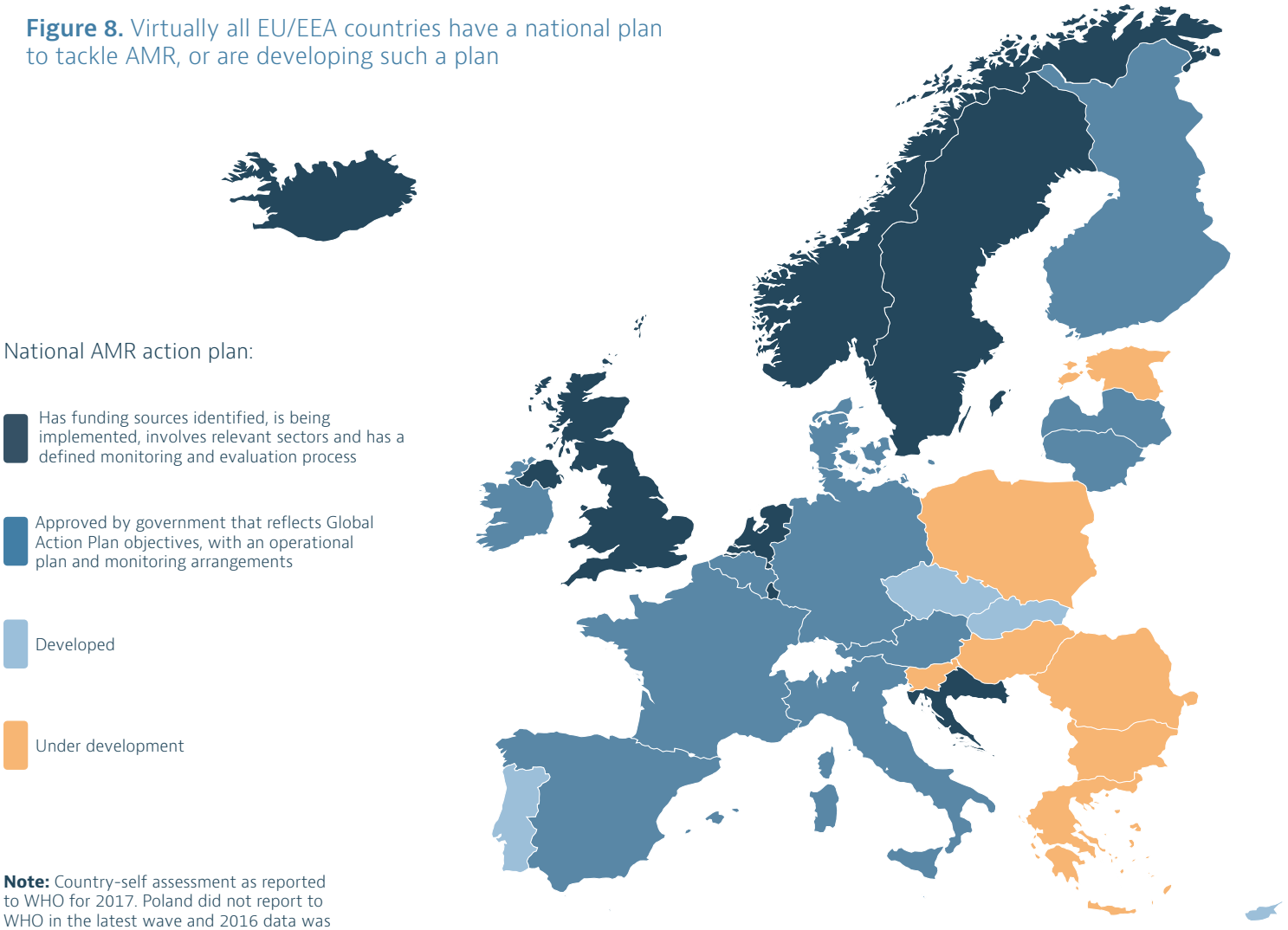
As of June 2018, 75% of EU and EEA countries developed a national action plan on AMR, with the remaining countries working to develop a plan (figure 8).

However, only a minority of countries declared having identified specific funding sources for the implementation of a national action plan and defined a monitoring and evaluation process.

At the same time, countries did not yet sufficiently invest in rolling out public health actions to tackle AMR. For example, only seven out 30 EU/EEA countries reported that they have guidelines to promote the prudent use of antibiotics and that data on antibiotic use are systematically fed back to prescribers.

In June 2017, the European Commission adopted a new European One Health Action Plan against AMR. The plan supports the EU and its Member States in delivering innovative, effective and sustainable responses to AMR, reinforces the research agenda on AMR, and enables the EU to actively promote global action and play a leading role in the fight against AMR.

Figure 8. Virtually all EU/EEA countries have a national plan to tackle AMR, or are developing such a plan



Note: Country-self assessment as reported to WHO for 2017. Poland did not report to WHO in the latest wave and 2016 data was used instead.

Source: OECD (2018), Stemming the Superbug Tide: Just a Few Dollars More. Available at: oe.cd/amr-2018.

What can EU/EAA countries do next?

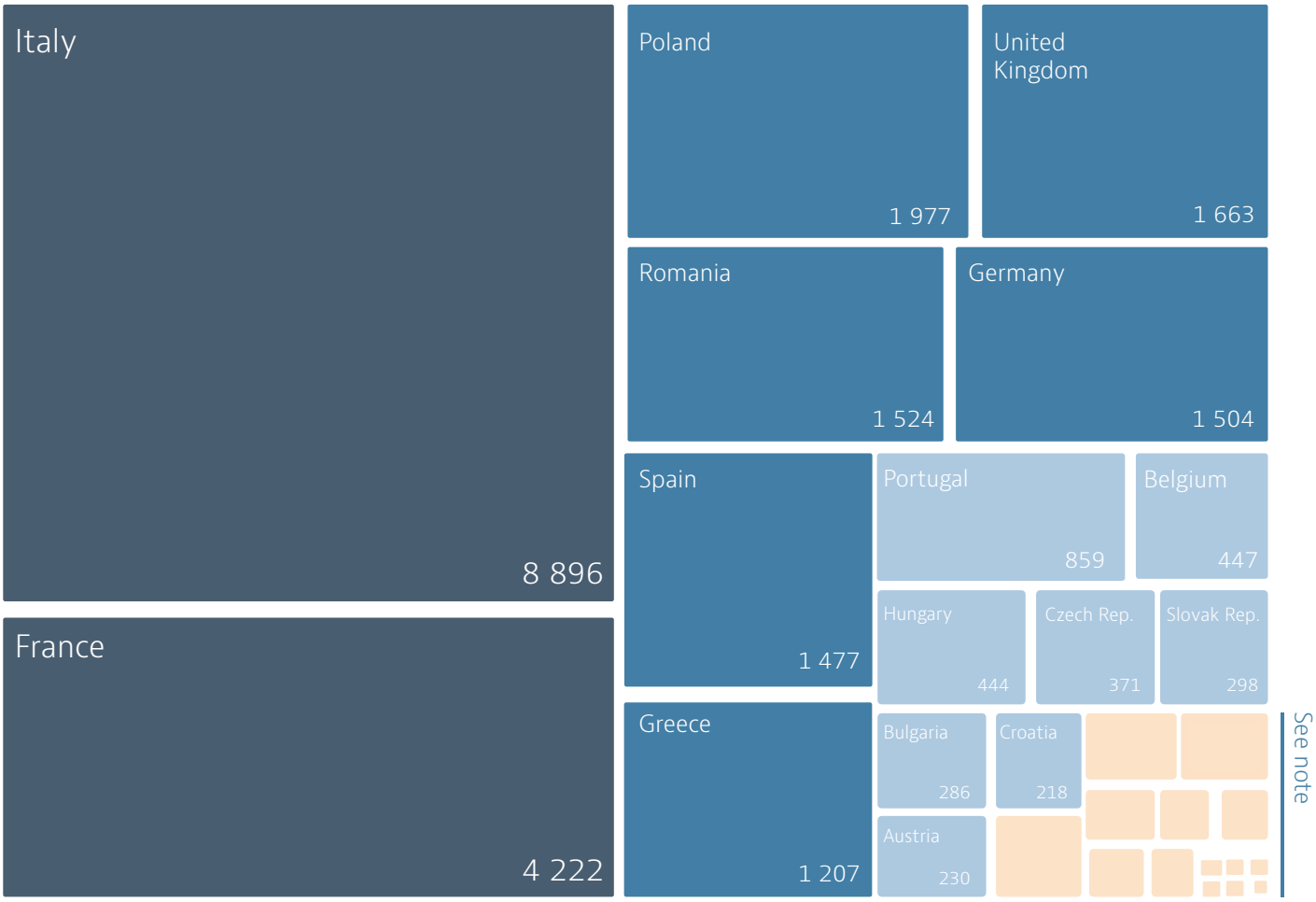
Public health actions to tackle AMR have a positive impact on population health…

The OECD has identified interventions that, for their impact on population health and heavy costs avoided, could be defined as 'best buys' to tackle AMR. The set of policies assessed is aligned with the WHO Global Action Plan on AMR and encompasses:

- improving hygiene in health care facilities, including promotion of hand hygiene and better hospital hygiene (e.g. disinfection of surfaces and equipment in hospitals);
- stewardship programmes promoting more prudent use of antibiotics to end decades of over-prescription;
- use of rapid diagnostic tests in primary care to detect whether an infection is bacterial or viral;
- delayed prescriptions; and
- public awareness campaigns.

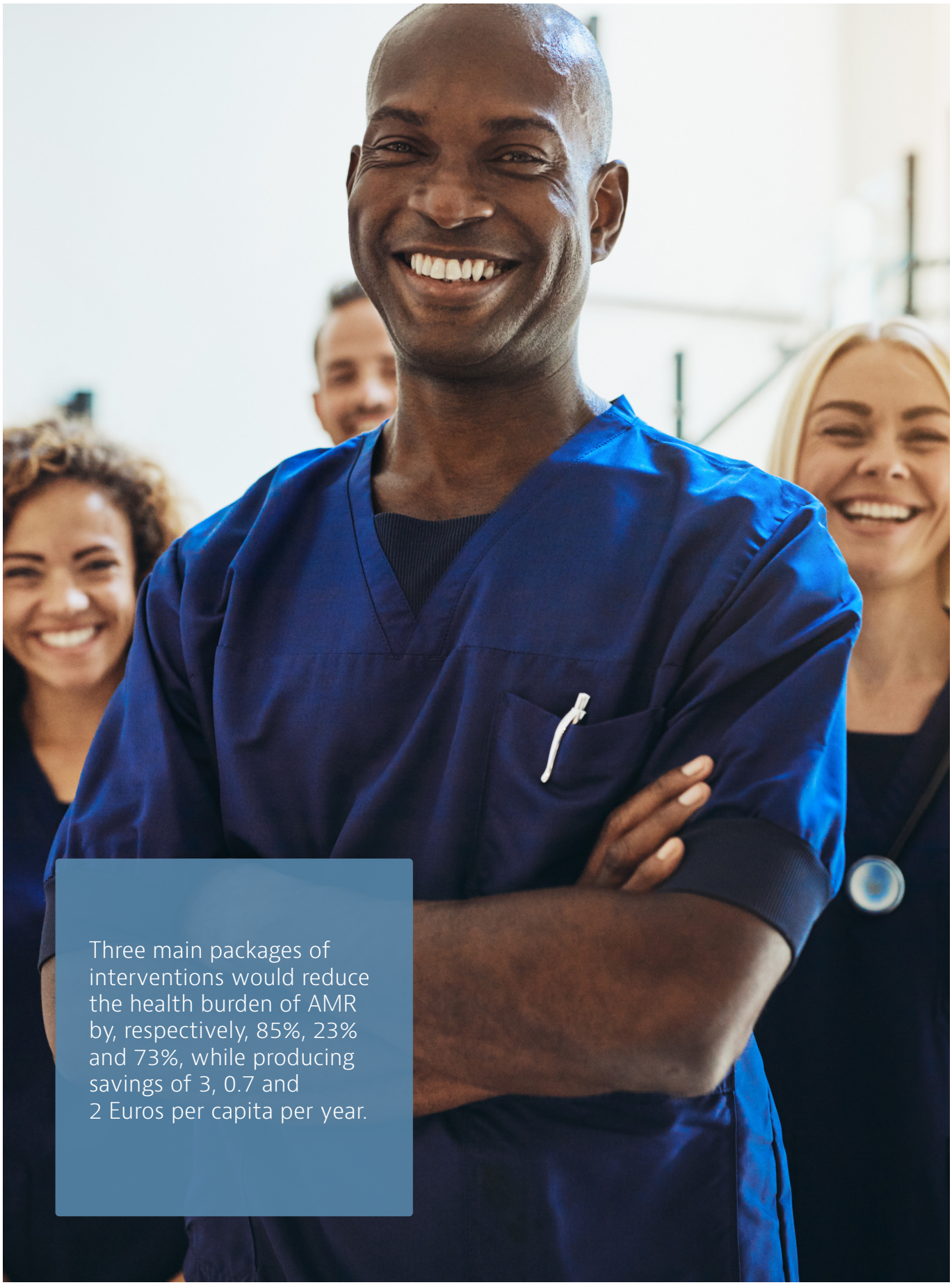
Simple measures, such as promoting hand hygiene and better hygiene in health care facilities more than halve the risk of death and decrease the health burden of AMR – measured in DALYs – by about 40%. Antibiotic stewardship programmes are similarly effective. Outside of hospitals, interventions designed to tackle AMR, such as the use of rapid diagnostic tests, delayed prescriptions and mass media campaigns would have a more limited health impact but remain important policies to address a multifaceted and complex phenomenon.

Figure 9. A mixed intervention package would save about 27 000 lives per year across EU/EEA countries



Note: The countries shown in orange are the following, by descending order: **The Netherlands** (193), **Ireland** (170), **Sweden** (149), **Denmark** (102), **Lithuania** (79), **Slovenia** (77), **Finland** (74), **Cyprus** (63), **Norway** (54), **Latvia** (33), **Malta** (25), **Luxembourg** (15), **Estonia** (14) and **Iceland** (1).

Source: OECD (2018), Stemming the Superbug Tide: Just a Few Dollars More. Available at oe.cd/amr-2018.


Three main packages of interventions would reduce the health burden of AMR by, respectively, 85%, 23% and 73%, while producing savings of 3, 0.7 and 2 Euros per capita per year.

...and are an excellent investment for EU/EEA countries

OECD analyses conclude that all these interventions are affordable for EU/EEA countries. Mass media campaigns, delayed prescriptions and improved hand hygiene cost from as little as 0.15 Euros up to 1.3 Euros per capita per year in many OECD countries. More resource-intense interventions can cost up to a few hundred Euros per hospitalised patient, as in the case of actions to improve hygiene in health facilities. Delayed prescriptions, improved hand hygiene and most antibiotic stewardship programmes generate health care savings that are higher than the implementation cost of these interventions.

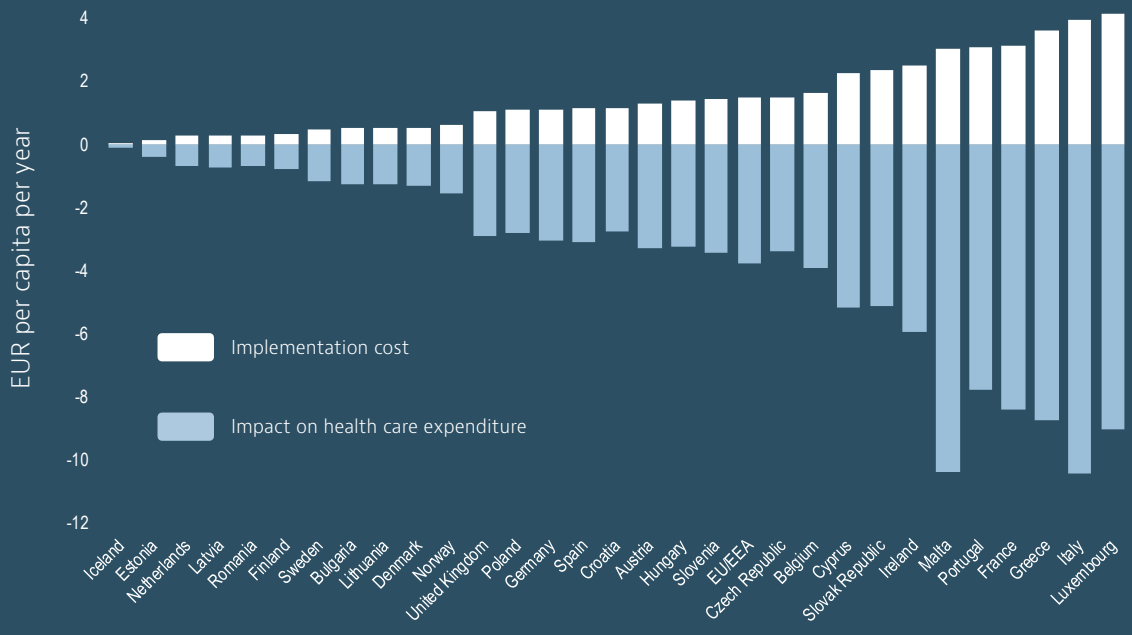
If interventions are implemented together by combining policies into a coherent strategy, the health and economic impact becomes even bigger. The OECD analysis considered three main packages of interventions:

1. The first package, for hospitals, includes improved hand hygiene, antibiotic stewardship programmes and enhanced environmental hygiene in health care settings.

2. The second package, for community settings, includes delayed antibiotic prescriptions, mass media campaigns and the use of rapid diagnostic tests.

3. The third package is a mix of interventions including antibiotic stewardship programmes, enhanced environmental hygiene, mass media campaigns, and the use of rapid diagnostic tests.

Figure 10. Economic assessment of the 'mixed-intervention' package: just a few Euros more produce substantial savings in health care expenditure



Note: Impact on health care expenditure also includes savings due to a reduction in infections susceptible to antimicrobials produced by interventions enhancing hygiene in the health care sector.

Source: OECD (2018), Stemming the Superbug Tide: Just a Few Dollars More.
Available at: oe.cd/amr-2018.

These packages would reduce the health burden of AMR by, respectively, 85%, 23% and 73%, while producing savings of 3, 0.7 and 2 Euros per capita per year. For example, the 'mixed-intervention' package would save about 27 000 lives each year across EU and EEA countries (figure 9). In terms of health expenditure, this policy approach would result in an annual average net saving (i.e. after accounting for the implementation cost of each intervention) of almost 4 Euros per capita (figure 10).

In practice, this would mean that millions of people in these countries would avoid AMR-related complications and health problems.

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Disclaimers

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