MISSION REPORT

ECDC country visit to Norway to discuss antimicrobial resistance issues

12-16 March 2018

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EUROPEAN CENTRE FOR DISEASE PREVENTION AND CONTROL

This report of the European Centre for Disease Prevention and Control (ECDC) was coordinated by Alessandro Cassini, Expert, Antimicrobial Resistance and Healthcare-Associated Infections, ECDC.

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Abbreviations

AMR	antimicrobial resistance
ARHAI	Antimicrobial Resistance and Healthcare-Associated Infections Disease Programme
ASP	Norwegian Antibiotic Centre for Primary Care
ATC	Anatomical, Therapeutic and Chemical (classification system)
CME	continuous medical education
CPE	carbapenemase-producing Enterobacteriaceae
CRE	carbapenemase-resistant Enterobacteriaceae
DDD	defined daily doses
EAAD	European Antibiotics Awareness Day
EARS-Net	European Antimicrobial Resistance Surveillance Network
EC	European Commission
ECTS	European Credit Transfer and Accumulation System
ESBL	extended spectrum beta-lactamase
ESCMID	European Society of Clinical Microbiology and Infectious Diseases
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EuSCAPE	European Survey on Carbapenemase-Producing Enterobacteriaceae
EU/EEA	European Union/European Economic Area
EULabCap	EU Laboratory Capability Monitoring System
GMO	genetically modified organisms
GP	general practitioner
HAI	healthcare-associated infection
ICM	Intersectoral Coordinating Mechanism
ICU	intensive care units
IPC	infection prevention and control
KAS	Norwegian National Centre for Antibiotic Use in Hospitals
KS	Norwegian Association of Local and Regional Authorities
KUPP	knowledge-based update visits (academic detailing)
LA-MRSA	livestock-associated MRSA
LTCF	long-term care facilities
MRSA	meticilin-resistant *Staphylococcus aureus*
NDM	New Delhi metallo-beta-lactamase
NFSA	Norwegian Food Safety Authority
NIPH	Norwegian Institute of Public Health
NORM	Norwegian Surveillance System for Antimicrobial Drug Resistance
NorPD	Norwegian Prescription Database
MSIS	National Notification System for Infectious Diseases
NRC	national reference centre
PPS	point prevalence survey
RELIS	Norway's regional medicine information and pharmacovigilance centres
RKS	Norway's regional resource centres for infection control
SSI	surgical site infections
TB	tuberculosis
VRE	vancomycin-resistant *Enterococcus faecium*
WAAW	World Antibiotic Awareness Week
WGS	whole genome sequencing
WHO	World Health Organization

Executive Summary

Rationale and purpose of the country visit

Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat that AMR poses to human health and advocates for a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for and is carrying out, upon invitation from national authorities, country visits to specifically discuss and assess the situation of the country regarding prevention and control of AMR through prudent use of antibiotics and infection control. These country visits also help document how Member States have approached this implementation and deployed national activities and they support the European Commission in evaluating the implementation.

The main output of the visit is a report from the ECDC team provided to the inviting national authority. To help the ECDC team ensure consistency of the visits and follow-up of progress of countries, an assessment tool has been developed. The assessment tool includes ten topics. These topics are regarded as core areas for successful prevention and control of AMR and are based on Council Recommendation 2002/77/EC and on Council Conclusions of 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

Following the official invitation by Director General Geir Stene-Larsen and Special Advisor Karl-Olaf Wathne, Royal Norwegian Ministry of Health and Care Services (10 November 2017), an ECDC country visit team conducted an assessment mission during the period 12–16 March 2018 to discuss antimicrobial resistance (AMR) issues in Norway. The overall objective of the mission was to provide an observation-based assessment of the situation in Norway regarding prevention and control of AMR through prudent use of antibiotics and infection control. This country visit also focused on the implementation of the 'National Strategy against Antibiotic Resistance 2015–2020', with the aim of providing useful comments for its monitoring and evaluation.

Conclusions

Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) show that the proportion of AMR in bacteria from bloodstream infections in Norwegian patients is consistently below the EU/EEA average and often among the lowest in Europe. Nevertheless, although considerably below the EU/EEA average, resistance to broad-spectrum antibiotics such as third-generation cephalosporins has been increasing over the past 10 years. This is the result of emergence of strains that produce an extended-spectrum beta-lactamase (ESBL), combined with increasing consumption of broad-spectrum antibiotics in healthcare.

Norway's consumption of antibiotics is below the EU/EEA average, both in the community (i.e. outside of hospitals) and in the hospital sector. Nevertheless, faced with a steadily increasing antibiotic consumption in the community since 2000, Norway first published a first cross-sectoral action plan to prevent antibiotic resistance (2000–2004), and then a 'National strategy for prevention of infections in the health service and antibiotic resistance (2008–2012)'. Finally, in 2015 Norway published its 'National strategy against antibiotic resistance 2015–2020' which took a 'One-Health' perspective, with sector-specific goals to be reached by 2020. These goals included substantial reductions of antibiotic consumption in human medicine and maintenance of the already low antibiotic consumption rate on the animal side, with specific initiatives for fisheries and turkey production. The national strategy also included AMR targets in food-producing animals, such as ensuring that livestock-associated meticillin-resistant *Staphylococcus aureus* (LA-MRSA) does not establish itself in the Norwegian pig population.

In 2016, the Norwegian Ministry of Health and Care Services published an 'Action plan against antibiotic resistance in the Norwegian health services with the aim of reducing the use of antibiotics in the Norwegian population by 30 percent by year-end 2020'. This included 20 measures, mainly covered by the existing budgetary framework at various levels. One notable exception is specific funding allocated to the establishment of a national steering committee and reference group to strengthen the Antibiotic Centre for Primary Care (ASP) and carry out academic detailing[1] for antibiotics in primary care (KUPP). This renewed momentum has already resulted in decreasing antibiotic consumption and it is likely that, if these actions are sustained, Norway will reach or even go below the antibiotic reduction targets in humans that it has set for 2020. It is currently too early to assess whether these reductions have had an effect on decreasing AMR.

Compared with many other European countries, Norway has a long-standing history of increased awareness of AMR issues, with a focus on controlling the spread of MRSA. The recent success towards eradication of LA-MRSA

[1] University or non-commercial-based educational outreach

from Norwegian pig herds, through 'One Health' collaboration, is another example of how targets, such as those in the National Strategy, and clear responsibilities result in rapid change.

Since 2010, many hospitals in Norway have experienced cases and sometimes substantial outbreaks of vancomycin-resistant *Enterococcus faecium* (VRE) by Norwegian standards. One university hospital is now facing an endemic situation. In addition, an increasing number of cases of carbapenem-resistant Enterobacteriaceae (CRE) have been reported in the country in recent years, particularly since 2015. These are sometimes referred to as $ESBL_{CARBA}$ although they are more resistant than the usual ESBL-producing strains. CRE are highly drug-resistant bacteria, that are even resistant to the safest last-line antibiotics - i.e. carbapenems - and options for the treatment of CRE-infected patients are even more limited.

According to the data that were presented to us, most CRE cases were related to hospitalisation abroad and/or international travel. However, a substantial proportion of cases could not be accounted for via this route of transmission and therefore there is a concern that patient-to-patient transmission in Norway has occurred, causing at least one outbreak.

Examples from other European countries show that if spread of VRE and CRE is not tackled at an early stage, these multidrug-resistant bacteria will inevitably spread within the affected hospitals, between hospitals and long-term care facilities (LTCFs) in affected regions, and ultimately between hospitals in different regions of the country. While Norway has been and continues to be quite successful at controlling MRSA, these new developments show that the control of VRE has not been equally successful. Once introduced into the healthcare system, CRE is even more difficult to control and the clinical consequences result in greater patient mortality and morbidity. There is concern that once this happens, the existing system for detection and control of CRE may fail, as has happened in some hospitals with VRE.

Thanks to its existing structures and the large number of experts, Norway is still in a good position to reverse these new trends in AMR. However, VRE, CRE and other emerging multidrug-resistant bacteria each require the implementation of a new set of well-coordinated, specific actions over and above the current sustained efforts to reduce antibiotic consumption in humans. The focus must be a rapid step-up of infection prevention and control in the country. This is essential if Norway wants to retain its good international position regarding AMR and secure the safety of its patients in healthcare.

Recommendations

Continue with the actions that are part of the current action plan against antibiotic resistance in the Norwegian health service which have already proven successful in reducing the consumption of broad-spectrum antibiotics.

Step-up hand hygiene and standard precautions in hospitals and all other healthcare settings, through a campaign that focuses on raising awareness. Process indicators relevant to infection prevention and control need to be established, including effective hand hygiene, through audits in all hospitals.

Increase all healthcare professionals' knowledge of VRE and CRE and the measures necessary to detect, prevent and control their spread. This can be achieved by various means such as awareness campaigns, training courses in hospitals and even academic detailing for VRE and CRE prevention and control measures. This, in turn, will require adequate numbers of professionals formally trained in infection prevention and control and would require establishing a career path in infection prevention and control. The current heterogeneity in the numbers of infection control nurses and doctors – as well as their background training – should be addressed by establishing clear complement requirements (e.g. a ratio of infection control nurses per bed), based on hospital type and size and indicating the basic level of training needed.

Support and coordinate control of VRE and CRE at national level by

- formally appointing one reference laboratory for VRE and CRE (this can be the same laboratory);
- ensuring that a strong epidemiological team at the Norwegian Institute of Public Health (NIPH) coordinates collection of data on VRE and CRE at national level and that these data are translated into support and field investigation where necessary (cases with unknown or unclear mode of transmission should be considered for root-cause analysis);
- ensuring a robust coordinating role and the regular link between these reference laboratories and the epidemiological team at NIPH;
- strengthening the department undertaking infection prevention and control at NIPH so that it can be more pro-active in providing standardised guidance to hospitals, as well as providing expert support in outbreaks, especially when they have the potential to involve different regions, hospitals and municipalities.

Control VRE and CRE at hospital level by ensuring (a) that the currently recommended screening programmes are properly applied and possibly expanded, (b) that the results are communicated rapidly, and (c) that the necessary control measures involving the infection control team are implemented. Norway could consider audits on preparedness for prevention and control of VRE and CRE in all hospitals. Ultimately, this could be

extended to other healthcare settings and in particular to LTCFs. To ensure the good use of available local data, Norway should consider training infection control teams on how to make sense of surveillance data and how to investigate outbreaks.

At AMR reference laboratories, phenotypic testing is essential to identify resistance due to currently unknown genes. At present this cannot be achieved by only performing next generation sequencing. In addition, AMR reference laboratories that do phenotypic testing can continue to provide advice and support to local clinical microbiology laboratories. It is essential for Norway that phenotypic testing for AMR is maintained at reference laboratories.

The actions on prevention and control of VRE and CRE would most probably need to be combined in an Action Plan for the prevention and control of multidrug-resistant organisms in Norwegian healthcare applicable to hospitals, LTCF and other settings, such as primary care.

Norway should consider including targets in this new action plan since in the current action plan the activities related to antibiotic reduction that have been successful are those with clear targets. In addition, specific funding should be allocated for the above-mentioned activities – or at least a mechanism should be put in place to ensure that national agencies and regions are prioritising these activities.

The national antibiotic guidelines for hospitals should be reviewed and revised where necessary. One particular issue that will need to be considered is situations where the current first-line regimen of penicillin/ampicillin + gentamicin should no longer be recommended because of increasing proportions of AMR.

Academic detailing on prudent use of antibiotics for GPs and in LTCFs has proven successful and, if the resources for continued national deployment are not available, **Norway should consider focusing on the prescribers of the highest numbers of antibiotics as this would provide the best value for money**.

In primary care, the introduction of electronic prescriptions represents an opportunity to collect, analyse and routinely feed back detailed information on antibiotic use by prescriber, type of patient and indication, without the need for the prescriber to have to request such information. **This data should routinely be fed back to prescribers whenever academic detailing is undertaken**.

In hospitals, the focus on reducing consumption of broad-spectrum antibiotics should continue. In addition, regions and hospitals should investigate the reasons for the high consumption of third-generation cephalosporins, for example by performing audits on prescription and giving feedback to prescribers. Behaviour change interventions should be introduced, aimed specifically at third-generation cephalosporins and carbapenems. These are already undertaken in some hospitals and include restricted laboratory reporting and the need for authorisation by an infectious diseases/microbiology expert before these antibiotics can be dispensed.

Finally, we would like to express concern that the operation of the WHO Collaborating Centre for Drug Statistics Methodology is currently at risk due to budget reduction. This centre is hosted at NIPH and financed by Norway. The Centre provides services and advice to WHO on the ATC/DDD[2] index which is the classification and metric used to perform surveillance of consumption of antibiotics and of other medicines. This system is used at WHO and worldwide and Norway is recognised globally for this contribution.

[2] ATC/DDD - anatomical, therapeutic and chemical (classification system)/defined daily dose

1 Background

1.1 Rationale for country visits to discuss antimicrobial resistance (AMR) issues

After the introduction of antibiotics in the 1940s, it soon became clear that antibiotic usage promoted the rise of antibiotic-resistant bacterial strains in common bacteria such as *Staphylococcus aureus* and *Mycobacterium tuberculosis* (TB). In the decades which followed, the increasing number of antibiotic-resistant strains could be managed thanks to the continuous availability of new antibiotics providing new means of treating patients infected with resistant bacteria. However, from the 1990s onwards, development of new antibiotics decreased and at the same time, the emergence of bacteria resistant to multiple antibiotics became an ever-increasing problem in clinical medicine. Treatment guidelines had to be rewritten and the need to take bacteriological samples for antibiotic susceptibility testing became essential.

Once a resistant bacterium has developed, it will spread from a colonised person to another person if appropriate hygienic precautions (e.g. hand hygiene, isolation) are not taken. The risk of resistant bacteria spreading is higher in crowded environments and even greater when people in the surrounding area are receiving antibiotics - a common situation in hospitals and other healthcare facilities.

Today, bacteria that are totally (or almost totally) resistant to antibiotics (i.e. untreatable with antibiotics) are spreading in Europe. This represents a patient safety issue.

In 1998, the Chief Medical Officers of the EU Member States recognised this evolving problem and took the initiative to arrange the first major conference on AMR, which resulted in the Copenhagen Recommendations (Report from the Invitational EU Conference on the Microbial Threat, Copenhagen, Denmark, 9–10 September 1998).

In November 2001, the EU Health Ministers adopted a **Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC)**, which covers most topics of importance for the prevention and control of AMR. The Commission has to report back to the Council on progress in implementing the Council Recommendation.

In 2005, the European Commission reported to the Council on progress in Member States in the Report from the Commission to the Council on the basis of Member States reports on the implementation of the Council recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine (COM (2005) 0684). This states that 'ECDC should be able to assist the Commission in the future preparation of implementation reports and of recommendation proposals.'

In June 2008, EU Health Ministers adopted Council Conclusions on antimicrobial resistance (AMR) that reiterated the call for action to contain antimicrobial resistance and called upon Member States 'to ensure that structures and resources for the implementation of the Council recommendation on the prudent use of antimicrobial agents in human medicine are in place and to continue with the implementation of specific strategies targeted towards the containment of the antimicrobial resistance'.

In June 2009, EU Health Ministers adopted a **Council Recommendation on patient safety, including the prevention and control of healthcare-associated infections (2009/C 151/01)**, which further stresses the importance of combating AMR as a patient safety issue.

In April 2010, the European Commission published its second report from the Commission to the Council on the basis of Member States' reports on the implementation of the Council Recommendation (2002/77/EC) on the prudent use of antimicrobial agents in human medicine. While acknowledging that Member States have made significant progress since 2003, this report highlights many areas where implementation is not optimal and identifies directions for future work.

In November 2011, the European Commission published a new five-year **action plan against the rising threats from antimicrobial resistance** with the aim of addressing AMR by implementing a coordinated approach in all those sectors concerned (public health, animal health, food safety, environment, etc.) and strengthening and further developing EU initiatives against AMR and healthcare-associated infections (HAI) at EU and international levels.

The new cross-sectorial approach has been further strengthened with the adoption of the **Council Conclusions on antimicrobial resistance of 22 June 2012** and the **Council conclusions on the next steps under a 'One Health' approach to combat antimicrobial resistance of 17 June 2016**.

On 29 June 2017, the European Commission published a new European One Health Action Plan against Antimicrobial Resistance (AMR)[3] containing concrete actions and offering EU added value that the European Commission will develop and strengthen as appropriate for a more integrated, comprehensive and effective approach to combating AMR.

ECDC's mission, as part of its **Founding Regulation No 851/2004**, is (i) to identify, assess and communicate current and emerging threats to human health from communicable diseases; (ii) in the case of other outbreaks of illness of unknown origin which may spread within or to the Community, the Centre shall act on its own initiative until the source of the outbreak is known; and (iii) in the case of an outbreak which clearly is not caused by a communicable disease, the Centre shall act only in cooperation with the competent authority upon request from that authority. As part of this mission, ECDC may be requested, by the European Commission, a Member State, or another country to provide scientific or technical assistance in any field within its mission.

1.2 Purpose

Council Recommendation of 15 November 2001 on the prudent use of antimicrobial agents in human medicine (2002/77/EC) outlines the threat posed by AMR to human health and advocates for a range of actions to be taken for its prevention and control. Council Conclusions on antimicrobial resistance (AMR) of 10 June 2008 reiterated this call for action.

To assist Member States in implementing the Council Recommendation, ECDC has developed a process for country visits. At the invitation of the national authorities, these visits are undertaken to specifically discuss and assess the national situation regarding prevention and control of AMR through prudent use of antibiotics and infection control. The country visits also help document how Member States have approached implementation and deployed national activities and they support the European Commission in evaluating implementation.

The main output of the visit is a report from the ECDC Team provided to the inviting national authority. To help the ECDC Team ensure consistency of the visits and follow-up of progress of countries, **an assessment tool** has been developed (see Annex 5.2 of this Report). The assessment tool includes ten topics. These topics are regarded as core areas for successful prevention and control of AMR and are based on Council Recommendation 2002/77/EC and on Council Conclusions of 10 June 2008. The assessment tool is used as a guide for discussions during the visit.

The ECDC country visit team consisted of Alessandro Cassini, ECDC Expert Antimicrobial Resistance and Healthcare-associated Infections (ARHAI), who led the mission, Dominique L. Monnet, Head of ECDC's ARHAI Disease Programme and three experts from EU/EEA countries: Michael Borg (Malta), Ute Wolff Sönksen (Denmark) and Walter Zingg (United Kingdom), as well as Andrea Nilsson (ECDC communication expert, only 12–13 March 2018). At national level, the visit was organised and coordinated by Karl-Olaf Wathne and Torstein Lindstad (Ministry of Health and Care Services). For the full list of national experts met during the ECDC country visit, please refer to Annex 5.1 of this report.

[3] https://ec.europa.eu/health/amr/sites/amr/files/amr_action_plan_2017_en.pdf

2 Overview of the situation in Norway[4]

2.1 Antimicrobial resistance (AMR)

Data on AMR in invasive bacterial isolates - mainly from bloodstream infections - are available from the European Antimicrobial Resistance Surveillance Network (EARS-Net), which Norway has participated in since 2000. Overall, the proportions of resistant isolates for the bacteria under surveillance by EARS-Net in 2016 were consistently below the EU/EEA average, often among the lowest in the EU/EEA.

However, according to data reported to EARS-Net, the proportions of resistant isolates increased for several bacteria under surveillance. The proportion of third-generation cephalosporin-resistant *Klebsiella pneumoniae*, although well below the EU/EEA average of 25.7%, increased from 1.5% in 2006 to 5.8% in 2016. The proportion of third-generation cephalosporin-resistant *Escherichia coli* was below 1% until 2006 and has since increased to reach 5.6% in 2016 (EU/EEA average: 12.4%). For *Streptococcus pneumoniae*, the proportion of isolates with penicillin resistance increased from 0.2% in 2007 to 1.2% in 2016, and the proportion of isolates with combined resistance to penicillin and macrolides increased from 0.5% in 2007 to 2.8% in 2016. The proportion of meticillin-resistant *Staphylococcus aureus* (MRSA) remained below 1% until 2012, when it increased to 1.3%, and in 2016 it was 1.2%.

Reports of carbapenem-resistant bacteria have been occasional and the proportions of carbapenem-resistant isolates are always much lower than the EU/EEA average, mostly occurring in *Pseudomonas aeruginosa* (6.7% in 2016) and in *Acinetobacter* spp. in 2014 (2.9%) and 2015 (9.4%). A publication from the European Survey on Carbapenemase-Producing *Enterobacteriaceae* (EuSCAPE) noted that: 'In Norway, the occurrence of carbapenemase-producing *Enterobacteriaceae* (CPE), KPC-, OXA-48- and NDM[5]-producing *Enterobacteriaceae*, has remained sporadic, with a small number of CPE cases (around 10 cases per year, including colonisation) since 2013. The majority of the identified cases had a link with foreign travel.' Another publication from the same project found that the prevalence of carbapenemase-producing *K. pneumoniae* and *E. coli* per 10 000 hospital admissions in Norway was the lowest of all participating European countries.

Occasional increases in the proportion of vancomycin-resistant *Enterococcus faecium* have been observed in Norway - in 2011 (1.8%), 2013 (2.4%), 2014 (1.8%) and 2016 (1.9%).

2.2 Healthcare-associated infections

In May–June 2012, Norway participated in the first ECDC point prevalence survey (PPS) of healthcare-associated infections (HAIs) and antimicrobial use in European acute care hospitals. A total of seven hospitals performed the PPS and country representativeness of the data was considered poor. The percentage of patients with at least one HAI (7.8%) on a given day in Norwegian hospitals was above the EU/EEA average (5.7%). In November 2017, Norway participated in the second ECDC PPS, although with a slightly different protocol for reporting the prevalence of HAIs (ECDC protocol for structure and process indicators at hospital level, as well the same definition for HAIs; however, the Norwegian PPS does not include all infection and antimicrobial use data as per ECDC protocol). Therefore comparisons with other EU/EEA countries should be made with caution. A total of 58 hospitals participated and 9 791 patients were assessed; country representativeness was considered to be good to optimal.

Norway contributes to the ECDC-coordinated surveillance of surgical site infections (HAI-Net SSI) through the national network for surveillance of surgical site infections (SSIs), coordinated by the NOIS programme (https://www.fhi.no/hn/helseregistre-og-registre/nois/) at the NIPH. In 2016, Norway reported data on more than 30 000 surgical procedures of five different types and from 60 hospitals. In 2016, the incidences of SSIs were 3.9% for coronary artery bypass graft, 3.4% for cholecystectomy, 10.8% for colon surgery, 3.8% for caesarean section and 2.3% for hip prosthesis. The Norwegian SSI surveillance system uses semi-automated data collection, can be considered well-representative of the country, and is characterised by comprehensive SSI case finding after hospital discharge, which results in increased sensitivity compared to most other EU/EEA countries.

Norway does not participate in the ECDC-coordinated surveillance of HAIs in intensive care units (HAI-Net ICU) or in the ECDC-coordinated surveillance of *Clostridium difficile* infections (HAI-Net CDI).

[4] Chapter 2 is completed in preparation of the country visit and based on available data sources at EU/EEA level.

[5] New Delhi metallo-beta-lactamase

2.3 Antimicrobial consumption

In 2016, antibacterial consumption for systemic use (ATC group J01) in the community in Norway was 15.2 defined daily dose (DDD) per 1 000 inhabitants per day, which was lower than the EU/EEA average of 21.9 DDD per 1 000 inhabitants per day, and significantly decreased from 16.9 DDD per 1 000 inhabitants per day in 2012. Quality indicators for consumption show that, in 2016, the majority of antibiotics prescribed in the community in Norway were beta-lactamase-sensitive penicillins (ATC group J01CE) (20.4% versus 2.3% in EU/EEA) and the ratio of broad-to-narrow-spectrum antibacterials in 2016 was among the lowest of all EU/EEA countries: 0.2 versus 13.4 (EU/EEA). It should be noted that in 2016 Norway had the highest consumption of methenamine (an antibacterial agent indicated for urinary tract infections, prophylactically and for longer treatments) of all EU/EEA countries. Norway is not included in the European Commission's Eurobarometer surveys on AMR.

Consumption of a number of commonly used antimicrobials in the community decreased between 2011 and 2016: fluoroquinolone consumption decreased from 0.56 to 0.41 DDD per 1 000 inhabitants per day, macrolide consumption decreased from 1.76 to 0.93 DDD per 1 000 inhabitants per day, and consumption of first-generation cephalosporins decreased from 0.11 to 0.06 DDD per 1 000 inhabitants per day. On the other hand, consumption of sulfonamides and trimethoprim combinations increased from 0.25 to 0.34 DDD per 1 000 inhabitants per day and consumption of combinations of penicillins, including beta-lactamase inhibitors, while remaining low, increased from 0.002 to 0.013 DDD per 1 000 inhabitants per day between 2011 and 2016.

In hospitals, consumption of antibacterials for systemic use (ATC group J01) was 1.38 DDD per 1 000 inhabitants per day in 2016 and remained stable under the EU/EEA average of 2.06 DDD per 1 000 inhabitants per day. It should be noted that consumption of carbapenems increased from 0.0141 DDD per 1 000 inhabitants per day in 2001 to 0.0397 DDD per 1 000 inhabitants per day in 2016, although there was a significant decrease in 2015 (from 0.0473 in 2014 to 0.0386 DDD per 1 000 inhabitants per day). In 2016, consumption of carbapenems was below the EU/EEA average of 0.052 DDD per 1 000 inhabitants per day. Consumption of polymyxins was 0.0007 DDD per 1 000 inhabitants per day in 2016 and remained stable under the EU/EEA average of 0.016 DDD per 1 000 inhabitants per day.

3 Observations

3.1 Development of an Intersectoral Coordinating Mechanism (ICM)

National strategy

The first 'National strategy for prevention of infections in the health service and antibiotic resistance (2008–2012)' was published in 2008 and was a multi-disciplinary strategy resulting from the cooperation of the Ministry of Labour and Social Inclusion, the Ministry of Fisheries and Coastal Affairs, the Ministry of Agriculture and Food, the Ministry of the Environment and the Ministry of Health and Care Services.

A knowledge gap exercise was undertaken between 2012 and 2015 and a 'National Strategy against Antibiotic Resistance 2015-2020' was published in 2015 by the Ministry of Fisheries, the Ministry of Agriculture and Food, the Ministry of Climate and Environment and the Ministry of Health and Care Services. The consultation process and development of the national strategy, together with its scope, goals and activities represent a rare example of a 'One Health' effort to combat AMR, combining human and animal health, research, environment and international relations. Moreover, the theme of AMR is high on the national agenda, together with the general public's increasing awareness. Norway's investments in ensuring that AMR remains an important international topic are substantial. The main goals of the national strategy are to reduce total antibiotic consumption, to enhance more appropriate use of antibiotics, to increase the body of scientific knowledge on what drives the development and spread of antibiotic resistance and to be an international mobiliser against AMR. These are completed by 14 ambitious, sector-specific goals. The national strategy is implemented through inter-ministerial meetings (at times also referred to as the 'Strategy Group') three times per year, but contacts between the various contributors to the strategy are reported to be more frequent.

The national strategy also lays out the following animal health and agricultural sector-specific goals, which are revised every six months:

- to monitor AMR in relevant animal populations and plants used in food production, as well as possible reservoirs of AMR, through the NORM-VET system;
- to stop the circulation of LA-MRSA in Norwegian swine production, using a One-Health approach to ensure this.;
- to reduce extended-spectrum beta-lactamase (ESBL)-producing bacteria in Norwegian poultry to a minimum, given that most recent outbreaks have originated in imported poultry. This activity is based on the assumption that the industry will continue to be involved and help through pro-active testing and monitoring. Between 2011 and 2014, the proportion of isolates producing an ESBL has been reduced from 30% to 10%;
- to reduce antibiotic consumption in animals for food production by at least 10% compared to 2013;
- to reduce antibiotic consumption in pets by at least 30% compared to 2013 (given that use of cephalosporins in pets is already very low);
- to stop the use of narasin and other coccidiostats in poultry production, in the knowledge that an increased use of vaccines will be crucial to achieving this goal.

The national strategy's goal for the fishing industry is to maintain or reduce the level of antibiotic consumption. In Norway, the low antibiotic consumption in fish farming is the result of successful vaccination campaigns.

The national strategy's goals in relation to the environment are to contribute to the body of knowledge (funding of NOK 2.5 million has been provided to the Norwegian Environment Agency, which is professionally independent, to achieve results in the area of AMR in the environment, AMR in the soil and AMR in genetically-modified organisms (GMOs) by 2021) and to increase international collaboration on environmental issues related to AMR.

Technical activities with international components concerning human and animal health, the environment and research are led by the relevant ministries and agencies, without input or coordination from the Ministry of Foreign Affairs. The latter is involved in the effort to combat AMR by focusing on increasing international awareness (e.g. earmarked funds and secondments to WHO); providing international cooperation to help other countries develop their own national action plans; offering support to other countries for the development of AMR surveillance; funding food security topics involving AMR and funding World Bank work on knowledge gaps.

National action plan

In 2015, the Ministry of Health and Care Services developed and published the 'Action plan against antibiotic resistance in the Norwegian health service – with the aim of reducing the use of antibiotics in the Norwegian population by 30 percent by year-end 2020'. A National Steering Committee was appointed to oversee the implementation of the action plan and this Committee meets twice a month. It is composed of the Norwegian

Directorate of Health (chair), the Norwegian Institute of Public Health, the Norwegian Medicines Agency and the Norwegian Directorate of eHealth. The National Steering Committee is assisted by a Reference Group, which ensures regional and professional support for the implementation of the action plan and meets at least twice per year. The Reference Group is composed of representatives from the offices of the county governors, the regional resource centres for infection control (RKS), the Norwegian Association of Local and Regional Authorities (KS)/local authorities, the Norwegian Medical Association, the Norwegian Dental Association, the Antibiotic Centre for Primary Care (ASP), the Norwegian National Centre for Antibiotic Use in Hospitals (KAS), and the regional medicines information and pharmacovigilance centres (RELIS).

Antibiotics are predominately consumed in primary care, therefore most measures pertain to reducing antibiotic prescription in primary care and are directed towards general practitioners (GPs). At present, more than 60% of antibiotics prescribed by GPs are for respiratory tract infections and, although narrow-spectrum antibiotics are predominantly prescribed in primary care, they seem to be used to shorten disease duration and alleviate the symptoms of infections. In comparison, antibiotic use in hospitals represents 7% of the total consumption and this is where more broad-spectrum antibiotics are prescribed to save lives and avoid complications.

In line with the national strategy and the action plan, Norway's human-health-specific goals are centred on antibiotic consumption and appropriateness of antibiotic use. For example, the national goals state that Norway aims to be one of the three European countries with the lowest consumption of antibiotics. In connection with this, specific goals aim to reduce antibiotic consumption by 30% compared to 2012; prescription of antibiotics shall be reduced from a current average of 450 to 250 prescriptions per 1 000 inhabitants per year and prescription of antibiotics for respiratory infections shall be reduced by 20% compared to 2012. Studies are also planned to investigate the possible effect of antibiotic usage being too low. Examples of enhancing appropriate use of antibiotics include promoting narrow-spectrum antibiotics such as penicillin instead of broad-spectrum antibiotics, while increasing access to penicillin and appropriate antibiotic use in other countries. Better diagnostics, surveillance and analysis of data are also stated as goals in the national strategy and/or the national action plan.

Other measures described in the national action plan aim at strengthening national organisations (steering and references groups, strengthening the Antibiotic Centre for Primary Care (ASP), increasing knowledge of antibiotics and immunisation in the general population, providing more suitable package sizes and reducing the length of validity of antibiotic prescriptions, strengthening antibiotic stewardship in the primary healthcare sector (academic detailing of GPs, peer-review of antibiotic prescriptions, diagnostic codes on prescriptions, electronic prescribing support), in the hospital sector (antibiotic management programme, updating guidelines), in dental institutions (appoint a dental committee to review antibiotic use in the dental health service), and in municipal health institutions (AMR surveillance in long-term care facilities (LTCFs), improvement of infection prevention and control in LTCFs, academic detailing for LTCFs).

Most activities in the action plan are foreseen within the available annual budget: however, NOK 5 million have been specifically allocated for the implementation of specific interventions, such as for the appointment of the steering committee, strengthening the ASP (the majority of the allocated funds) and to pilot test academic detailing of GPs and LTCFs for antibiotics.

The Norwegian Institute of Public Health (NIPH) has an official antibiotic committee, which includes microbiologists, infection prevention and control (IPC) and AMR specialists. The committee's responsibilities are generally limited to human health, although an agreement is in place with the Norwegian Food Safety Authority (NFSA) based on a general memorandum of understanding - i.e. not specifically centred on AMR. The NIPH and the NFSA meet 4-6 times per year, but collaboration can be more frequent when outbreaks occur involving both institutions.

3.2 Organised multi-disciplinary and multi-sectoral collaboration at local level

During the country visit, we were presented with an example of local collaboration between animal health and human health sectors, focusing on livestock-associated MRSA (LA-MRSA).

MRSA, including LA-MRSA, is a notifiable disease in Norway and its incidence has remained stable since 2014, although MRSA colonisation has increased (maybe due to increased screening and mainly in travel-related cases). The MRSA cases were increasingly reported as being infected outside of Norway or with unknown place of acquisition. Most MRSA cases in humans were not outbreak-related, although some had outbreak potential.

Three main MRSA cluster outbreaks in humans have been identified and studied by sampling 26 swine herds, two slaughterhouses, and including 36 human isolates. They were all independent (i.e. resulting from primary introductions) and did not appear to originate from pigs. The joint multi-disciplinary group of medical doctors, veterinarians, epidemiologists and microbiologists investigating these outbreaks found that the pigs were infected by humans (LA-MRSA-positive farm workers).

Only 20 pigs were imported into Norway between 2007 and 2014, which is an indication that Norway is self-sufficient in the production of pigs. Antimicrobial consumption in food-producing animals such as pigs is low in Norway, representing only 11% of the total antimicrobial consumption (humans and animals combined).

Norway's approach to LA-MRSA is not only to prevent spill-over of LA-MRSA to humans, but to eradicate LA-MRSA from food animals. In 2014, nationwide surveillance of MRSA in livestock was implemented, whereby all pig populations are regularly sampled for MRSA by the NFSA. When a case is identified, measures are implemented to eradicate LA-MRSA and these include trade restrictions for the farm (no import/export of pigs) as well as depopulation and local containment measures (sanitation and disinfection). The trade restrictions are lifted only when eradication of LA-MRSA at the farm has been confirmed. Simultaneously, contact-tracing activities are initiated in humans. Eradication of LA-MRSA is costly and is financed partly from state subsidies, and partly by farmers and their insurance.

In the future, the national goal is to focus on preventing the spread of LA-MRSA by screening humans in contact with pigs for LA-MRSA carriage, carrying out annual surveys of the pig population for LA-MRSA carriage, and undertaking targeted testing where there is a suspicion of LA-MRSA introduction into the country. This example shows an effective working relationship (the peak observed in 2015 has now inverted its trend) and involvement of all stakeholders. The NFSA and the NIPH have also collaborated in a socio-economic study on the costs of LA-MRSA eradication. The application of a similar approach is currently being considered for other relevant antimicrobial-resistant bacteria such as ESBL-producing E. coli and antimicrobial-resistant *Salmonella* spp. and *Campylobacter* spp.

3.3 Laboratory capacity

In 2016, the EU Laboratory Capability Monitoring System (EULabCap) index of Norway was 8.3, which slightly improved since 2013 (8.1). Other data from the EULabCap indicated that the public health microbiology system had a high and stable level of capability/capacity. Antimicrobial susceptibility testing in all laboratories is based on the implementation of EU standards (EUCAST) and molecular and genomic surveillance is fully deployed. The EU 'One Health' surveillance protocol is applied to AMR monitoring and reporting in zoonotic pathogens. However, not all clinical laboratories are accredited according to ISO/national standards (which are not required to obtain biosafety authorisation for BSL2/CL2 operations) and key national diagnostic testing guidelines are not monitored for compliance in clinical practice.

All 24 clinical microbiology laboratories in the country are properly equipped, financed by the public health system and include microbiologists in their staff. All GPs can send isolates from the community clinics and/or LTCFs to the clinical microbiology laboratories, although it is not clear if and when GPs receive feedback on preliminary results. Concerns about long waiting times for laboratory results were expressed in one hospital that we visited, which reported an average of four days between taking the sample and getting the results. Reportable pathogens are referred from clinical microbiology laboratories to national surveillance, in addition to the reporting of cases by clinicians.

There are several AMR reference laboratories in Norway. For example, the MRSA reference laboratory is in Trondheim, whereas Enterobacteriaceae isolates resistant to carbapenem and/or colistin are referred to the clinical microbiology laboratory at the University Hospital of North Norway in Tromsø. Isolates of reportable antimicrobial-resistant pathogens are sent to reference laboratories for phenotypic confirmation, genetic resistance mechanism identification, and whole genome sequencing (WGS).

Significant investments have recently been made at the NIPH reference laboratory with the aim of shifting from mainly phenotypic testing for antimicrobial susceptibility to WGS. However, concerns were expressed about the ability of the NIPH reference laboratory to detect emerging, but currently unknown, antimicrobial resistance

mechanisms if only WGS methods are used, particularly given the 10% budget cut imposed on the NIPH reference laboratory, which de facto results in the reduction of routine, phenotypic antimicrobial susceptibility testing.

3.4 Monitoring of antibiotic resistance

Monitoring of AMR in Norway is based on four pillars: routine data such as that providing information to EARS-Net and considered of good quality; surveys based on the Norwegian Surveillance System for Antimicrobial Drug Resistance (NORM) specific protocols; the National Notification System for Infectious Diseases (MSIS) hosted at NIPH, and data reported from reference laboratories.

The notification pathway starts with a microbiology laboratory identifying a resistant isolate and sending this isolate to the reference laboratory for confirmation. Once confirmed, both the primary and the reference laboratory send a notification to MSIS and the primary laboratory sends the result to the treating physician. The latter will send a pre-defined referral to the MSIS with epidemiological and clinical information to obtain a complete picture of the reported case. Reference laboratories do not receive the clinical and epidemiological information on the tested isolate, thus limiting their possibility to investigate outbreaks or perform root-cause analysis of infection or carriage of resistant bacteria. It was reported that the notification rate from GPs is declining, although drivers for this trend are unclear. During the visit, the team noticed that GPs rarely perform screening tests to detect carriage of resistant bacteria, and when this was done it was generally only for MRSA.

No formal notification system exists between hospitals and communication is generally on a voluntary basis. This informal system is perceived as being sufficient and formalisation is not considered necessary.

Every year a combined NORM/NORM-VET report is produced describing the proportions of AMR in bacteria from humans, animals and the environment, together with special topics of relevance. These results are based on routinely collected surveillance data, mainly from hospital laboratories that also test isolates sent in by primary care facilities (almost all laboratories in Norway participate). Data are generally sent from microbiology laboratories and epidemiological information is usually limited and/or not standardised. For aggregate data visualisation there is NORM-atlas, with restrictions on personal case-based data for privacy reasons. The NORM-atlas allows municipalities to monitor themselves and compare their resistance proportions with that of other regions and municipalities. We were shown an example from a large university hospital that publishes local surveillance data every month.

During the visit, we were presented with the latest epidemiological information published by NORM. Around 6% of *E.coli* from bloodstream and urinary tract infections are ESBL producers and this proportion has increased in recent years. The number of cases of carbapenemase-producing Enterobacteriaceae (CPE) cases – mainly *E. coli* and *K. pneumoniae* – has also been increasing, particularly between 2014 and 2015, with the most frequent carbapenemase being OXA-48 and cases mainly seen in patients having travelled outside of Norway. Several outbreaks of vancomycin-resistant *Enterococcus* spp. (VRE) have been reported, with a *VanB* strain linked to a specific hospital infectious disease ward. Infected and colonised cases of MRSA have increasingly been registered, predominantly in primary care and LTCFs, with about half of the cases having been acquired outside of Norway.

The NORM protocols are based on specific epidemiological questions and research objectives. Good quality of the datasets is a priority and they are checked for completeness and validity. For example, reporting of categorical susceptibility data based on results from automated systems is not accepted.

Norway has established a national advisory unit on detection of AMR (K-res), with the aim of building up competence to ensure that AMR is detected in accordance with national guidelines; to act as a reference to other microbiology laboratories for the definition of phenotypic and molecular analysis for the detection and characterisation of resistant bacteria, and to promote research at a high international level in collaboration with the national and international scientific community (K-res is a European Society of Clinical Microbiology and Infectious Diseases (ESCMID) collaborative centre and a EUCAST laboratory, and promotes the exchange of students and supervision of PhD projects).

3.5 Monitoring of antibiotic usage

Personal data, such as individual prescriber's name, patient's age, sex and geographical location, can be linked to prescriptions and these data are hosted by the Norwegian Prescription Database (NorPD) at the NIPH. However, for primary care prescriptions, the indication, diagnosis or infection related to a prescription are not collected in NorPD due to privacy issues. For hospitals, information on prescription is based on sales, and the hospital pharmacy is able to obtained detailed information of antimicrobials for each ward. Other information on antibiotic consumption in hospitals is collected through point prevalence surveys, although this information is limited to antibacterials for systemic use (ATC group J01). Similarly, information on antibiotic consumption in LTCFs is obtained from wholesale databases and prevalence surveys. The above-mentioned data collection systems are financially supported by the government, but further analyses of the data depend on the particular initiatives and interests of researchers.

The NIPH is hosting and financing the WHO Collaborating Centre for Drug Statistics, which is responsible for the maintenance and development of the ATC/DDD methodology used by WHO and globally for the monitoring of drug consumption, including consumption of antimicrobials. However, recent budget cuts at the NIPH are threatening the prominent role of this WHO Collaborating Centre.

Antibiotic consumption is low in Norway compared to other EU/EEA countries, and public awareness on the effects of inappropriate antibiotic consumption is high, which helps to keep the prescription of antibiotics low. In primary care, prescriber's information is generally used for self-assessment of the consistency of prescriptions with guidelines, and in hospitals aggregated data are used for local group discussions on antibiotic prescribing. Nevertheless, individual prescribers do not receive regular feed-back on their own antibiotic prescription patterns compared with that of their colleagues.

One target of the national strategy and action plan is to lower the number of antibiotic prescriptions by 30% by 2020. To help achieve this goal, a proper level of consumption has been estimated at country, regional and municipal level based on national and local indicators and benchmarks. Moreover, the trends in antibiotic consumption are monitored, by age group and indication, based on the epidemiology of infectious diseases and on guidelines.

3.6 Antibiotic utilisation and treatment guidance

On average, GPs account for 80% of antibiotic prescriptions, 5% in dental practices, 6% in long-term care facilities (LTCFs) and the remaining 7–8% of prescriptions occur in hospitals. All prescriptions, except for those in hospitals, must serve the purpose of alleviating symptoms and shortening the duration of infections, not necessarily saving patient lives.

A few targeted interventions aiming to further reduce the number of prescriptions have been implemented in several primary care areas. In LTCFs, for example, discussion with doctors and nurses in five counties on the appropriateness of prescribing antibiotics for the frequent number of urinary tract infections in LTCF residents have resulted in a 15–18% reduction in the number of prescriptions.

Other measures include tailored guidelines for GPs, dentists and prescribers working in LTCFs. Primary care guidelines are available via a dedicated website (www.antibiotika.no) and a phone application which has been downloaded more than 15 000 times. GPs were extensively involved in the development of the guidelines and related decision support trees (also embedded into patient electronic charts), resulting in the guidelines being the most used source of information on antibiotic prescribing. The system includes information on rapid diagnostic testing and how to interpret the results. Information on conferences and continuous medical education (CME) courses is also available.

In addition, the intervention 'Riktigere Antibiotikabruk i Kommunene' is built around the use of academic detailing and consists of three group meetings in supplementary education groups and an e-learning course. At the core of the intervention is the antibiotic report tailored for each attending GP, based on data from the prescription registry. In this report, GPs learn about their own prescription rates, the distribution of the types of antibiotics used and their indications. GPs can benchmark their prescription pattern with that of other GPs in the same local area, the same county and the whole country. The report is an important tool in the discussions among colleagues in the education groups. Since the beginning of the intervention, attended by 40–50% of GPs, a 15% reduction in total GP prescriptions has been observed, with a 22% increase in the use of penicillin V for respiratory infections, a decrease in the prescription of tetracyclines and macrolides, and a 4–6% decrease in the prescription of quinolones for urinary tract infections.

As part of intervention, an antibiotic-free prescription ('Antibiotikafri resept') information leaflet (available in six languages) has been developed for distribution by GPs to patients when an antibiotic is not prescribed. The leaflet describes how long the infection will last, the reasons why an antibiotic prescription was not necessary, information on AMR and what to do if the infection persists.

During our interactions, GPs expressed their satisfaction with the amount of time allocated for patient consultations. This allows for thorough clinical examination and exchange of information, including raising awareness on AMR and antibiotic use, as well as the appropriateness of antibiotic prescription, which in turn increases acceptance from patients when an antibiotic is not prescribed.

The Norwegian Directorate of Health is responsible for developing national antimicrobial prescription guidelines in hospitals. The latest guidelines were published in 2013 and 30 000 copies have been printed and distributed amongst hospital prescribers. A computer and phone application is also available and is accessed on average 50 000 times per month. The 2013 guidelines have not been updated because of the lack of resources. It has been reported that many regional and local guidelines are available, although the examples provided date from before 2013.

The National Centre for Antibiotic Use in Hospitals (KAS) was established in 2011 and has a budget of EUR 360 000 from the Ministry of Health and Care Services. It is a multidisciplinary unit with infectious disease specialists,

pharmacists and nurses and staffing of 2.5–3 full-time equivalents, located within the Division of Patient Safety of the 'Helse Bergen' and Haukeland University Hospital. The main activities of KAS are to network and promote antibiotic stewardship teams through meetings, conferences, website resources and reports on antibiotic use, to prepare and distribute material for European Antibiotic Awareness Day (EAAD), and to assist other hospitals in antibiotic stewardship programmes.

In one hospital that we visited, a multi-disciplinary antibiotic stewardship team was in place, which included an infectious disease physician (leading the team), a microbiologist, an infection control physician, an infectious disease nurse, a surgeon and delocalised physicians at the same hospital. As in other hospitals in Norway, information on consumption is based on sales of antibiotics; however, a new electronic system will soon be in place, which will include the indication for the antibiotic prescription and other patient and prescriber information. Some prescription restrictions are already in place, such as the need to obtain an infectious disease opinion and agreement before prescribing carbapenems or colistin. Some challenges and areas for improvement were presented, such as the need to further involve hospital leadership, define/monitor/evaluate knowledge requirements for all prescribers and perform regular audits on the compliance to prescription guidelines.

In another hospital that we visited, a multi-disciplinary antibiotic team was in place and was responsible for stewardship both at hospital and community levels. The team has many tasks, ranging from developing antibiotic consumption reports (stratified by hospital unit), to developing communication strategies (also for EAAD), improving microbiology testing, and monitoring and evaluating stewardship activities within the different clinical units and delocalised healthcare centres. The latter intervention, for example, ensured a 50% reduction in the prescription of broad-spectrum antibiotics in a local hospital. However, the antibiotic team voiced their concern regarding the difficulties of involving leadership. Other concerns are related to the tendency of prescribers to substitute broad-spectrum antibiotics with penicillin, even when an antibiotic is unnecessary in the first place. However, the antibiotic team managed to achieve relevant outcomes, such as increasing knowledge of prescription guidelines and raising awareness on the positive effects of prudent use of antibiotics.

Adherence to prescription guidelines is assessed through specific audits and projects. In one hospital that we visited, a recent audit on the implementation of antibiotic stewardship (mainly based on mandatory e-learning for prescribers and a two-day course for nurses) through interviews of leaders showed that, although a good general structure is in place, there was a lack of clear goals, a need to empower nurses and a need to facilitate the review of prescriptions after three days.

3.7 Infection prevention and control

Infection prevention and control (IPC) in Norwegian healthcare is based on two legislative frameworks; the first dating from 1996 regulating the screening of healthcare workers for antibiotic-resistant bacteria and the second, in 2005, regulating HAIs and antibiotic consumption. The latter was the basis for the implementation of the Norwegian Surveillance System for Healthcare-Associated Infections (NOIS) hosted at the NIPH. It became mandatory for all healthcare institutions to have an infection control programme, written guidelines and surveillance of HAIs. Moreover, an IPC committee was formally established. However, the legislation does not cover IPC in dental services, home-based care and other institutions for the elderly.

The legislative framework defines the roles and responsibilities of all actors in the healthcare system. All municipal health institutions are required to have an IPC programme, and ensure assistance and training for IPC. Regional competence centres for IPC are established, which are responsible for initiating IPC programmes in hospitals, facilitating an appropriate distribution of IPC personnel, developing and coordinating IPC activities in the region, assisting the municipal authorities when requested and providing expert assistance (counselling, surveillance, competence-building measures for personnel, research and outbreak investigation) in cooperation with the NIPH. The NIPH coordinates activities related to IPC, is responsible for national surveillance, prepares annual statistics on HAIs, stimulates professional development, provides assistance in outbreaks, and coordinates the development of guidelines and surveys. The Norwegian Directorate of Health is responsible for the overall IPC strategy, sets IPC standards and formulates requirements for education in IPC.

Norway does not have a national programme or action plan on IPC. Hospitals and LTCFs generally have written IPC programmes, although implementation and updating was reported to be limited in most settings. Other healthcare services are not required to have an IPC programme. Moreover, Norway does not have a national programme or action plan on IPC. All hospitals have IPC nurses, but many lack formal education – no formal IPC education is required to become an IPC nurse – and they also work in areas other than IPC. A recent survey showed that smaller hospitals have one IPC nurse per 250 beds, whereas large hospitals have, on average, one IPC nurse for 488 beds. Most hospitals either do not have an IPC doctor or only allocate a small proportion of a doctor's time to IPC. It should be noted that IPC is not a topic in the education of medical personnel.

Compliance with hand hygiene measures was not reported to be audited on a regular basis, and auditing is mainly done according to structural indicators. One university hospital that we visited had an IPC centre was in place. It consisted of two doctors and four nurses who meet regularly. They report on HAIs and can initiate root-cause

analysis during outbreaks, and report on antibiotic consumption to the wards and discuss stewardship with the prescribers. They are also responsible for the hospital IPC programme and preparedness planning, counselling, education and internal audits. They are involved in the remodelling of hospital buildings and assisting in the revision of regional and national IPC guidelines. In another university hospital, the IPC team, which is also responsible for antibiotic stewardship and surveillance, is placed within the patient safety unit and is multi-disciplinary (infectious disease physician, microbiologist, nurses and pharmacist). They perform daily rounds in clinical wards and aim to improve IPC through leadership commitment and discussions with nurses. A monthly epidemiological review is undertaken that will inform risk assessments and guidelines, as well as counselling and education.

IPC in LTCFs is considered the responsibility of the municipality and it is common for IPC personnel not to be on site. Staff involved in home-based care and dentistry do not require specific IPC training.

National guidelines for hand hygiene were published in 2017. These guidelines were developed by the NIPH together with representatives from all regions and municipalities. NIPH has set up a dedicated hand hygiene website, and develops educational materials and posters to hang in hospital wards for communication with healthcare workers and the general public.

National guidelines also exist for the prevention of catheter-associated urinary tract infections (2013), for the screening and handling of patients with MRSA (2009) and for the isolation of patients (2004). National guidelines on IPC are currently being developed at the NIPH. All hospitals and most LTCFs have local IPC guidelines, although these are not regularly updated or based on scientific evidence. It was suggested that the latter might represent an unnecessary use of resources.

The compulsory tasks of NOIS include the implementation – twice a year and ongoing since 2002 – of point prevalence surveys (PPSs) of HAIs and antimicrobial consumption in hospitals and LTCFs (60% of all LTCFs), and to implement prospective surveillance of surgical site infections based on ECDC surveillance protocol, focusing on five types of surgical interventions (coronary artery bypass grafting, hip replacement, Caesarean section, cholecystectomy and colon surgery). The results from the last PPS in 2017 show a decrease in the prevalence of HAIs to below 5% in hospitals and in LTCF. The PPS also showed that 28% of hospitalised patients were given antibiotics, of which 33% were broad-spectrum agents (about one third were used to treat HAIs). Of those HAIs treated with broad-spectrum antibiotics, 72% had a clinical microbiology sample, compared to 78% for other antibiotics. The most commonly prescribed broad-spectrum antibiotics were piperacillin-enzyme inhibitor combinations and third-generation cephalosporins. Patient data are anonymised in NOIS and the data represent a public quality indicator at institutional level.

The Norwegian Board of Health Supervision is responsible for IPC audits. The number of audits in LTCFs and of home care workers is unknown. Other audits carried forward by the Board related to isolation and IPC in ten health trusts (2006), IPC in six intensive care units (ICUs) (2002) and IPC services in municipalities (2002). In addition, local audits are being performed. Only 10% of hospitals report having audits for IPC, 60% report having audits for antibiotic use and very few audits have been performed for hand hygiene.

An IPC education programme for nurses in training will start in August 2019 and this will correspond to 60 (ECTS) credits. However in Norway, IPC is neither a medical specialty, sub-specialty, or academic discipline. While 70% of training sessions in hospitals focus on appropriate antibiotic use, only 30% are centred on IPC and very little research on IPC is promoted.

'Sykehusbygg' is a competence organisation owned by the regional health trusts and used when planning and building hospitals. 'Sykehusbygg' is currently developing guidelines on how IPC should be considered when building hospitals. An indicator survey found that 44% of the rooms in Norwegian hospitals are single rooms and that around 13% of patients have their own toilet and shower. Concerns were raised on the isolation capacity in hospitals, particularly in ICUs where there seems to be insufficient isolation rooms and personnel to care for isolated patients. Most hospital beds have alcohol hand rub dispensers for hand hygiene, although during our visit the team found several empty dispensers and the dispenser was often not easily accessible (i.e. not at the foot of the bed).

Screening policies for resistant bacteria in hospitals are claimed to be based on 'search and destroy' tactics. Upon admission, patients will be considered for screening of MRSA, VRE and ESBL-producing Enterobacteriaceae if they have been admitted to a hospital outside of the Nordic region in the previous 12 months, if they have been admitted from a Nordic hospital with an ongoing outbreak or if the patient has previously had a positive result for MRSA, VRE or ESBL. In addition, patients or healthcare workers are screened for MRSA if they have worked in a hospital outside of the Nordic region or if they have been in close contact with a known carrier. High-risk units are advised to consider screening all patients for carbapenemase-producing organisms (CPOs), although the application of this recommendation seemed to differ in the hospitals we visited. Some hospitals have slightly different screening policies and, for example, will screen any patient hospitalised abroad, even from a Nordic country. On the other hand, the same hospital might not screen a returning traveller (e.g. backpacker) requiring hospitalisation who may well be carrying an ESBL-producing Enterobacteriaceae.

In one hospital that we visited, a VRE outbreak that started in 2011, and looked as if it was under control by 2015, seems to have started again in 2017, is ongoing in the hospital, and has now extended (same strain according to whole genome sequencing) to LTCFs in the region. The extent of this outbreak in the region is unclear, and it is also unclear whether, in 2018, the VRE strain has spread to other hospitals and other regions in the country.

In Norway, the target influenza vaccination rate is set to 75% for the defined population at risk (healthcare workers, general population over 65 years and/or affected by a chronic condition). However, during the 2016–2017 season, only 17% of healthcare workers having contact with patients were vaccinated (15% in the general population overall and 28% in the population at risk). The vaccination coverage rates have increased during the 2017–2018 season, although they are still far from the target.

3.8 Educational programmes on AMR

A goal of the national action plan is to improve the knowledge of nurses on AMR and increase their training in antibiotic stewardship. As described above, a Nordic education programme in IPC will start in August 2019 as part of the training for nurses and doctors, but also other types of health personnel.

Antibiotic stewardship and AMR are topics in undergraduate medical and nursing schools, although the approach is not standardised and curricula may differ between universities. There is no formal postgraduate, ongoing education and training on antibiotic stewardship in Norway. Industry-sponsored workshops no longer exist as pharmaceutical companies do not seem to be interested in promoting antibiotics in Norway.

Knowledge-based update visits (KUPP), an experimental implementation of academic detailing for antibiotics prescribed by GPs has been ongoing since 2015, promoted by St. Olavs hospital, Trondheim, and the Central Norway RELIS (regional medicines information and pharmacovigilance centre). A focus group composed of clinical pharmacologists, pharmacists and GP representatives discussed the information available from antibiotic prescription guidelines and other published scientific evidence. The focus group prepared a distilled set of independent a priori key messages for GPs trained by the group in order to maximise the effectiveness of the 20-minute academic detailing meeting with individual GPs in their office. These messages focus on appropriate antibiotic prescription, screening and patient education. The messages are presented and interactively discussed with the GP visited, although their specific prescription patterns are not reviewed. The GP visited is given the opportunity to reflect on whether their own practice is in accordance with the best available evidence, and make changes if needed. All GPs in the Trondheim area were offered a visit and 80% accepted, with many welcoming a subsequent re-visit during which the key messages were repeated and reinforced.

The first results from the deployment of academic detailing to 450 GPs, during which the main messages centred on appropriate use of antibiotics for respiratory infections and choosing penicillins over macrolides and fluoroquinolones, showed that prescriptions for penicillins increased by 5.6% in the intervention group compared to a 7.6% decrease in the control group. Prescription of fluoroquinolones showed a 21.2% decrease in the intervention group compared to a decrease of only 12.5% in the control group.

3.9 Public information related to AMR

Norway has implemented communication campaigns focusing on the prudent use of antibiotics and has been participating in European Antibiotic Awareness Day (EAAD) since 2008. Most of the communication activities around antibiotic resistance in Norway take place between November and January.

A campaign was launched in 2016, with the objective of informing the general public about the relationship between overuse of antibiotics and emergence of antibiotic-resistant bacteria. This was done in collaboration with a communication agency, and after working with focus groups to determine what the public knew and thought about antibiotics and antibiotic resistance. The findings of the focus groups showed that the Norwegian population, in particular the parents of small children, have confidence in their doctor and a good overall knowledge of the issue. However, the technicalities of antibiotic resistance, its impact on their own lives and the actions that they could take, were not common knowledge among focus group participants. Taking this into account, the Norwegian Directorate of Health and the NIPH have developed a campaign with two practical objectives: appealing to emotions with messages about what could happen in a world without antibiotics, and producing materials with key data translated into simple messages. Social media results indicate that the campaign was successful among the selected audience but also with health professionals. Information on travel-related risks of infection or colonisation with antimicrobial-resistant bacteria has still not been included as part of the awareness campaigns.

Communication efforts in other areas are also ongoing - e.g. smaller campaigns on hand hygiene and IPC, as well as prevention and treatment of sexually-transmitted diseases. Age segments where antibiotic consumption is high, such as people aged 55 years and above, are not targeted through communication initiatives. Norway is also working with Sweden, Finland, Denmark and Iceland on a Nordic project, with the aim of sharing and translating materials.

Public relations are relevant and well managed and there is close cooperation with key journalists across the country. Media interest is high with regard to AMR and hospital safety, and an increase in coverage has been visible since 2011. The latter could be attributed to the international interest in the topic due to EAAD and the World Antibiotic Awareness Week (WAAW), as well as national efforts and strategies.

Evaluation measurements include process indicators, such as media clippings or social media statistics (e.g. reach, video views and reactions.) These were high for the campaign in 2016 and the follow-up efforts in 2017. Perception studies are not available in the country and Norway is not included in the European Commission's Eurobarometer surveys on AMR.

Collaboration between ministries and professional groups is well established. However, there does not seem to be any link up with other groups developing campaigns on AMR awareness, such as MSF Norway or the Norwegian Cancer Society.

Hard-to-reach populations have been identified and are being targeted for communication on many health-related topics, including antibiotics. Outreach is done through community leaders, by translating key messages and using simple language that can be understood by individuals learning Norwegian.

'One Health' campaigns and other communication efforts have been discussed. The first initiative will involve communicating to dentists, veterinarians and doctors about the change in the duration of antibiotic treatments. Other plans might include a campaign for veterinarians taking care of small animals and horses.

3.10 Marketing related issues

The Norwegian Medicines Agency aims to ensure that information on medicines is independent and is disseminated to prescribers. Guidelines have been developed for this purpose by the Directorate of Health, the ASP, the NIPH, public hospitals, KUPP and public primary care providers.

Ethical guidelines on the relationship between physicians and the pharmaceutical industry are in place ('A doctor may not interact with the pharmaceutical industry in a manner that may affect trust in the doctor's decision'). Personal gifts or other benefits given by the industry are illegal.

In Norway, a doctor's salary is completely unrelated to prescriptions. Advertising for antibiotics is restricted and there is no advertising on antibiotics for systemic use.

4 Conclusion and recommendations

4.1 Conclusions

Data from the European Antimicrobial Resistance Surveillance Network (EARS-Net) show that the proportion of AMR in bacteria from bloodstream infections in Norwegian patients is consistently below the EU/EEA average and often among the lowest in Europe. Nevertheless, although significantly below the EU/EEA average, resistance to broad-spectrum antibiotics such as third-generation cephalosporins has been increasing over the past 10 years. This is the result of emergence of strains that produce an extended-spectrum beta-lactamase (ESBL), combined with increasing consumption of broad-spectrum antibiotics in healthcare.

Norway's consumption of antibiotics is below the EU/EEA average, both in the community (i.e. outside of hospitals) and in the hospital sector. Nevertheless, faced with a steadily increasing antibiotic consumption in the community since 2000, Norway first published a first cross-sectoral action plan to prevent antibiotic resistance (2000–2004), then a 'National strategy for prevention of infections in the health service and antibiotic resistance (2008–2012)'. Finally, in 2015 Norway published its 'National strategy against antibiotic resistance 2015–2020' which took a 'One-Health' perspective, with sector-specific goals to be reached by 2020. These goals included substantial reductions of antibiotic consumption in human medicine and maintenance of the already low antibiotic consumption rate on the animal side, with specific initiatives for fisheries and turkey production. The national strategy also included AMR targets in food-producing animals, such as ensuring that livestock-associated meticillin-resistant *Staphylococcus aureus* (LA-MRSA) does not establish itself in the Norwegian pig population.

In 2016, the Norwegian Ministry of Health and Care Services published an 'Action plan against antibiotic resistance in the Norwegian health services with the aim of reducing the use of antibiotics in the Norwegian population by 30 percent by year-end 2020'. This included 20 measures, mainly covered by the existing budgetary framework at various levels. One notable exception is specific funding allocated to the establishment of a national steering committee and reference group to strengthen the Antibiotic Centre for Primary Care (ASP) and carry out academic detailing[6] for antibiotics in primary care (KUPP). This renewed momentum has already resulted in decreasing antibiotic consumption and it is likely that, if these actions are sustained, Norway will reach or even go below the antibiotic reduction targets in humans that it has set for 2020. It is currently too early to assess whether these reductions have had an effect on decreasing AMR.

Compared with many other European countries, Norway has a long-standing history of increased awareness of AMR issues, with a focus on controlling the spread of MRSA. The recent success towards eradication of LA-MRSA from Norwegian pig herds, through 'One Health' collaboration, is another example of how targets, such as those in the National Strategy, and clear responsibilities result in rapid change.

Since 2010, many hospitals in Norway have experienced cases and sometimes substantial outbreaks of vancomycin-resistant *Enterococcus faecium* (VRE) by Norwegian standards. One university hospital is now facing an endemic situation. In addition, an increasing number of cases of carbapenem-resistant Enterobacteriaceae (CRE) have been reported in the country in recent years, particularly since 2015. These are sometimes referred to as $ESBL_{CARBA}$ although they are more resistant than the usual ESBL-producing strains. CRE are highly drug-resistant bacteria, that are even resistant to the safest last-line antibiotics - i.e. carbapenems - and options for the treatment of CRE-infected patients are even more limited.

According to the data that were presented to us, most CRE cases were related to hospitalisation abroad and/or international travel. However, a substantial proportion of cases could not be accounted for via this route of transmission and therefore there is a concern that patient-to-patient transmission in Norway has occurred, causing at least one outbreak.

Examples from other European countries show that if spread of VRE and CRE is not tackled at an early stage, these multidrug-resistant bacteria will inevitably spread within the affected hospitals, between hospitals and long-term care facilities (LTCFs) in affected regions, and ultimately between hospitals in different regions of the country. While Norway has been and continues to be quite successful at controlling MRSA, these new developments show that the control of VRE has not been equally successful. Once introduced into the healthcare system, CRE is even more difficult to control and the clinical consequences result in greater patient mortality and morbidity. There is concern that once this happens, the existing system for detection and control of CRE may fail, as has happened in some hospitals with VRE.

Thanks to its existing structures and the large number of experts, Norway is still in a good position to reverse these new trends in AMR. However, VRE, CRE and other emerging multidrug-resistant bacteria each require the implementation of a new set of well-coordinated, specific actions over and above the current sustained efforts to reduce antibiotic consumption in humans. The focus must be a rapid step-up of infection prevention and control in

[6] University or non-commercial-based educational outreach

the country. This is essential if Norway wants to retain its good international position regarding AMR and secure the safety of its patients in healthcare.

4.2 Recommendations

Continue with the actions that are part of the current action plan against antibiotic resistance in the Norwegian health service which have already proven successful in reducing the consumption of broad-spectrum antibiotics.

Step-up hand hygiene and standard precautions in hospitals and all other healthcare settings, through a campaign that focuses on raising awareness. Process indicators relevant to infection prevention and control need to be established, including effective hand hygiene, through audits in all hospitals.

Increase all healthcare professionals' knowledge of VRE and CRE and the measures necessary to detect, prevent and control their spread. This can be achieved by various means such as awareness campaigns, training courses in hospitals and even academic detailing for VRE and CRE prevention and control measures. This, in turn, will require adequate numbers of professionals formally trained in infection prevention and control and would require establishing a career path in infection prevention and control. The current heterogeneity in the numbers of infection control nurses and doctors – as well as their background training – should be addressed by establishing clear complement requirements (e.g. a ratio of infection control nurses per bed), based on hospital type and size and indicating the basic level of training needed.

Support and coordinate control of VRE and CRE at national level by

- formally appointing one reference laboratory for VRE and CRE (this can be the same laboratory);
- ensuring that a strong epidemiological team at the Norwegian Institute of Public Health (NIPH) coordinates collection of data on VRE and CRE at national level and that these data are translated into support and field investigation where necessary (cases with unknown or unclear mode of transmission should be considered for root-cause analysis);
- ensuring a robust coordinating role and the regular link between these reference laboratories and the epidemiological team at NIPH;
- strengthening the department undertaking infection prevention and control at NIPH so that it can be more pro-active in providing standardised guidance to hospitals, as well as providing expert support in outbreaks, especially when they have the potential to involve different regions, hospitals and municipalities.

Control VRE and CRE at hospital level by ensuring (a) that the currently recommended screening programmes are properly applied and possibly expanded, (b) that the results are communicated rapidly, and (c) that the necessary control measures involving the infection control team are implemented. Norway could consider audits on preparedness for prevention and control of VRE and CRE in all hospitals. Ultimately, this could be extended to other healthcare settings and in particular to LTCFs. To ensure the good use of available local data, Norway should consider training infection control teams on how to make sense of surveillance data and how to investigate outbreaks.

At AMR reference laboratories, phenotypic testing is essential to identify resistance due to currently unknown genes. At present this cannot be achieved by only performing next generation sequencing. In addition, AMR reference laboratories that do phenotypic testing can continue to provide advice and support to local clinical microbiology laboratories. It is essential for Norway that phenotypic testing for AMR is maintained at reference laboratories.

The actions on prevention and control of VRE and CRE would most probably need to be combined in an Action Plan for the prevention and control of multidrug-resistant organisms in Norwegian healthcare applicable to hospitals, LTCF and other settings, such as primary care.

Norway should consider including targets in this new action plan since in the current action plan the activities related to antibiotic reduction that have been successful are those with clear targets. In addition, specific funding should be allocated for the above-mentioned activities – or at least a mechanism should be put in place to ensure that national agencies and regions are prioritising these activities.

The national antibiotic guidelines for hospitals should be reviewed and revised where necessary. One particular issue that will need to be considered is situations where the current first-line regimen of penicillin/ampicillin + gentamicin should no longer be recommended because of increasing proportions of AMR.

Academic detailing on prudent use of antibiotics for GPs and in LTCFs has proven successful and, if the resources for continued national deployment are not available, **Norway should consider focusing on the prescribers of the highest numbers of antibiotics as this would provide the best value for money**.

In primary care, the introduction of electronic prescriptions represents an opportunity to collect, analyse and routinely feed back detailed information on antibiotic use by prescriber, type of patient and indication, without the

need for the prescriber to have to request such information. **This data should routinely be fed back to prescribers whenever academic detailing is undertaken**.

In hospitals, the focus on reducing consumption of broad-spectrum antibiotics should continue. In addition, regions and hospitals should investigate the reasons for the high consumption of third-generation cephalosporins, for example by performing audits on prescription and giving feedback to prescribers. Behaviour change interventions should be introduced, aimed specifically at third-generation cephalosporins and carbapenems. These are already undertaken in some hospitals and include restricted laboratory reporting and the need for authorisation by an infectious diseases/microbiology expert before these antibiotics can be dispensed.

Finally, we would like to express concern that the operation of the WHO Collaborating Centre for Drug Statistics Methodology is currently at risk due to budget reduction. This centre is hosted at NIPH and financed by Norway. The Centre provides services and advice to WHO on the ATC/DDD[7] index which is the classification and metric used to perform surveillance of consumption of antibiotics and of other medicines. This system is used at WHO and worldwide and Norway is recognised globally for this contribution.

[7] ATC/DDD - anatomical, therapeutic and chemical (classification system)/defined daily dose

Annexes

Country visit team and people met during the ECDC country visit to Norway to discuss AMR issues

ECDC Team

- Alessandro Cassini, Expert for Antimicrobial Resistance and Healthcare-associated Infections, ECDC, Stockholm, Sweden
- Dominique L. Monnet, Head of Antimicrobial Resistance and Healthcare-associated Infections (ARHAI) Programme, ECDC, Stockholm, Sweden
- Michael Borg, National Focal Point for AMR, National Focal Point for Antimicrobial consumption, National Focal Point for Healthcare-Associated Infections, Malta
- Ute Wolff Sönksen, Clinical Microbiology specialist, National Focal Point for AMR and for Antimicrobial Consumption, Bacteria, Parasites & Fungi, Statens Serum Institut, Copenhagen, Denmark
- Walter Zingg, Infection Control Programme of the University of Geneva Hospitals in Switzerland; Infection control programme, Imperial College NHS Trust, London, United Kingdom
- Andrea Nilsson, Communication Specialist Press and Media, Communication Support, ECDC, Stockholm, Sweden (12 and 13 March)

Persons met

Monday 12 March 2018

Meeting on the status of the Norwegian strategy for antimicrobial resistance, governance and action at ministerial level: Ministry of Health and Care Services, Ministry of Agriculture and Food, Ministry of Trade, Industry and Fisheries, Ministry of Climate and Environment and Ministry of Foreign Affairs, Norwegian Veterinary Institute

Ministry of Health and Care Services, Oslo

- Lise Albreschtsen, Senior Advisoer, Ministry of Foreign Affairs
- Kjersti Nilsen Barkbu, Senior Advisor, Ministry of Agriculture and Food
- Solveig Crompton, Senior Adviser, Ministry of Climate and Environment
- Carl Andreas Grøntvedt, Scientist, Norwegian Veterinary Institute
- Merete Hofshagen, Director of Animal Health and Food Safety Department, Norwegian Veterinary Institute
- Ragnhild Holst, Senior Adviser, Ministry of Health and Care Services
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Casper Linnestad, Senior Adviser, Ministry of Climate and Environment
- Stig Atle Vange, Ministry of Health and Care Services
- Anne Margrete Urdahl, Senior Researcher, Norwegian Veterinary Institute
- Nina Eriksen Vinje, Senior Adviser, Ministry of Trade, Industry and Fisheries
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Meeting to discuss implementation of the AMR strategy with a 'One Health' approach: Ministry of Health and Care Services, Norwegian Institute of Public Health, Norwegian Veterinary Institute, Norwegian Food Safety Authority, Norwegian Environment Agency and Norwegian Agency for Development Cooperation

Ministry of Health and Care Services, Oslo

- Petter Elstrøm, Researcher, Norwegian Institute of Public Health
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Aina Nedal, Senior Adviser, Norwegian Environment Agency
- Line Vold, Director of Zoonotic, Food- and Waterborne Infections Department, Norwegian Institute of Public Health
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services
- Kine Rautio Øverland, Senior Adviser, Norwegian Environment Agency

Detailed discussion on AMR in Health and Care Services: Ministry of Health and Care Services, Directorate of Health, Norwegian Institute of Public Health, Norwegian Medicines Agency, Norwegian Dental Association, University Hospital of North Norway, National Centre for Antibiotic Use in Hospitals (KAS), Independent drug information for healthcare professionals (RELIS), Antibiotic Centre for Primary Care (ASP)

Ministry of Health and Care Services, Oslo

- Per Espen Akselsen, Academic Director, National Centre for Antibiotic Use in Hospitals (KAS), Haukeland University Hospital
- Øyvind Asmyr, Head of Political Affairs and Continuing Education, the Norwegian Dental Association

- Hege Salvesen Blix, Senior Researcher, Norwegian Institute of Public Health
- Ulf Reidar Dahle, Laboratories Director, Norwegian Institute of Public Health
- Roar Dyrkorn, Chief physician, Independent drug information for healthcare professionals (RELIS)
- Hanne-Merete Eriksen, Acting Director of Resistance and Infection Prevention Department, Norwegian Institute of Public Health
- Svein Hoegh Henrichsen, Senior Adviser, Directorate of Health
- Sigurd Hortemo, Senior Physician, Norwegian Medicines Agency
- Harald Christian Langaas, Leader, Independent drug information for healthcare professionals (RELIS)
- Børge Myrlund Larsen, Senior Advisor, Directorate of Health
- Siri Jensen, Senior Advisor Researcher, Antibiotic Centre for Primary Care (ASP)
- Morten Lindbæk, Professor and Leader of the Antibiotic Centre for Primary Care (ASP)
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Ingrid Kristine Ohm, Advisor, Directorate of Health
- Gunnar Skov Simonsen, Head of Microbiology Department and Head of NORM, University Hospital of North Norway
- Andreas Skulberg, Senior Adviser, Directorate of Health
- Line Vold, Director of Zoonotic, Food- and Waterborne Infections Department, Norwegian Institute of Public Health
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Tuesday 13 March 2018

Visit to the University Hospital of North Norway (UNN HF): National Reference Laboratory for AMR, clinical microbiology laboratory, infection control unit, antibiotic stewardship team, intensive care unit, infectious disease ward, gastrointestinal surgery ward

University Hospital of North Norway, Tromsø

- Einar Bugge, Deputy CEO, University Hospital of North Norway
- Anne-Sofie Furberg, NORM, University Hospital of North Norway
- Bjørg Haldorsen, Norwegian National Advisory Unit on Detection of AMR, University Hospital of North Norway
- Haakon Lindekleiv, Chief Medical Officer, University Hospital of North Norway
- Annelin Lyshoel, Section Leader of the Infection Control Unit, University Hospital of North Norway
- Torni Myrbakk, Senior Physician of Infection Control, University Hospital of North Norway
- Markus Rumpsfeld, Head of Infectious Diseases and Internal Medicine, University Hospital of North Norway
- Ørjan Samuelsen, Norwegian National Advisory Unit on Detection of AMR, University Hospital of North Norway
- Jeanette Schultz Johansen, Pharmacist and member of the Antibiotic Stewardship Team, University Hospital of North Norway
- Gunnar Skov Simonsen, Head of Microbiology Department and Head of NORM, University Hospital of North Norway
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Visit to Nordbyen Regular General Practitioner officeTromsø

- Trygve Sigvart Deraas, General Practitioner, Nordbyen GP Centre
- Lise Zimowski Johansen, General Practitioner, Nordbyen GP Centre
- Gunnar Skov Simonsen, Head of Microbiology Department and Head of NORM, University Hospital of North Norway
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Wednesday 14 March 2018

Visit to the Haukeland University Hospital: infection control unit, antibiotic stewardship team, hospital pharmacy, National Centre for Antibiotic Use in Hospitals, microbiology laboratory, intensive care unit, infectious disease ward, surgery ward

Haukeland University Hospital, Bergen

- Per Espen Akselsen, Academic Director, National Centre for Antibiotic Use in Hospitals (KAS), Haukeland University Hospital
- Marit Helen Ebbesen, Clinical Microbiologist, Haukeland University Hospital
- Hans Flaatten, Intensive Care Unit, Haukeland University Hospital
- Merete Gjerde, IPC Nurse, Haukeland University Hospital
- Clara Gram Gjesdal, Deputy CEO and Director of Research and Development, Haukeland University Hospital
- Eivind Hansen, CEO, Haukeland University Hospital
- John-Helge Heimdal, Clinical Director Surgery, Haukeland University Hospital
- Janiche Heltne, Head of Gastro-surgical Department, Haukeland University Hospital

- Arild Horn, Gastrosurgical ward, Haukeland University Hospital
- Kristin Kilhus, IPC Physician, Haukeland University Hospital
- Frank Jørgensen, Hospital Pharmacist, Bergen Hospital Pharmacy
- Christoffer Lindemann, Microbiological Laboratory, Haukeland University Hospital
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Marion Neteland, Pharmacist, KAS and Antibiotic Stewardship Team, Haukeland University Hospital
- Dorthea Oma, IPC Physician, Haukeland University Hospital
- Brita Skodvin, KAS and Antibiotic Stewardship Team, Haukeland University Hospital
- Steinar Skrede, Infectious Disease ward, Haukeland University Hospital

Visit to the University of Bergen: Department of Clinical Dentistry at the University of Bergen

University of Bergen, Bergen

- Trond Berge, Professor, Department of Clinical Dentistry, University of Bergen
- Siv Kvinnsland, Specialist in Endodontology, Department of Clinical Dentistry, University of Bergen
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Bodil Lund, Professor, Department of Clinical Dentistry, University of Bergen

Visit to the Bergen city centre local pharmacy

VitusApotek Nordstjernen, Bergen

- Tonje Cecilie Mohn, Pharmacist
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Csaba Pataki, Pharmacist

Visit to the Attendo Kleppestø Nursing Home: infection control, antibiotic utilisation and treatment guidance related to nursing homes

Attendo Kleppestø, Askøy

- Kjellaug Enoksen, Public Health Medical Doctor, Kleppestø Nursing Home
- Janne Halvorsen, Head Nurse, Kleppestø Nursing Home
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services

Visit to Regular General Practitioner: infection control, antibiotic utilisation and treatment guidance related to general practice

Kokstad Medical Center, Kokstad

- Roger Borge, General Practitioner, Kokstad Medical Center
- Hege-Vala Førland, General Practitioner, Kokstad Medical Center
- Karina Koller-Løland, General Practitioner, Kokstad Medical Center
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Torstein Ljones, General Practitioner, Kokstad Medical Center

Thursday 15 March 2018

Visit to the Visit of Lovisenberg Deaconale Hospital

Lovisenberg hospital, Oslo

- Bjørn Brandsaeter, Chief Physician Infectious Diseases, Lovisenberg Deaconale Hospital
- Bjørn Magne Eggen, Chief Medical Officer, Lovisenberg Deaconale Hospital
- Per Gerlyng, Internal Medicine physician, Lovisenberg Deaconale Hospital
- Urszula Jadczak, Infection Control Nurse, Lovisenberg Deaconale Hospital
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Anne Marit Pedersen-Bjergaard, Pharmacist, Lovisenberg Deaconale Hospital

Visit to the microbiology laboratories at the Norwegian Institute of Public Health

Norwegian Institute of Public Health, Oslo

- Martha Bjørnstad, Microbiology, Norwegian Institute of Public Health
- Torbjørn Bruvik, Microbiology, Norwegian Institute of Public Health
- Nadia Debech, Microbiology, Norwegian Institute of Public Health
- Pal Kristiansen, Director of Bacteriology Department, Norwegian Institute of Public Health
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Anne Torunn Mengshoel, Mycobacteria microbiologist, Norwegian Institute of Public Health
- Martin Steinbakk, AMR microbiologist, Norwegian Institute of Public Health

Visit to the Infection Control Unit at the Office of the Health Authority in the Oslo Municipality

Health Authority, Oslo

- Catrine Dahl, Health Agency, Oslo Municipality
- Kirsten Marie Garder, Health Agency, Oslo Municipality
- Øystein Riise, Health Agency, Oslo Municipality
- Siri Seterelv, Nursing Home Agency, Oslo Municipality
- Tore W. Steen, Health Agency, Oslo Municipality
- Ingvild Vik, Medical Doctor, Antibiotic Centre for Primary Care and Oslo Accident and Emergency Outpatient Clinic (AEOC)
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Friday 16 March 2017

Preliminary report debriefing from the ECDC Team to Bent Høie, Minister of Health

Ministry of Health and Care Services, Oslo

- Bent Høie, Minister of Health
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Preliminary report debriefing from the ECDC Team to representatives of the Ministry of Health and Care Services, Ministry of Agriculture and Food, Ministry of Trade, Industry and Fisheries, Ministry of Climate and Environment, Ministry of Foreign Affairs, Norwegian Veterinary Institute, Norwegian Food Safety Authority, Norwegian Environment Agency, Directorate of Health, Directorate of eHealth, Norwegian Medicines Agency, Norwegian Medical Association, Norwegian Dental Association, Norwegian Institute of Public Health and the Antibiotic Centre for Primary Care

Ministry of Health and Care Services, Oslo

- Per Espen Akselsen, Head of the National Advisory Unit for Antibiotic Use in Hospitals
- Elin Anglevik, Head of Public Health Department, Ministry of Health and Care Services
- Øyvind Asmyr, Head of Political Affairs and Continuing Education, the Norwegian Dental Association
- Kjersti Nilsen Barkbu, Senior Advisor, Ministry of Agriculture and Food
- Hege Salvesen Blix, Senior Researcher, Norwegian Institute of Public Health
- Geir Bukholm, Division Director, Norwegian Institute of Public Health
- Petter Elstrøm, Researcher, Norwegian Institute of Public Health
- Frode Forland, Specialist Director, Norwegian Institute of Public Health
- Svein Hoegh Henrichsen, Senior Adviser, Directorate of Health
- Ragnhild Holst, Senior Adviser, Ministry of Health and Care Services
- Børge Myrlund Larsen, Senior Advisor, Directorate of Health
- Siri Jensen, Senior Advisor Researcher, Antibiotic Centre for Primary Care (ASP)
- Svein Lie, Director of Primary Care, Directorate of Health
- Torstein Lindstad, Senior Advisor, Department of Public Health, Ministry of Health and Care Services
- Ingrid Kristine Ohm, Advisor, Directorate of Health
- Øystein Riise, Health Agency, Oslo Municipality
- Gunnar Skov Simonsen, Head of Microbiology Department and Head of NORM, University Hospital of North Norway
- Andreas Skulberg, Senior Adviser, Directorate of Health
- Karl-Olaf Wathne, Special Advisor, Department of Public Health, Ministry of Health and Care Services

Assessment tool for ECDC country visits to discuss antimicrobial resistance (AMR) issues

The mechanisms behind emerging antimicrobial resistance (AMR) are complex. However, two main issues that stand out offering opportunity for control efforts are: the use of antibiotics and the epidemiological spread of resistant microbes.

The complexity of the problem makes it difficult to grade which interventions are most successful. Where interventions have been introduced few of them have been evaluated. This may partly be because few systematic interventions have been used.

The Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) lists a number of areas that have an impact on controlling AMR. Most of the following tentative indicators are based on the Council Recommendation. Some are based on experience from different countries. These indicators are either structure- or process-related. Outcome indicators are collected by dedicated surveillance networks.

1. Development of an Intersectoral Coordinating Mechanism (ICM)

Due to the complexity of the issue there is a need for coordination to make an interventional strategy work. There is also a need for close cooperation from fields such as epidemiology, microbiology clinical medicine, infection control, veterinary medicine, pharmacology and behavioural sciences. It also requires cooperation from practitioners working in different medical specialities as well as government departments and healthcare providers.

In the Council Recommendation on the prudent use of antimicrobial agents in human medicine (2002/77/EC) and the World Health Organization (WHO) Global Strategy for Containment of Antimicrobial Resistance (WHO/CDS/CSR/DRS/2001.2) the establishment of a coordinating group is regarded as essential.

Member States have different administrative organisations. There should be a group at the highest administrative level where representatives from regulatory bodies and professionals from the different sectors coordinate.

Tentative indicators for 1

Structures

- Multidisciplinary composition
- Regular meetings
- Minutes from meetings
- National strategy plan available
- Defined governmental mandate
- Financially supported by government.

Functions

- Coordinates analysis of consumption and plans and supports interventions
- Proposes national objectives and policies
- Proposes, plans and supports interventions
- Provides policymakers, media and public with continues updated and structured data
- Provides support to local working groups.

2. Organised multidisciplinary and multisectoral collaboration at local level

One of the main elements for control strategies is to lower the selective pressure of antibiotics by restricting usage to appropriate indications. There is much evidence showing that antibiotics are overused. Prescribers need to be well acquainted with the AMR problem and the rational of using antibiotics appropriately.

A non-regulatory intervention that has had some influence on prescribing habits is a local activity whereby practising physicians discuss local data on consumption and bacterial resistance patterns, supported by epidemiologists, pharmacists and infection control. This proves to be an appropriate opportunity to revise local usage patterns, develop local guidelines (based on national guidelines) and organise local meetings with prescribers to promote rational use of antibiotics. In addition, topical issues can be discussed, such as problems related to MRSA or *Clostridium difficile* 027.

Practising doctors have limited time available. It is essential that there is a good collaboration with and support from the national/regional group to provide background data and help with scientific updates.

Tentative indicators for 2

Genera/

Structures

- Are there local activities in some places?
- Are there nationally disseminated local activities?
- Are activities in hospitals and primary healthcare coordinated at the local level?

Primary health care

Structures

- Are there local activities in primary health care?
  - If yes:
  - Mostly multidisciplinary
  - Private practitioners are taking part
  - Have access to local surveillance data on AMR
  - Have access to local antibiotic consumption data
  - Have public funding
  - Meet regularly.

Functions

Primary areas of work are:

- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions
- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

Hospitals

Structures

- Are there local activities in hospital health care?
  - If yes:
  - Mostly multidisciplinary
  - Have access to local surveillance data on AMR
  - Have access to local antibiotic consumption data
  - Have public funding
  - Meet regularly.

Functions

Primary areas of work are:

- Infection control
- Diagnostic practices/habits
- Analysis of local consumption and resistance data
- Educational activities
- Coordination of interventions

- Provide local guidelines
- Convene local meetings with prescribers at least once a year.

3. Laboratory capacity

Laboratory capacity is essential for many reasons:

- To be able to follow trends in antimicrobial resistance;
- To discover newly emergent resistant strains;
- To enable prescribers to make informed antibiotic choices. For this there is a need for timely feedback to clinicians.

It is important to characterise isolates that may have clinical importance. Often this cannot be done in all laboratories so a referral system to specialised laboratories should exist.

All laboratory work should be quality assessed regularly.

Tentative indicators for 3

General

Structures

- How many diagnostic laboratories are appropriately equipped for microbiological diagnostic work (minimum requirement: performance of gram-stain, aerobe culture and antimicrobial susceptibility testing)?
- What proportion of microbiological laboratories have at least one specialist clinical/medical microbiologist?
- Is there a formal referral structure to reference laboratories supported by public (alternatively through insurance system or equivalent) funding?
- Does a national external quality assessment scheme exist?
- Does an accreditation system exist for microbiological laboratories that requires regular QC and EQA?

Hospitals

Functions

- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 12 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) via telephone or clinical rounds to the submitting clinician within the first 24 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- What proportion of microbiological laboratories provides species identification of blood culture isolates to the submitting clinician?
- Who pays for the analysis of samples sent in?

Out patients

Functions

- What proportion of general practitioners can submit clinical specimen for microbiological investigation to an appropriately equipped microbiological laboratory within 12 hours?
- What proportion of microbiological laboratories provide preliminary and individual feedback (gram stain, rapid tests, culture results) to the submitting clinician within the first 24 hours of receiving diagnostic specimen?
- What proportion of microbiological laboratories provides susceptibility test results to the submitting clinician within 48 hours of receiving a diagnostic specimen?
- Who pays for sent in sample analysis?

4. Monitoring of antibiotic resistance

Resistance patterns should regularly be followed. This should be done using a standardised method. The method should be quality assessed on a regular basis.

To be able to guide prescribers in prudent usage of antibiotics, surveys of different clinical conditions should be carried out to define which pathogens and their susceptibility profiles for antibiotics. The resistance pattern may vary from area to area so local monitoring may be needed.

Data should be gathered nationally and internationally to follow long term trends.

Tentative indicators for 4

- Local, time limited studies have been performed
- Local continuous, monitoring is done in a few laboratories
- Are duplicates excluded?
- National monitoring with standardised methodology on clinically and epidemiologically relevant bacterial pathogens is on-going
- Country wide local monitoring with standardised methodology in communities and hospital unites is on-going
- Data from hospitals and out-patient settings are treated separately
- Data collection is financially supported by government
- Regular surveys of resistance patterns for pathogens in population based syndromes are performed
- Regular feedback of resistance patterns to prescribers and local groups is given.

5. Monitoring of antibiotic usage

As antibiotic usage is the driving force for emerging resistance it is important to monitor usage. Therefore, reliable surveillance systems of antibiotic consumption are essential to complement antibiotic resistance data and develop instruments for assessing effective strategies to foster appropriate antibiotic use in all European countries.

Current antibiotic use surveillance systems are mostly monitoring trends and shifts in usage patterns. However, to deepen our understanding of antibiotic prescribing, more detailed information is needed on patients' age and gender, the prescriber, the indication and pathogen. Although prescriber data are felt as sensitive, this kind of data can be used for the self-assessment. Aggregated data may be used for local group discussions.

Tentative indicators for 5

- Are valid national data on outpatient antibiotic use available?
- Are valid national (or at least representative sample) data on hospital antibiotic use available?
- Is collection of data on antibiotic use legally supported?
- Is data collection financially supported by the government?
- Are data available per prescriber/ clinical diagnosis/micro-organism?
- Is there regular feedback of prescription patterns to prescribers?
- Are anonymous data fed back to local groups?

6. Antibiotic utilisation and treatment guidance

Antibiotics should be used properly. 'Proper use' is a difficult term both in human and veterinary medicine. There is still a need to find some common view on what is 'proper'. Guidelines are a way of agreeing locally or nationally.

Antibiotics allow treatment of serious bacterial infections. The largest volume of antibiotics is prescribed in ambulatory care. This use is increasingly recognised as the major selective pressure driving resistance, which in turn makes them ineffective. Therefore antibiotics should be used appropriately - i.e. (no) antibiotics for those who will (not) benefit from the treatment. In addition, unnecessary use of antibiotics requires more resources, motivates patients to re-consult and exposes them to the additional risk of side effects, whereas under-prescribing could be associated with higher risk of complications of untreated infections.

A 'proper' level of usage is difficult to define. The levels are mostly for following trends and shifts in usage patterns. With these data related to other data there might be a way of defining a 'proper' range of usage. One benchmark value at European level cannot be given, because for different countries the demographical characteristics and epidemiological situation can influence this indicator. Individual countries should position themselves and define their own benchmark, This should be based on the epidemiology of infectious diseases and national guidelines. A range of acceptable antibiotic use should be defined rather than one threshold value. If the use is outside the limits of the range, more detailed assessment is recommended in order to define the action required. For any action planned explicit targets should be set.

Most guidelines define treatment for specific diagnosis. This means that the diagnosis has to be made correctly before guidelines are applicable.

That also means that antibiotic usage must be directed by medical diagnosis and decisions. This is why systemic antibiotics are prescription-only medicines in the European Union.

Tentative indicators for 6

- Availability of OTC (over-the-counter) antibiotics
- Availability of national treatment guidelines
- Availability of locally adapted treatment guidelines
- Has the compliance to guidelines been assessed?
- Defined standardised criteria for clinical diagnosis
- What is the rate of laboratory diagnostics use before deciding on use of antibiotics for sore throat (% of patients)?
- What is the rate of blood cultures before use of antibiotics for perceived bacteremia with sepsis (% of patients)?

7. Infection control

Healthcare and hospitals in particular have historically been a major source of spread for epidemics. This has been shown for a wide variety of microbes – for example smallpox and early outbreaks of Lassa fever. A recent well-known example is SARS. Another very well-known bacterium that spreads in healthcare settings is MRSA.

All hospitals have defined procedures and hygienic principles although these may not always be based on the latest scientific knowledge. Implementation of guidelines and adherence to procedures is another problem. Surveys have shown that adherence to infection control guidelines many times is poor.

More and more people with complicated medical conditions are given home-based care. Many of them are elderly. Such patients may have indwelling catheters, a lower immunity and often use antibiotics. Infection control guidelines are difficult to follow in a home setting and many of the care staff have little or no training in infection control. Increasingly MRSA is reported to also be a problem in these settings.

Tentative indicators for 7

General

- Is there a national committee on issues related to infection control?

Hospitals

- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Guidelines for hygienic procedures including standardised barrier precautions in >90% of hospitals
- Specific guidelines for MRSA in >90% of hospitals
- At least one infection control nurse/doctor per hospital
- Time allocated for infection control?
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in ICUs? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in surgical wards? (% of hospitals)
- What numbers of hospitals do surveillance of healthcare acquired infections (HAI) regularly in internal medicine wards? (% of hospitals)
- Are there legal requirements for infection control system in hospitals?
- Is implementation of infection control practice regularly evaluated?

Health care settings outside hospitals

- Alcohol-based hand disinfection recommended for non-diarrhoeal disease
- Alcohol-based hand disinfection available in >90% of outpatient clinics
- Alcohol-based hand disinfection available in >90% of health care settings for elderly
- Guidelines for infection control are available for elderly and long term care staff
- Implementation of infection control practice in elderly and long term care is regularly evaluated.

8. Educational programmes on AMR

Understanding the problem with AMR is the basis for having an impact with interventional programmes. This can partially be achieved with educational programmes. Educational programmes should be an integrated part of undergraduate studies. All healthcare-related professionals need to have an understanding of the AMR problem.

'Education' in the context of AMR is more than just pharmacology of antibiotics or resistance patterns in microbes. It encompasses the relationship between microbes, antibiotics and the epidemiology of resistant strains. It describes the complex interrelation between all aspects brought up in this document.

Regular, repetitive, independent educational material best provided by locally-based colleagues in discussion groups seems to be one of the better success factors.

Tentative indicators for 8

- Doctors have in their curriculum AMR as undergraduate course
- Hospital health care workers have some education on AMR
- Community health care workers have some education on AMR
- Specific post-graduate courses for doctors in antibiotic resistance are provided
- Regular educational programmes in antibiotic resistance are provided for health staff
- It is compulsory for all prescribers to take part regularly in a session on AMR
- <60% of information on AMR is industry sponsored.

9. Public information related to AMR

Many prescribers blame patients for demanding antibiotics irrespective of their condition. This can only be changed if the public is well informed about what antibiotics can and cannot do. Hence, educational activities for the wider public are important.

Tentative indicators for 9

- No information provided
- Topic sometimes covered in media
- Some material for media and/or internet from official sources
- Occasional national campaigns
- Repeated, structured national campaigns
- Regular, structured information provided by professional bodies
- Public perception assessed.

10. Marketing related issues

Economics also have an impact on prescribing habits, irrespective of diagnosis or best practice. This should be discouraged.

Tentative indicators for 10

- Independent (not industry supported) drug information is available
- Ethical guidelines for interrelation between physicians and industry are in place
- Physician's prescriptions do not influence on physician's salary
- Personal gifts from industry to physicians are illegal.

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