



AMR Next

EU Antimicrobial Resistance One Health ministerial conference 2016

 Veterinary Health

 Human Health

 One Health

Introduction

Antimicrobial Resistance, from intentions to action!



Minister of Health, Welfare and Sport, Schippers

From the very beginning the European Union continuously faced political, social and economic challenges. Today the migration crisis, terrorism, climate change and international tensions demand our immediate response and continuing attention. At the same time we cannot afford to neglect Antimicrobial Resistance, a threat that is evolving slowly but progressively, jeopardising the health of all people.

If antibiotics are not effective anymore, modern healthcare is at stake. Without antibiotics, common infections can no longer be treated. Even routine operations will be too risky. Already 25,000 people die every year in Europe due to untreatable bacterial infections.

Alarming signals

Infection prevention and prudent use of antibiotics, both in human and animal healthcare, are crucial in the fight against Antimicrobial Resistance. We need new antibiotics or other effective medicines against infections. This requires new business models. Also, we need to develop new, affordable and quick diagnostic instruments. Commitment is important, but commitment alone will not stop the spread of multiresistant bugs. It is alarming that recent data of the European Centre for Disease Prevention and Control show that Antimicrobial Resistance is still progressing in the EU. It is time to act!

One Health approach

That is why Antimicrobial Resistance is a top priority on our Health Agenda during our EU-presidency in the first half of 2016. We hope to meet you in Amsterdam, where we purposefully bring together European Ministers of Health, and Ministers of Agriculture. Because the Netherlands believes

the One Health approach, when all disciplines work together, is crucial in combating Antimicrobial Resistance.

‘Commitment is important, but commitment alone will not stop the spread of multiresistant bugs’

This newspaper is meant as a source of inspiration. It provides good practices both from the human healthcare sector and the veterinary sector of different Member States. It shows that we are not powerless in the fight against Antimicrobial Resistance and that joining forces within the EU allows tailor-made solutions fitting individual Member States.

Realistic dilemmas

You will also find a sneak preview of our programme, which includes a scenario-based policy discussion that will confront us with realistic dilemmas on the topic of Antimicrobial Resistance. This is an important part of the conference. Our experience is that an interactive approach supports us in moving from intentions to actions. We are looking forward to meeting you in Amsterdam on 9 and 10 February 2016!

Edith Schippers,
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Antimicrobial Resistance in the European Union: what's the big deal?

Antibiotics are one of the most important therapeutic discoveries in medical history. They enabled us to treat many infectious diseases caused by bacteria that were once life-threatening. Moreover, many advanced medical interventions such as chemotherapy, organ transplants and placement of artificial prostheses, depend critically on the availability of antibiotics, in both treatment as well as prophylaxis. Nowadays, we face a huge increase of antibiotic resistant bacteria.

Unfortunately, the use of antibiotics (both appropriate as well as inappropriate use) in human and in animal health inevitably involves the emergence of Antimicrobial Resistance. Hence inappropriate use of antibiotics should be minimised. Besides inappropriate use of antibiotics, inappropriate infection prevention practices, for example not observing simply hygienic measures such as washing hands after examination or other handling of patients, cause an increase in the spread of resistant pathogens. Infection prevention and control programmes in human health care exist in the EU, but not in all Member States. Also the 'prevention is better than cure' principle is incorporated in the proposal for the EU Animal Health Law. This regulation could contribute to a better health status by introducing measures for prevention of animal diseases.

How big is the problem in Europe?

In the EU, more than 25,000 patients die each year from infections caused by antibiotic resistant bacteria. Today, antibiotic resistant bacteria are regularly found in many hospitals in the EU, infecting about 4 million patients every year. Data on antimicrobial resistance in human health care in Europe are provided by the European Centre of Disease Prevention and Control (ECDC) and are collected through EARS-net (European Antimicrobial Resistance Surveillance Network) and the FWD-net (Food-and Waterborne Diseases and Zoonoses Network). Some countries like Sweden, Denmark and the Netherlands collect integrated (human and veterinary) data on Antimicrobial Resistance and use of antibiotics. EU legislation obliges Member States to monitor trends in Antimicrobial Resistance in different bacteria in food and animals. The European Food and Safety Authority (EFSA) in cooperation with ECDC analyses and publishes these data.

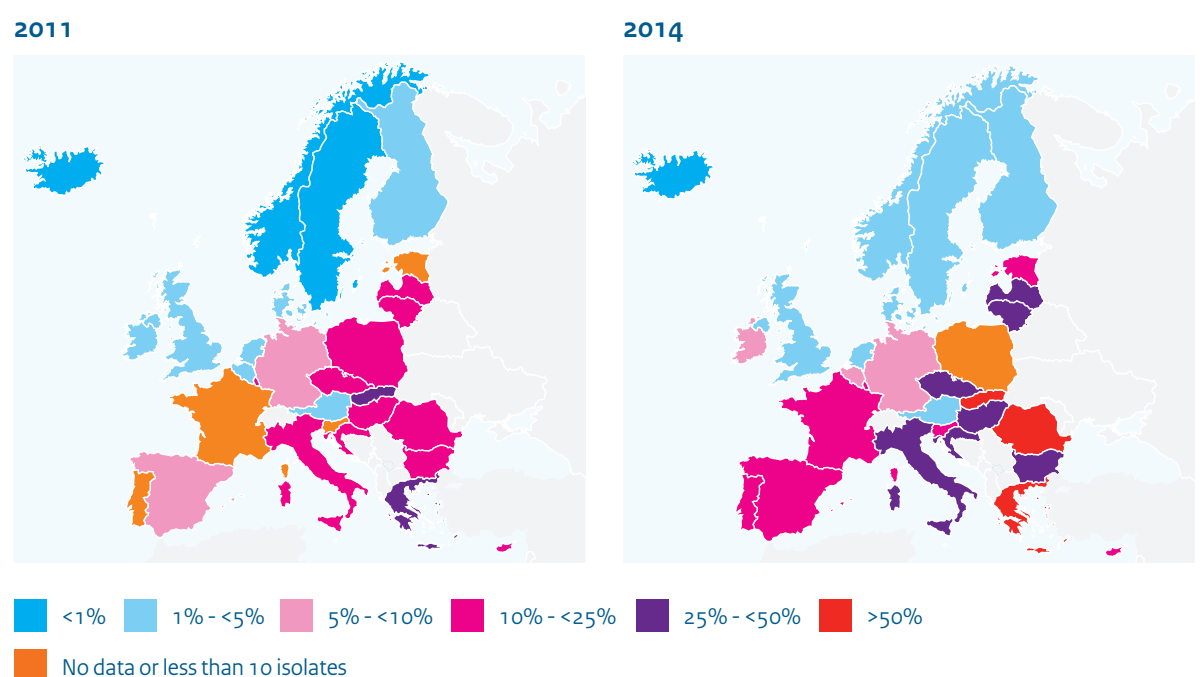


Figure 1: *Klebsiella pneumoniae*: percentage of invasive isolates with combined resistance to third-generation cephalosporins, fluoroquinolones and aminoglycosides, EU/EEA, 2011 and 2014. Source: ECDC

Recent figures from the ECDC show that Antibiotic Resistance is an increasing problem in the EU (see figure 1). The Antimicrobial Resistance situation in Europe displays large variations depending on the bacterium, antimicrobial group and geographical region. For several antimicrobial group-bacterium combinations, a north-to-south and west-to-east gradient is evident in Europe. In general, lower resistance

percentages are reported by countries in the north and higher percentages by countries in the south and east of Europe. These differences are most likely related to differences in antimicrobial use, infection control and healthcare utilisation practices in the countries (see figure 1).

One of the most worrisome developments is the rise in CPE (Carbapenemase-Producing Enterobacteriaceae), one of the most threatening forms of resistance. The European survey of CPE (EuSCAPE) project, reported in November 2015 that the situation regarding CPE worsened over the last two years. In 2015, 13 out of 38 countries reported inter-regional spread of or an endemic situation for CPE, compared with 6 out of 38 in 2013. Only three countries replied that they had not identified one single case of CPE. The ongoing spread of CPE represents an increasing threat to patient safety in European hospitals (Figure 2).

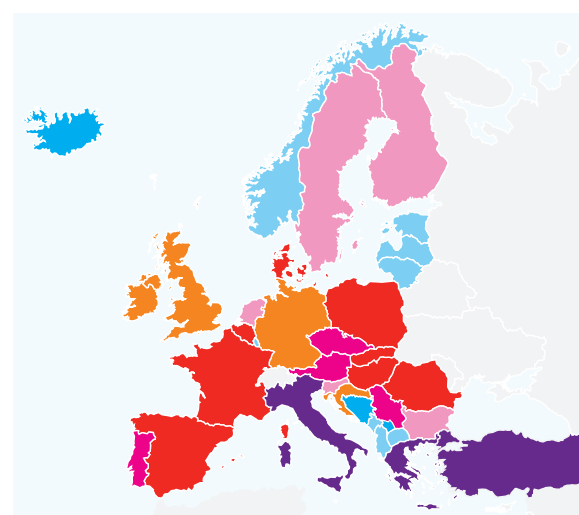
How many antibiotics do we use in the EU?

As mentioned above, the use of antimicrobials in human as well as in animal health has added to the problem of Antimicrobial Resistance in the EU. Data on the use of antimicrobial consumptions in humans are collected through ESAC-net (European Surveillance of Antimicrobial Consumption Network). The quantity of antimicrobial drugs used is not at the same level throughout the EU. Also here, a clear north-south gradient exists: in northern Member States the consumption of antimicrobial drugs per 1000 inhabitants and the ratio broad-/narrow-spectrum antibiotics are lower than in the south. These differences between countries and regions imply that cultural differences have a large influence on the use of antimicrobials. They could lead to different health care practices, but also to a different use of health care organisations and pharmacies by patients. EMA (European Medicines Agency) analyses and publishes each year data on the sales of veterinary antimicrobial agents, corrected for the size of the animal population, in EU/EEA countries. A large difference between most and least selling countries is observed. This difference is partially due to variations in the composition of the animal population in the various countries. Figure 3 shows a comparison of biomass corrected consumption of antimicrobials in humans and food producing animals by country.

Socioeconomic burden of Antimicrobial Resistance

In the health care sector, control and prevention of Antimicrobial Resistance could lead to decreased costs. In France and Belgium, the national campaigns aimed at improving the use of antibiotics were associated with cost savings of €850 million (2002-2007) and €642 million (1999-2015), respectively. In general, economic opportunities exist in the development of new antimicrobial drugs.

However, only very few pharmaceutical companies in the world are carrying out research to develop new antibiotics. The fact that Antimicrobial Resistance is a serious public health threat, has also created a serious socioeconomic burden. Economic issues related to Antimicrobial Resistance extend well beyond the health sector. Increased health care costs and productivity losses are estimated to be €1.5 billion per year in the EU. Furthermore, domestic animals suffer increasingly from resistant bacterial infections, resulting in costly production losses and risks for livestock farmers. The estimated future burden of Antimicrobial Resistance are potentially large. It is estimated in the O'Neill report



Epidemiological stages, 2014-2015

- Countries not participating
- No case reported (Stage 0)
- Sporadic occurrence (Stage 1)
- Single hospital outbreak (Stage 2a)
- Sporadic hospital outbreaks (Stage 2b)
- Regional spread (Stage 3)
- Inter-regional spread (Stage 4)
- Endemic situation (Stage 5)

Figure 2: Occurrence of carbapenemase-producing Enterobacteriaceae in Europe, 2015. Source: ECDC

(<http://amr-review.org>) that by 2050, when no action is taken, Antimicrobial Resistance results in 10 million premature deaths worldwide. This means that Antimicrobial Resistance could impose a substantial cost to the world economy.

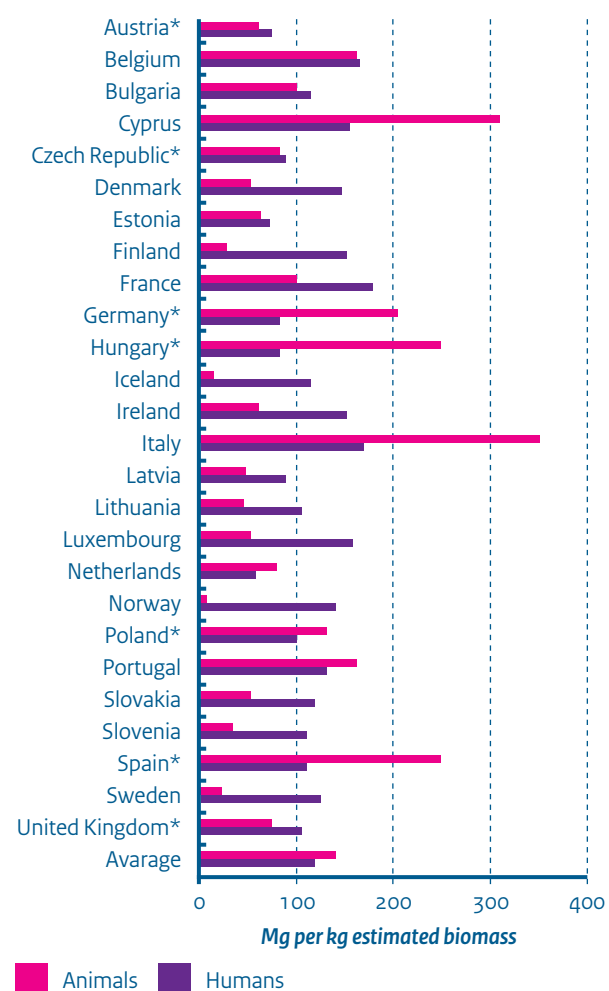


Figure 3: Comparison of biomass-corrected consumption of antimicrobials (milligrams per kilogram estimated biomass) in humans and food-producing animals by country in 26 EU/EEA countries in 2012.

Source: ECDC/EFSA/EMA first joint report on the integrated analysis of the consumption of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from humans and food-producing animals. Stockholm/Parma/London: ECDC/EFSA/EMA, 2015. EFSA Journal 2015;13(1):4006, 114 pp. doi:10.2903/j.efs.2015.4006

Scenario-based policy discussion

From awareness to concrete actions

By means of a film, the European Ministers of Health and Agriculture and their delegations will experience the challenges Member States and the EU faces in tackling the increasing problem of Antimicrobial Resistance (AMR), in both human and veterinary health. The film is divided in three short film clips. After every clip specific AMR related (political) dilemmas will be discussed, both in the area of human and veterinary medicine.

Part one of the film will show the first AMR related policy dilemmas on Health policy and on Agriculture. All participants will have the opportunity to give their opinion on a few statements. After each part of the film statements with possible responses will be shown on a screen. Ministers will have five minutes to consult their delegations, after which they will be asked to vote anonymously for the possible responses. The summarised results of all votes will be projected on screens and the moderator will use this outcome as the starting point for a discussion. The scenario will continue with a number of escalating developments. A second film clip will be shown and new triggering questions will be posed to both Ministers of Health and Agriculture. In the second round, again Ministers will be asked to make use of the voting system to support the subsequent discussion. The last film illustrates (joint) action is needed to bring the AMR scenario to a positive end. It invites Ministers to further discuss concrete national and EU actions.

Three policy dilemmas

Illustrated by three short films

- 1. Identified risk of antibiotic resistance**
Is the approach of Antimicrobial Resistance purely a national problem? How do Ministers of health and agriculture see the risks and are actions needed?
- 2. Serious developments**
Which actions are needed and who is responsible?
- 3. EU approach on AMR**
How can we realise the ambitions in the EU, which actions and how?

Objectives

- Find common ground and share awareness on the challenges of Antimicrobial Resistance
- Work towards a shared vision on the One Health principle
- Confirm a joint sense of urgency to take concrete national and EU actions to tackle AMR challenges

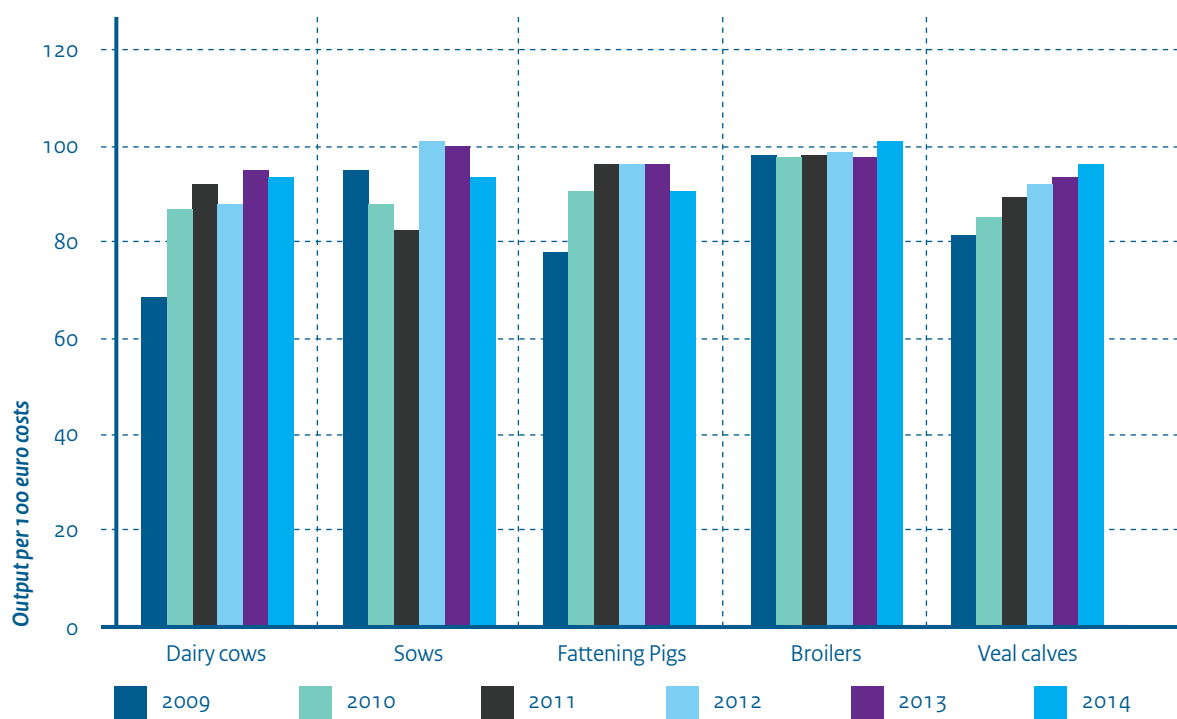
Place and time

Date: 10 February 2016
Location: MEA Amsterdam
Time: 10.30 – 13.00 (2,5 hours)



Substantial reduction in antibiotic use appears not to affect profits

Between 2009 and 2014 the use of antibiotics in Dutch livestock decreased by 58%. This does not appear to have affected farm profits: the animal husbandry sector did not diminish in size and the average technical and economic results do not appear to have worsened.



This figure shows the trends in the 'rate of return' (output-costs ratio). This profitability index indicates the revenues for every 100 euros spent. If the total costs, including calculated costs for deploying unpaid labour and capital, are not totally covered by revenues, the profitability index falls below 100. If revenues are higher than the costs, the profitability is greater than 100.

Fluctuation in profitability

Most sectors show an annual fluctuation in profitability. In none of the sectors is the trend downwards. The fluctuations are the greatest for the pig sector, while a definite upward trend is only visible in the veal calf sector. It is difficult to compare sectors because of the differences in calculated costs for private labour and capital. The profitability in the dairy

sector is relatively low because of the high calculated costs of land (capital). In none of the cases has a reduced usage of antibiotics appeared to have lowered profitability.

Data collection

The trend was studied in three indexes which could be affected by reduced antibiotic use on pig and broiler farms in

the Farm Accountancy Data Network (FADN): animal health costs, mortality rates and feed conversion. This European data network gathers accountancy data from farms to determine incomes and to perform a business analysis of agricultural holdings. The Dutch part of FADN is a major source of information in the Netherlands, collecting current data on a wide range of subjects from a large number of agricultural businesses that jointly represent around 95% of Dutch production.

Animal healthcare costs

The marked decrease in use of antibiotics in sows and broilers has not led to lower animal health costs. Probably the farms had to spend more on preventive healthcare, for example, on obtaining advice and guidance from vets or on vaccination. In the fattening pig sector the annual healthcare costs showed a distinct reduction in the period 2009-2011 and they remained lower in subsequent years as well.

Mortality

There is some annual fluctuation in mortality in each sector. For piglets there is a slight increase and for broilers a decrease, especially in 2011. This decrease was probably caused by the implementation of the animal welfare legislation, with upper limits regarding mortality and meat production per square metre of animal housing space. In general, mortality is certainly not on the increase.

Feed conversion

Feed conversion for fattening pigs and broilers fluctuates but the trend is downwards and therefore favourable. Feed conversion represents how many kg of feed was necessary for 1 kg of growth in pigs or poultry.

How do farmers view the situation?

A survey of 42 pig farmers in 2012 showed that 90% of them did not believe the enormous reduction in antibiotic usage was having an adverse effect on economic results. Furthermore, an analysis of the technical and economic results from 80 pig farms and 21 broiler farms showed that farms with more than 50% reduction in antibiotic usage in the period 2009-2011 did not perform better or worse than farms where antibiotic reduction was not achieved.



Pig farm Van de Nieuwelaar in Roosendaal

Successful animal health team

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Broiler farmer in Brabant

Rely on the animal's natural resistance

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Broiler farmer Van Harten in Fochtelloo

Focus on quality of day-old broilers and yield

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Pig farm Harbers in De Heurne

Keeping animals free of stress and infection

p. 21



A pre-operative screen-and-treat strategy of Staphylococcus aureus reduces surgical infections with 60%

Little effort and small financial investments make a big difference

Nasal carriage of Staphylococcus aureus (S. aureus) is a major risk factor for surgical infections. Researchers from the Amphia Hospital Breda (The Netherlands) investigated the impact of the so-called screen-and-treat strategy aimed at identification and removal of S. aureus shortly before surgery. This simple strategy significantly reduces surgical infection rates and hospital costs.

The Amphia Hospital Breda uses a simple non-invasive screen-and-treat strategy to prevent surgical infections with S. aureus. The strategy entails rapid identification of S. aureus by means of screening (a real-time polymerase-chain-reaction assay), followed by treatment with mupirocin nasal ointment and chlorhexidine soap.

A cost saving of €1,900

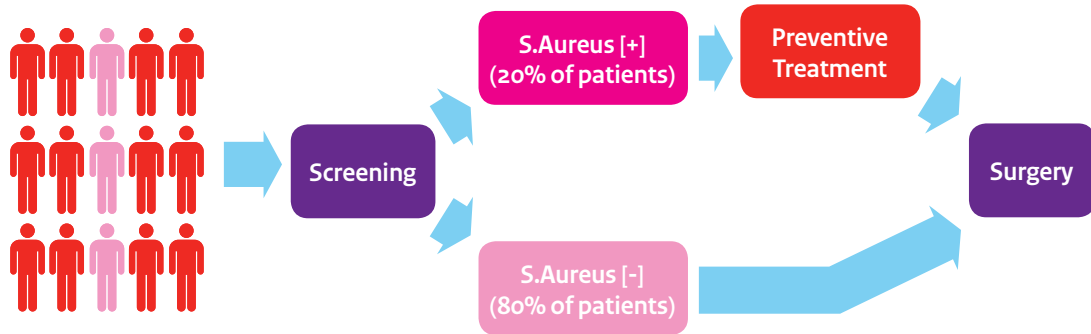
In addition, the screen-and-treat strategy is highly cost-effective from a healthcare perspective. Kluytmans and colleagues took all costs made during the 12 months after (cardiothoracic or orthopaedic) surgery into account. The mean total hospital costs for a screened-and-treated

Practical barriers?

The (cost-)effectiveness is proven and mupirocin nasal ointment and chlorhexidine soap are considered relatively safe. Still, some practical barriers may hinder widespread adoption and implementation. First, pre-operative screening and treatment demands some time and effort from healthcare personnel, even though this is only a few minutes. Second, when patients enter the hospital shortly before surgery, the healthcare personnel have no opportunity to treat them. In those cases the physician should facilitate treatment at home by sending a prescription to the pharmacy. Nevertheless, these are slight practical barriers compared to the large benefits in terms of patient safety and quality of care.

Benefits

The results of the screen-and-treat strategy are remarkable. Apart from the significant reduction of S. aureus infection, the strategy could save a total of €400,000 per thousand surgeries. This is based on the nasal S. aureus carriage rate of 20%. Worldwide millions of surgical procedures are performed each year. Huge numbers of patients could therefore benefit from this screen-and-treat strategy, accompanied by large savings. Meanwhile, the US Centers for Disease Control have decided to include this strategy in their top recommendations for safer healthcare.

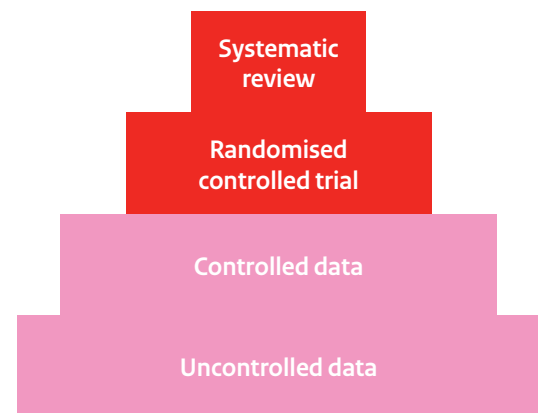


The screen-and-treat strategy to prevent surgical S. aureus infections

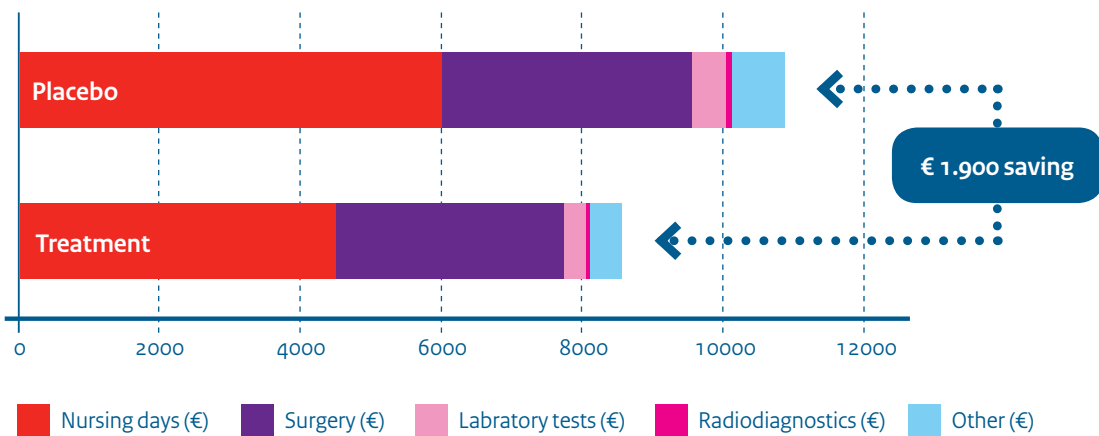
60% reduction of surgical infections

Medical microbiologist Jan Kluytmans and colleagues studied the effectiveness of the screen-and-treat strategy in five Dutch hospitals. Their study was the first to use a double-blind, randomised, controlled trial design. The results were striking: the screen-and-treat strategy results in a statistically and clinically significant reduction in S. aureus infections during surgery. The rate of S. aureus infection was 3.4% (17 of 504 patients) in the screen-and-treat strategy group, compared to 7.7% (32 of 413 patients) in a placebo group. The risk of hospital-associated S. aureus infection was reduced by nearly 60%. These results provide solid evidence for preventive effectiveness. Moreover, a Cochrane review conducted by researchers from the same study group confirmed effectiveness.

patient undergoing surgery were considerably lower than costs for a placebo treated patient (€8,600 versus €10,500). This difference was primarily caused by a reduction in hospital stay of almost two days due to fewer infections. Much less nursing time at the IC was therefore required. The financial investments for the screen-and-treat strategy are almost negligible. Screening is relatively cheap (around €20), and treating even cheaper (€5 for the mupirocin nasal ointment and €5 for the chlorhexidine soap).



Evidence for the business case



Mean hospital costs per patient for placebo and treatment group

Background MRSA

S. aureus is worldwide the most common hospital-acquired infection. Meanwhile infection rates are increasing each day due to the widespread dissemination of methicillin-resistant S. aureus (MRSA). In 2008 there were an estimated 380,000 infections in EU hospitals. MRSA accounts for 5,400 attributable deaths and for more than 1 million in-hospital days. The hospital costs caused by MRSA are also considerable, reaching approximately €380 million annually. Effective prevention strategies are much needed. Hospitals traditionally focus on preventing cross-infection between patients to control S. aureus. But most S. aureus infections originate from patients' own flora (presence in the nose). Approximately 20% of the healthy population carries S. aureus. This is a major risk factor for subsequent infection in various patient groups.



Multidrug-resistant and extensively drug-resistant tuberculosis

According to 2007 official data, 1.5% of new tuberculosis (TB) cases registered in Portugal were multidrug-resistant tuberculosis (MDR-TB) and 48% of them extensively drug-resistant tuberculosis (XDR-TB). In June 2007, Portugal's National Directorate of Health created the National Reference Centre for M/XDR-TB. Facing the need to decentralise the management of M/XDR-TB cases in a regional structure, the National Directorate of Health proposed the creation of one Regional Reference Centre for MDR-TB in each of the seven health regions of the country.

The Northern Regional Reference Centre started its activity in July 2009. The team is composed of a pulmonologist (group coordinator), an infectious disease specialist, a public health physician, a microbiologist, a pharmacist, and a thoracic surgeon. Certain standard operational procedures are applied in the regional reference centre.

the clinician responsible for the patient from the hospital, outpatient clinic (public or private), primary health care centre, prison or other location. The therapeutic approach and the decision whether to hospitalise or not and follow-up are also discussed.

With this strategy, 73% of patients followed by the reference centre during 2010-2013 have had therapeutic success

Multidrug-resistant TB strain

When a multidrug-resistant M. tuberculosis strain is detected, the laboratory notifies the reference centre and the clinician responsible for the patient. The clinical case is discussed with

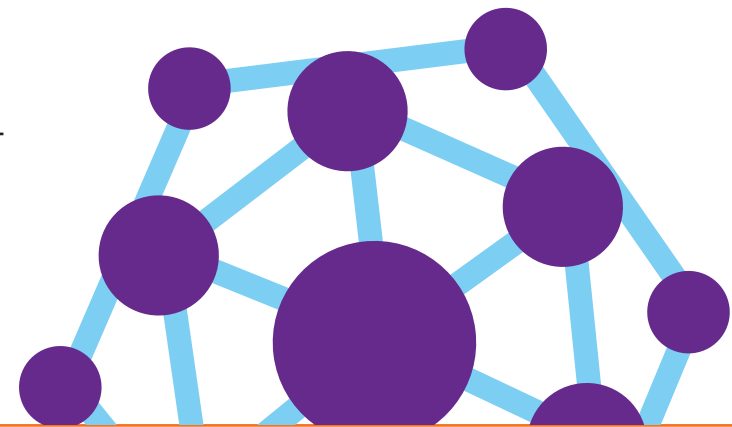
Hospitalisation

Hospitalisation is the first choice (not mandatory) at the beginning of treatment and until smear sputum conversion. The regional centre is responsible for the clinical management

of patients, including the choice of treatment regimen, the purchase of second-line drugs and the provision of medication to the health service where the patient is being treated (hospital, outpatient clinic). Directly observed treatment is provided throughout the whole process. After discharge, local nurses provide the medication, preferably at the patient's home. The regional reference centre provides periodic appointments to the patients, with the aim of assessing disease progression and occurrence of adverse events. The reference centre, together with the family physician and public health authority, identifies the best strategy for contact tracing.

Constant decline

All MDR-TB cases are notified and the NTP analyses data regionally and nationally. The number of cases of MDR-TB in the region has consistently declined in the last years, and no cases of XDR-TB have been detected since 2010. With this strategy, 73% of patients followed by the reference centre during 2010-2013 have had therapeutic success.



Systematic risk management by a joint human and veterinary AMR task force

The Finnish Antimicrobial Resistance strategy focuses on zoonoses and animal disease control, herd health programmes and legislation on the use of medicines in animals. Consumption of antimicrobials in food-producing animals has remained on a relatively low level, but systematic multidisciplinary actions involving all parties are necessary to promote prudent use of antimicrobials.

Making profit on the sales of medicines by veterinarians is banned and using antimicrobials for systemic treatment is subject to veterinary prescription since 1949. Systematic resistance monitoring has been carried out in Salmonella species since 1983 and Finres-Vet programme covering resistance monitoring in major zoonotic and indicator bacteria was initiated in 2002. Indication-based recommendations for the use of antimicrobials in animals have been in place since 1995.

Recommendations and guidelines

Consumption figures of antimicrobials have been published annually since 1995. Detailed recommendations, such as on the use of (fluoro)quinolones in 1998 have been published when needed. Veterinarians have a legal obligation to follow the official recommendations and guidelines on the use of antimicrobials. The use of certain human last resort antimicrobials in animals was banned in 1999. Also the use of antimicrobials for salmonellosis was banned in poultry in 2006 and for swine and cattle in 2011. A joint human and veterinary Antimicrobial Resistance task force was established in 2012 although the human-veterinary co-operation had already started in 1997.

Special requirements for group treatments

In 2014, new legislation on the medication of animals with special emphasis on the use of antimicrobials came into force. The legislation emphasises on the role of veterinarian i.e. clinical diagnosis and microbiological analyses as a prerequisite for antimicrobial treatment. Special requirements are laid down for group treatments and recurrent infections. There are also rules for prioritising the choice of antimicrobial for treatment and restrictions are set on the use of human critically important antimicrobials (HCIA). New legislation also gives more responsibility for herd health programmes to set criteria for responsible use and follow the use of antimicrobials in animal production units. Herd health programmes are run by the private food industry and their goal is to prevent and control contagious animal diseases and improve the health of production animals.

Awareness and education

Awareness and education of all parties, including industry, veterinarians and animal owners, has contributed positively in tackling Antimicrobial Resistance in Finland. Cooperation between all sectors has resulted very low occurrence of animal diseases and zoonotic agents in food animal production

warranting consequently very limited need to treat animals with antimicrobials. The strict policy in using antimicrobials has prevented development of Antimicrobial Resistance.

Narrow spectrum antimicrobials

Consumption of antimicrobials in food-producing animals has remained on a relatively low level, according to ESVAC reports. In Finland antimicrobials are used for treatment of individual animals rather than groups, and narrow spectrum antimicrobials are first choice. The overall resistance situation is good, in particular, in zoonotic bacteria (Finres-Vet reports) although increasing resistance is seen in some animal pathogens. Systematic multidisciplinary actions involving all parties (human and veterinary medicine, animal industry) are necessary to promote prudent use of antimicrobials. Combatting Antimicrobial Resistance therefore needs endurance and strong motivation of all parties as well as multiple actions.





Regional AMR groups

The decision to establish regional Antimicrobial Resistance management groups was taken in Lithuania by the Ministry of Health in 2015. The leading role to create and support the group activities is given to a regional public health centre where regional epidemiologists are located. There are ten regions in Lithuania and currently groups are being established in all the regions.

The composition of groups varies among the regions depending on specific problems and available resources. Basically they include representatives from public health centres, territorial patient funds, public health bureau, municipalities, health care institutions, veterinary service and universities.

After a successful pilot it was decided to promote such groups in all regions

Public health centres

The regional model was created and piloted in 2012-2013 during the ImPrim project (Improvement of public health by promotion of equitably distributed high quality primary health care systems) under the Baltic Sea programme (2007-2013). It is based on Swedish experience and the Strama-model was used as inspiration. After a feasibility study, the first regional group was created including members

from public health centres (epidemiologists), territorial patient funds, the public health bureau, universities, health care institutions (clinicians, infection control doctors, family doctors, microbiologists) and municipalities (municipality doctors). The regional public health centres have undertaken the leading role in controlling infectious diseases in the region. After a successful pilot it was decided to promote such groups in all regions.

Support local groups

Establishment of regional groups has initiated several activities on a regional level and the start of collaboration between institutions, specialists and policy makers. Before, there were no institutions on a regional level where Antimicrobial Resistance control or any related surveillance was listed among functions or activities. It is important to support local groups and create their network. Yearly network meetings are planned to ensure the exchange of good practices.

Training courses

Coordinating national institution is helpful to initiate twinning and collaboration between groups. Initial seminars were organised for group members in every region by the Institute

Coordinating national institution is helpful to initiate twinning and collaboration

of Hygiene. Specific problems were discussed during seminars and the first steps were taken to draw up their own action plans. To deal with inequalities in knowledge on Antimicrobial Resistance among members of the AMR management group, training courses are scheduled in all regions.



Involvement of all parties responsible for animal health, food safety and human health

National Residue Monitoring Plan

In the context of the National Residue Monitoring Plan (NRMP), implemented in Italy according to European directives 96/22/CE and 96/23/CE, a large amount of samples of products of animal origin are tested for traces of antimicrobial substances from medicinal treatment. This research is very important in Italy to monitor and reduce the development of Antimicrobial Resistance. Italy therefore suggests to adopt the One Health approach in every Member State, with the involvement of all the parties responsible for animal health, food safety and human health.

The contribution of residues of antibiotics in food may not be very significant in comparison to the impact of resistant bacteria in or on foodstuff. However, residues of antimicrobials used in farms, for treatment and prevention of diseases, may end up in the environment, following their excretion from the animals via faeces or urine, exerting pressure on clinically relevant bacteria. This diffusion in the environment may lead to a development of acquired Antimicrobial Resistance and potential spread of such resistant microorganism to animals and humans. Focused research into this kind of residues should also have a deterrent effect on illegal or non-compliance treatment with veterinary medicines, favouring the concept of prudent use of antimicrobials.

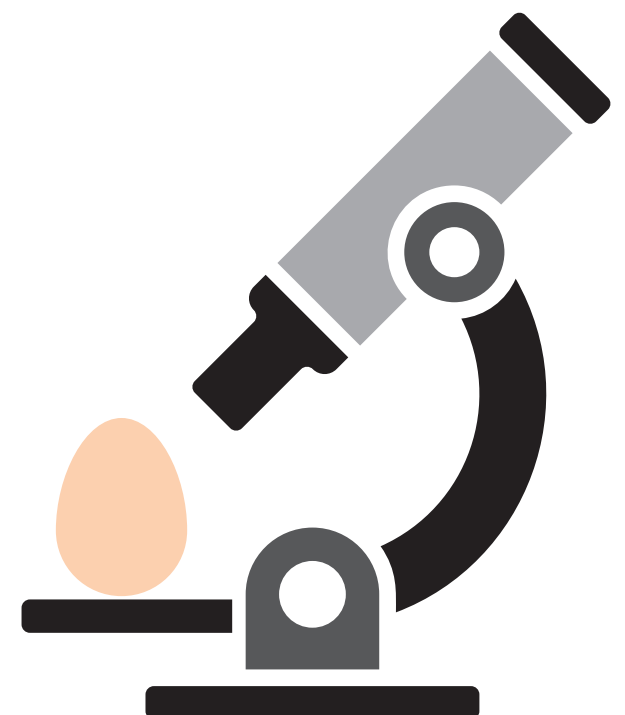
Constant interaction

Italy has chosen to keep the system of food hygiene controls, including the system regarding the research of residue of veterinary medicines, NMRP, under the care of the Ministry of Health and the National Health Service. This is important to ensure the constant interaction with other services, to

obtain updated information on human and animal health, for example about authorised veterinary medicines and to guarantee scientific uniformity in view of the One Health approach. The choice to assign expertise in food safety to the Ministry of Health dates from the late 50s. The Ministry of Health has produced the annual plan since 1988, updating every year the researches, according to criteria based on non-compliance in previous years, particular emergencies highlighted by local authorities and cases of alerts.

Whole system approach

The National Residue Monitoring Plan monitors the breeding animals process and the primary processing of animal origin products. It's implemented at central level by the Ministry of Health - Directorate General for Food Hygiene Food Safety and Nutrition with the collaboration of the Regional Health Authorities, Local Health Units National Reference Laboratories and Institutes Experimental Zooprophyllactic (IZS).





Outbreak prevention programmes in hospitals contribute to sustainable healthcare

Outbreak control versus outbreak prevention

In 2012, the Antonius Hospital Nieuwegein (the Netherlands) experienced a Vancomycin-Resistant Enterococcus (VRE) outbreak. After controlling the outbreak, the hospital implemented a successful outbreak prevention programme.

The investments needed to control the outbreak were about eight times higher than the yearly costs for routine outbreak prevention. In addition, routine outbreak prevention reduces the risk of multiresistant bacteria to become endemic, preventing additional downstream costs.

Until 2012 the Antonius Hospital Nieuwegein had never experienced any problems with VRE. But then a VRE bacterium was detected on a nursing ward. Eventually, three bacterial clones were involved, of which one highly contagious. Carriership of VRE was demonstrated in 250 patients, twelve of them were infected. The infected patients were mainly treated on nursing wards for internal medicine and oncology. The hospital took several measures to control the outbreak: weekly hospital-wide screening, isolation of patients carrying VRE, closure of wards, and disinfection of rooms. Also, the hospital increased the awareness of healthcare workers for basic hygiene measures by information, training and audits. The efforts and costs to control the outbreak were considerable. The hospital spent more than €2 million. These costs included personnel costs on the wards (cleaning and disinfecting the nursing wards, additional personnel for treating isolated patients), material costs (gowns, gloves, hydro alcoholic solutions, disinfection procedures), and diagnostic procedures.

Elements of success

After controlling the outbreak, the Antonius Hospital Nieuwegein implemented a successful outbreak prevention programme. Within two years this resulted in full elimination of VRE infections. Moreover, the prevention programme had some spillover effects to other possible infection threat. The programme is based on a collaborative working atmosphere in an open dialogue culture, based on openness and trust. The key elements of the prevention programme are:

- Hospital-wide surveillance
- Daily monitoring of cultures by an infection control team
- Reminders and feedback from the lab to hospital units
- Definition of patients at risk
- Low threshold for closing of nursing wards
- Isolated treatment of VRE positive patients
- Closely monitoring of hygiene guidelines

Outbreak prevention

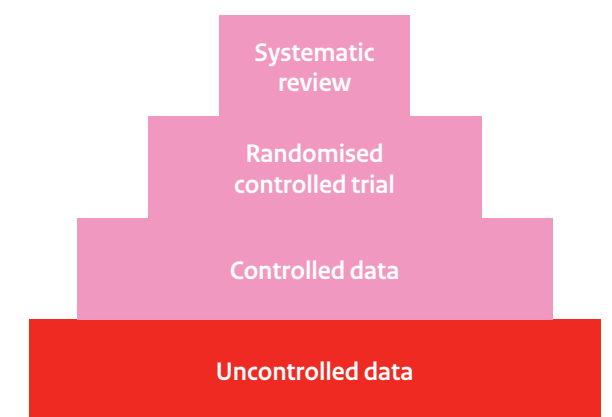
The Antonius Hospital Nieuwegein made an estimation for the costs associated with the VRE outbreak prevention programme. Approximately 200 additional VRE screening cultures are taken each month. Each culture costs €50, including assessment and feedback by the microbiologist. Around €10,000 is therefore spent each month on VRE screening cultures, adding up to €120,000 on a yearly basis. The cultures are taken by nurses, which takes on average 20 hours (€50 per hour) per week. This adds up to €12,000 on a yearly basis for personnel costs. In the case of early detection, VRE spread is limited, and only a limited number of patients will have to be isolated. Incidentally closure of a ward may be necessary. The additional costs of nursing and materials are estimated at €150,000 per year. The total costs for the VRE outbreak prevention programme are estimated at €280,000 per year.

Yearly cost-savings

The Antonius Hospital Nieuwegein also made an estimation of the potential health and financial gain of VRE outbreak prevention. Yearly, more than 45,000 patients are being hospitalised at the hospital. Without preventive strategies, VRE would have become endemic and approximately 10% to 20% of the hospitalised patients would carry VRE. This adds up to 4500 to 9000 patients annually. As approximately 3% to 6% of the VRE carriers would get infected, around 135 to 270 bloodstream infections would occur per year. Given the VRE associated mortality rate of 20%, 27 to 54 patients with VRE bloodstream infections would die each year. Yearly 27 to 54 intensive care admissions would be associated with VRE. Given the average length of stay of 7 days (€2000 for each day), this accumulates to €378,000 to €756,000 each year. Knowing the €280,000 yearly costs for prevention, a break-even point will be reached within a few months. Moreover, €100,000 can be saved annually by implementation of intensive VRE outbreak prevention.

Patient safety

The example of the Antonius Hospital Nieuwegein underlines the burdensome and costly consequences of an outbreak of a multiresistant bacteria strain, emphasising the urgency of implementing routine prevention programmes. Although based on uncontrolled data, the hospital gives an indication of the effort and costs required for an outbreak prevention programme. Even though the yearly costs for preventive strategies are high (€280,000), the costs are still substantially lower than the costs for controlling an outbreak (>€2,000,000) and the additional costs related to endemicity (€378,000 – €756,000). In addition, the contribution of prevention to patient safety and health is huge. Implementation of a hospital-wide outbreak prevention programme therefore helps to keep healthcare sustainable.

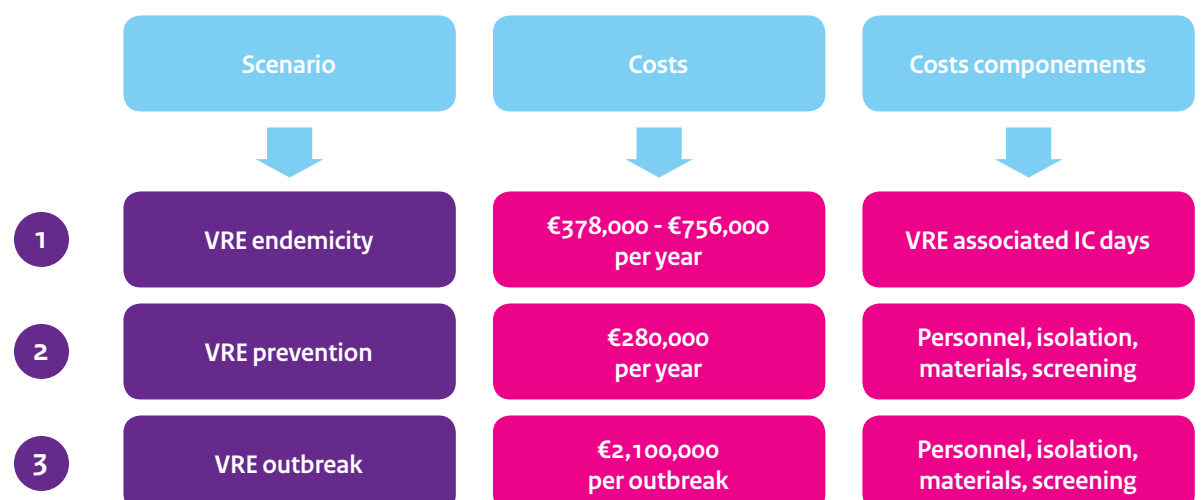


Evidence for the business case

A hospital outbreak

Hospital-acquired infections with multiresistant bacteria occur worldwide and are among the major causes of death and increased morbidity among hospitalised patients. An unusual or unexpected increase of these hospital-acquired infections is a so-called outbreak. An outbreak should be identified and eliminated as early as possible. Not only to maintain patient safety, but also to avoid huge expenses to control the outbreak.

Spread of Vancomycin-Resistant Enterococcus
VRE is a bacterial strain resistant to the antimicrobial Vancomycin. The bacterium is found in the bowel and on the skin of humans. It is usually spread via contact with hands, surfaces or medical equipment. VRE does not affect healthy and young people, but VRE can be life-threatening for patients with weakened immune systems. An outbreak of VRE is therefore a concern of every hospital.



The estimated costs for three different scenarios



Behavioural analysis proves effective on reducing antibiotic prescribing

A programme of work is currently being conducted by England's PHE's Behavioural Insights Team to reduce antibiotic prescribing with an initial focus on general practice, where the majority of antibiotic prescribing occurs. They conducted an extensive evidence review and 'behavioural analysis' in partnership with the Department of Health. They reviewed more than 150 scientific articles, assessing available evidence about key behaviours that support antibiotic stewardship among the public and patients, primary care, and secondary care.

The behavioural analysis identified key behaviours and importantly, drivers for those behaviours that may be amenable to change. This evidence informed a national randomised controlled trial that PHE ran in partnership with the Behavioural Insights Team and the Department of Health. They tested two interventions to reduce antibiotic prescribing among 1,581 practices whose prescribing rate was in the top 20% in their area: 1) a letter from England's Chief Medical

Return-on-investment

The key outcome monitored from September 2014 to April 2015 was the rate of antibiotics dispensed. The inclusion of practices that did not receive the interventions enabled definitive calculation of the independent effect of each intervention. Use of publicly-available prescribing data enabled low-cost and robust evaluation. This work

Use of publicly-available prescribing data enabled low-cost and robust evaluation

Officer providing social norm feedback that the practice was prescribing antibiotics at a higher rate than 80% of practices in their area, 2) patient-focused information that linked unnecessary antibiotic use to future personal consequence. The letter was a fraction of the cost of the patient-focused information.

will provide strong evidence of effectiveness and return-on-investment and final results have been submitted for publication in a high profile peer-reviewed journal. The Behavioural Insights teams are now working to implement and further test evidence-based behaviour change messages in routine and automated feedback to GPs.



Strengthening surveillance systems

Antibiotic consumption data collection project

A report which combines veterinary antimicrobial sales and antibiotic susceptibility of veterinary pathogens is published annually by the Veterinary Medicines Directorate (VMD). However, sales data do not permit accurate analysis of antibiotic consumption by animal species or production category and this means it isn't possible to target interventions where they will be most effective, or evaluate the effectiveness of interventions that are put in place. Therefore, the VMD has committed to strengthening surveillance of veterinary antibiotic use, and has initiated work to facilitate collection of antibiotic consumption data from the major food producing species.

The UK also has a long-standing clinical surveillance programme which monitors antibiotic resistance in veterinary pathogens in samples sent to government laboratories for veterinary investigation, and has now added to this the recently initiated EU statutory harmonised monitoring programme for resistance in zoonotic and indicator bacteria.

Extensive stakeholder engagement

Since 1993 the VMD has collected, collated and published figures on UK sales volumes of active antimicrobial ingredients in products authorised for use in animals. In 2013, these sales data were published in a report together with the clinical surveillance data on antibiotic susceptibility of veterinary pathogens for the first time. Since then the report has been developed to include resistance to zoonotic and indicator bacteria from EU harmonised monitoring, and in 2015, preliminary results from the voluntary, industry-run

antibiotic consumption data collection system in meat poultry. With extensive stakeholder engagement across animal health and livestock production sectors, further antibiotic consumption data collection systems are being developed in pig and cattle sectors. These are being led by those working in the agriculture industry and veterinary profession, facilitated and guided by the Veterinary Medicines Directorate.

Central government data hub

The data described above are published on a yearly basis in the UK-VARSS report. For the antibiotic consumption data collection project, the UK has developed a central government data hub to receive antibiotic sales/use and surveillance data from the industry. The British Poultry Council (BPC: 90% of the poultry sector) submitted their antibiotic consumption data to the VMD for publication in the UK-VARSS report for the first time in 2015. The pig sector is currently developing

an electronic Book Medicine (eMB-pig) antibiotic (and other medicines) consumption data collection system to be launched in 2016. The cattle sector is meeting in January 2016 to progress the development of their antibiotic consumption data collection system.

Develop One Health surveillance

In terms of strengthening surveillance systems, it is important to have systems which collect antibiotic consumption data rather than sales, and it is also important to be able to compare these data between other countries, and also with surveillance data from humans. These data will help better understand use of antibiotics (appropriate and inappropriate), and take appropriate, evidence-based action on the development of resistance to antimicrobial medicines that are vital in the treatment of infections in both humans and in animals. We are working with the medical colleagues in government to develop strengthened One Health surveillance in the UK.

Tailored to each sector's need

Working in partnership with stakeholders in the different agriculture sectors requires investment of time and effort, but ensures development of systems tailored to each sector's need. In some sectors it has additional benefits such as encouraging farmers to move from paper records to electronic recording of data on all medicines, not just antibiotics, and is a useful clinical tool for vets and farmers for overall herd health optimisation (which in turn can reduce the need to use antibiotics).



Intervention programme to reduce resistance in an endemic situation

CP-KP (Carbapenemase-Producing *Klebsiella Pneumonia*), a carbapenem-resistant microbe, has been determined as an important pathogen in most tertiary care hospitals in Greece. These organisms are sustained in a healthcare facility by continuous influx of already colonised patients as well as by cross-transmission from patient to patient when the infection control practices are inadequate. The aim of the present study was to examine the impact of a bundle of measures on the containment of CP-KP in a haematology unit where the incidence of infections was high.

The study was conducted from June 2011 to December 2014 in a 31-bed haematology unit of a tertiary-care hospital in Athens. The intervention programme was launched in June 2011 and consisted of active screening for CP-KP rectal colonisation, separation of carriers or infected patients (single rooms or cohorting), assignment of dedicated nursing staff, contact precautions, and promotion of hand hygiene.

Evaluate trends in colonisation rates

The primary outcome was the incidence of CP-KP bloodstream infections (BSIs). Secondary outcomes included the incidence and prevalence of CP-KP colonisation. The antibiotic consumption was calculated and expressed in Defined Daily Dosages (DDD) per 100 patient-days. For BSIs Interrupted Time Series Analysis was performed using generalised least-squares method. To evaluate the trends in colonisation rates and antibiotic consumption, trend analysis was performed using the Mann-Kendall test. P values <0.05 were considered significant.

High adherence

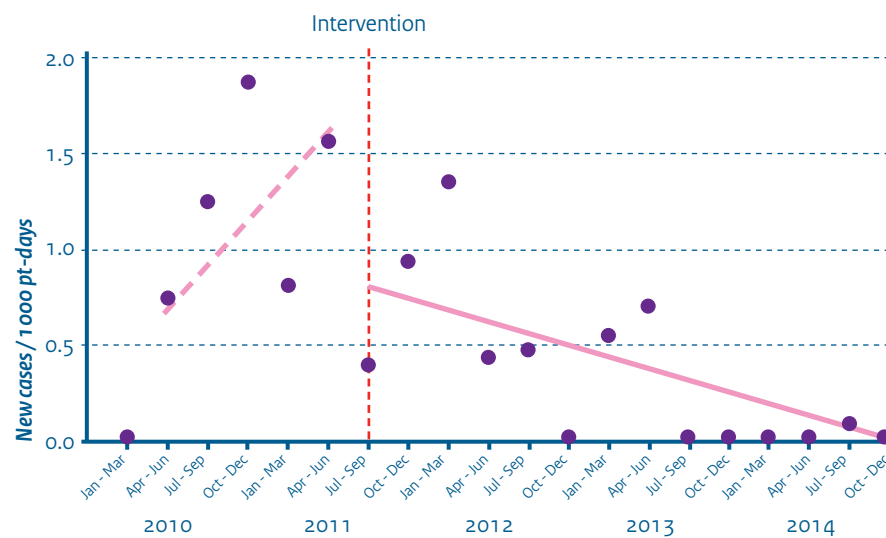
Adherence to most components of the intervention bundle was high. Surveillance cultures for rectal colonisation were obtained in 90.7% of patients admitted into the haematology unit (1.827 out of 2.015 admissions). All CP-KP carriers were separated from non-carriers in private rooms or in a cohort room. Dedicated nursing staff was assigned only during the morning shift. Compliance with hand hygiene among the medical and nursing staff ranged between 50% and 77% whereas compliance for the auxiliary staff was below 20%. Weekly surveillance rectal swabs were collected from all patients who were negative upon admission.

Point prevalence

The point prevalence of CP-KP carriers on May 2011, before the intervention, was 28.6% (8 of 28 hospitalised patients were colonised). Continuous influx of already colonised patients was observed during the study period; the prevalence of CP-KP carriage on admission ranged from 0 to 10.2%. After intervention, 40 patients were found to be carriers; 23 on admission and 17 during hospitalisation. Of note, 23% of colonised patients developed BSIs caused by CP-KP strain exhibiting identical PFGE type with that of colonisation.

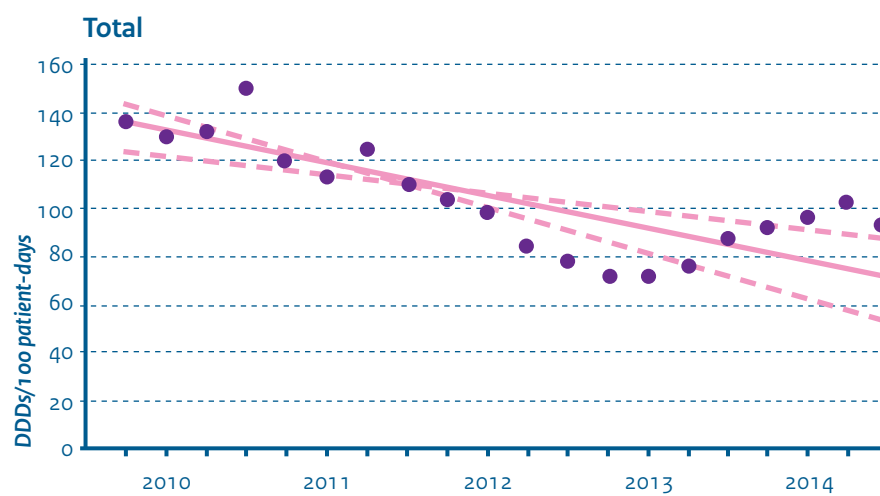
Active surveillance cultures

The implementation of a bundle of infection control measures consisted of active surveillance cultures on admission and subsequent separation of carriers, coupled with contact precautions and improved hand hygiene compliance. This was associated with significant reductions in CP-KP colonisation and infection in a haematology unit. In endemic areas the role of screening of carriers is of crucial importance for the control of the CR-KP spread in healthcare settings.



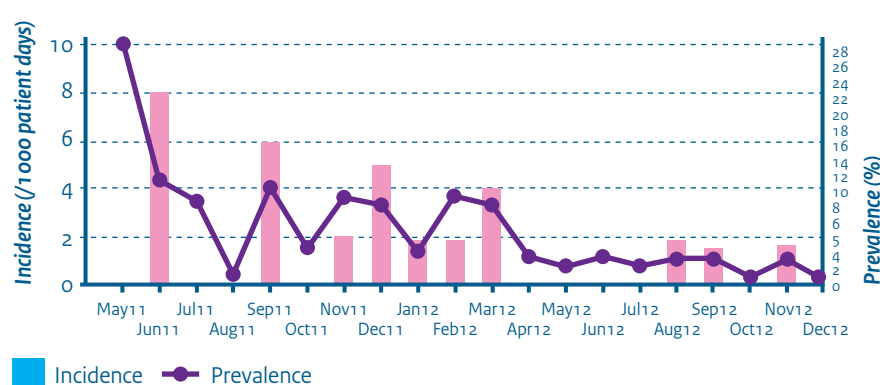
Incidence Rate of CP-Kp BSIs Before and After Intervention

Intervention resulted in significant decline in the incidence of CP-KP BSIs (change in level, P value=0.014; change in slope, P value=0.006)



Total Antibiotic consumption

Significant decline in total antibiotic consumption was observed (P < 0.001)



Prevalence and Incidence Rates of CP-Kp Rectal Colonisation Among Hospitalised patients



Responsible use of antibiotics according to OIE/WHO/EU recommendations

Ecoantibio plan

The Ecoantibio plan aims to reduce antibiotic use in veterinary medicine by 25% between 2012 and 2016. The general idea is that only strictly necessary and appropriate amounts should be prescribed and administered to animals. With a specific focus on C3-C4 generations and fluoroquinolons (-25% in 3 years 2014-2016). France advises to set a national plan for reducing antibiotic use in veterinary medicine, with quantitative and qualitative objectives, under the One Health approach and according to OIE/WHO/EU recommendations.

According to France, a prudent use of antibiotics is based on a set of recommendations and practical measures to avoid or reduce the selection, emergence and spread of antibiotic-resistant bacteria and to improve the health of food producing animals and pets. It is all about taking care of animals so that they are kept in good health whilst preserving the effectiveness of antibiotics. This means ensuring efficient use of antibiotics to prevent or limit the transfer of resistant bacteria within animal populations and also between animals, humans and the environment. This will preserve and prolong the effectiveness and usefulness of antibiotics for humans. At the same time this will protect consumer health by ensuring the safety of food of animal origin and by avoiding the risk of transmission of resistant bacteria.

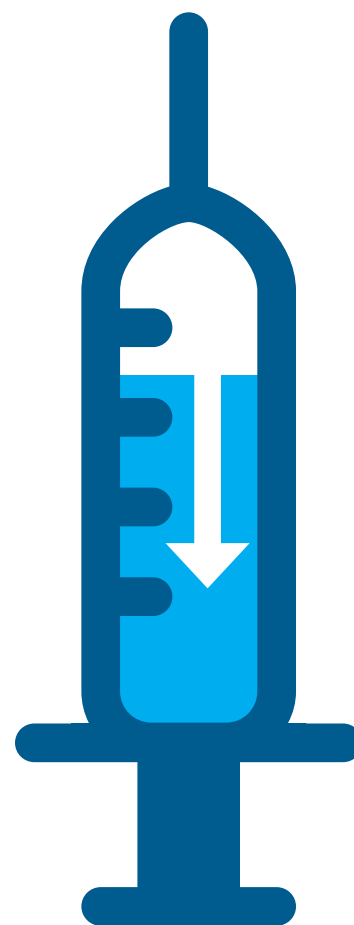
Animal Level of Exposure to Antimicrobials

The Ecoantibio plan is operational since December 2011. The global volume of antibiotics sold in 2013 reached 699 tonnes: -11% between 2012 and 2013, and -34% over the past five years. In 2013, the exposure of animals to antibiotics lessened by -7,3% compared to 2011 and by -15,7% over the past five years. The exposure of animals to antibiotics is calculated in the Animal Level of Exposure to Antimicrobials (ALEA). This is

the level of exposure by dividing the weight of animals treated with the weight of the population potentially consuming antimicrobials. The ALEA indicator has been followed for each animal sector and each antibiotics family every year since 1999.

National plan

France would like to have the support of other Member States on two essential points relating to the current negotiations on the draft regulation on veterinary medicinal products and the draft regulation on medicated feed. First of all, the requirements imposed on animals imported from third countries must be identical to those applicable to foodstuffs from those countries. This principle must apply to both regulations. Secondly the internet sales of veterinary medicines subject to prescription (in the buyer's country) must be prohibited. France believes that for action to be effective and coherent in relation to the objective of protecting public health, the prohibition of internet sales of veterinary medicines subject to prescription (in the buyer's country) must be included in the regulation itself and not left to national authorities, since such medicines are health products rather than ordinary consumer goods.



More good practices

All good practices are described within the 12 pages 'Decree of 22 July 2015 on good employment practices medicines containing one or more antibiotic substances in veterinary medicine'.



Public campaigns on responsible use of antibiotics

The first French national plan on antibiotics in 2002 aimed to raise awareness of the prudent use of antibiotics among the general public. Nationwide mass media campaigns were launched. The overall antibiotic consumption fell by 10.7% between 2000 and 2013.

The public campaigns used a range of tools, including TV and radio spots, information booklets for parents of young children, for a larger public, an exhibition entitled 'micro-organisms in questions' touring around France, and press releases giving advice on good antibiotic use for those likely to use them more (young mothers, young workers, old people).

Online guidelines and tools

At hospital level, each hospital must have a person responsible for antibiotic treatment (help with prescriptions, distribution of guidelines, follow up). Moreover, guidelines and tools are available online to help count antibiotics. Tools for pediatric professionals were also created and distributed to nursery nurses, and to directors of crèches. These measures led to a decrease in antibiotic consumption in the community: the overall antibiotic consumption fell by 10.7% between 2000 and 2013. A 5.9% increase in antibiotic consumption has been observed since 2010.



Antibiotics are not automatic

The National Health Insurance launched several public campaigns:

- 2002-2006: to break the reflex: common diseases. Slogan used: "Antibiotics are not automatic"
- 2007-2009: a focus on a new idea: viral disease. Slogan used: "An antibiotic cannot heal"
- 2010: focus on good practices, illustrated by diseases for which unnecessary antibiotic prescriptions are common (tonsillitis, bronchitis). New slogan for public awareness raising: "Antibiotics, if you use them incorrectly, they will be less strong"

Tools for physicians

- Guidelines on treating infectious, leaflets on respiratory diseases, specific website with all guidelines, but currently hardly used (18% of GPs used them regularly)
- Streptotests: free of charge for physicians (since 2002), but currently hardly used (18% of GPs used them regularly)
- Visits to GPs by local members of the national health insurance, with information on which drugs, and especially antibiotics, the GP has prescribed, compared to the average in the geographic area

Pig farm Van de Nieuwelaar in Roosendaal

Successful animal health team

The veterinary use of antibiotics was high on many Dutch livestock farms until 2009, when many vets and livestock farmers went into action. It turned out that on many farms it was possible to achieve unexpectedly significant improvements in animal health and a much lower antibiotic use by adopting a series of relatively simple and not particularly expensive management measures. These included checking the animal housing climate more often, giving animal behaviour more attention, improving the quality of the drinking water and applying hygiene measures.

This is a farrow-to-finish pig farm with at least 500 sows and 4,500 fattening pigs. The piglets remain in the farm until they can be slaughtered as fattened pigs.

The farmer's vision

In 2011, the pig farmer began implementing improvements which would lead to reduced dependence on medication administered to all the animals via the feed. For example, he took part in the project initiated by the innovation network for antibiotic-free animal husbandry. He believes it is important not to concentrate only on production but to be in contact with the general public as well. This is also the aim of the Supply Chain for Sustainable Pork (KDV) in which the farm participates.

'My aim is to produce tasty, healthy pork and to be able to look the consumers in the eye. We supply an honest product and that deserves to be recognised. That is why I'm actively involved in setting up a farmers' market in Roosendaal so I can sell my own meat there and have direct contact with the consumers.'

His own target in 2011 was to reduce antibiotic use in sows and piglets from about 16 to less than 5 Animal Daily Doses per sow per year. The figure shows that he had already more than reached his target by 2012.

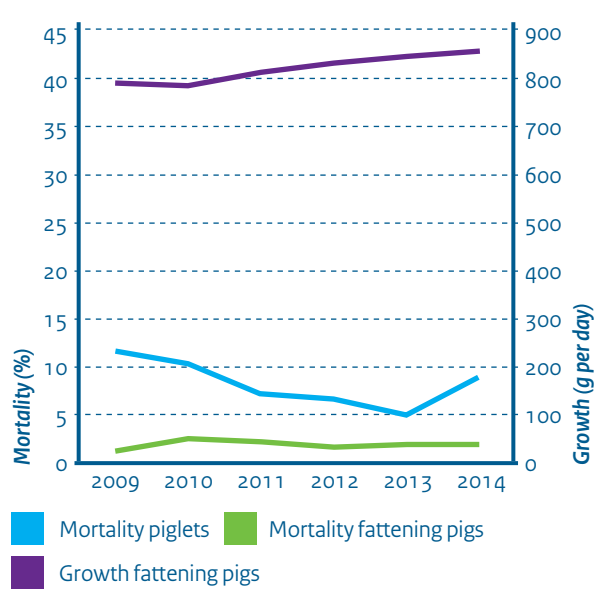
Results

The figures show that not only antibiotic use had lessened drastically after 2011 but also that the gross margin for each animal and the technical results were greatly enhanced. On this farm, improvements in management and animal housing have also led to lower total animal health costs (medicines plus vet fees).

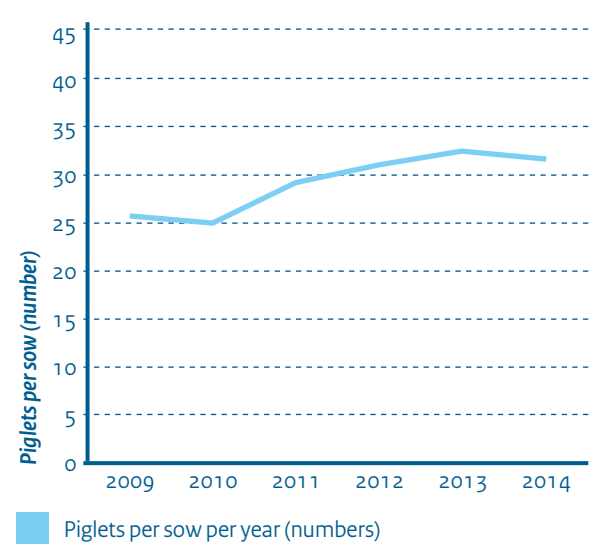
Mentality change

On this pig farm there have been huge changes in mentality and practice in terms of animal health. This farmer has had some personal experience of the damaging side-effects antibiotic treatment can cause. A treatment interferes with the natural balance, giving diseases the chance to develop whereas they were never a problem before. 'You should use antibiotics only if they're absolutely essential!', Van de Nieuwelaar says. 'I can give the pigs just one 'bucketful' of attention each day. How can I use that time to realise a maximum return? If you spend extra time on something for a short while, it always improves. I wanted to change things in such a way that those improvements became permanent.' One of the most important measures introduced on the farm was to set up an animal health team consisting of the pig farmer, his wife, the employees, the feed consultant and the vet. All measures are discussed in this team and if there is agreement on a particular point then this is always put into

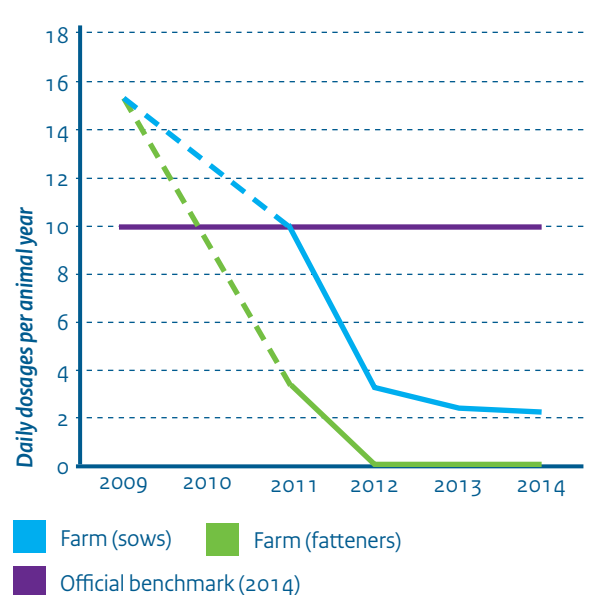
Production results - mortality and growth



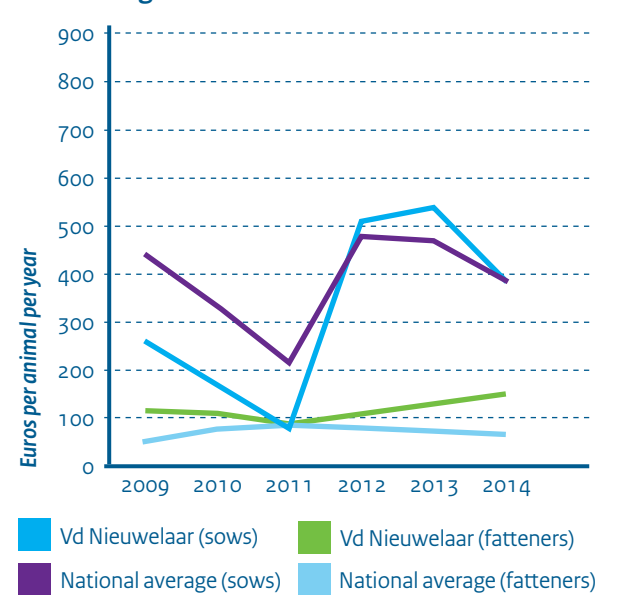
Production results - piglets per sow



Antibiotic use



Gross margin



Sources: Antibiotic use: Figure for 2009 is not available. Figure for 2010 is the overall use of sows and fatteners together. The official benchmark 2014 was laid down by the Netherlands Veterinary Medicines Authority (SDA); Gross margin and Production results: figures from Agrovision; national average: LEI Wageningen UR/FADN.

action completely and consistently. The farm's success hinges on this way of working.

Technical improvements

Van de Nieuwelaar has invested about €20,000 in technical improvements over the last five years. The truck that comes to collect manure no longer needs to drive up to the animal housing unit but is connected up at a distance via pipework. Access routes in the farm have been altered; sows no longer have to pass through the housing for the piglets. The risk of

external contacts introducing infections is further minimised by delivering the fattening pigs through special delivery pens outside the pig housing. Quarantine housing has also been installed. Young sows are delivered to this unit every 10 weeks. The annual costs of these investments amount to about €3,000. At a cost of about €1,200 per year, the team also consults a coach who helps them to analyse problems and to draw up plans for improvement twice a year. These extra costs are more than compensated for by the improved technical and economic results.



Antimicrobial stewardship limits antimicrobial resistance successfully

Face-to-Face with the A-team

To control the spread of antimicrobial resistance, the Dutch government has made an antimicrobial stewardship team mandatory for every hospital. The main objective of the so-called A-teams is to stimulate appropriate antimicrobial use. Costs are associated with the development of stewardship teams. However, the A-teams also reduce antimicrobial resistance rates, the use of expensive restricted antimicrobials, and the length of hospital stay. A-teams enhance quality of care, while also yielding large cost-savings, not only in the long run, but also shortly after implementation. The A-team of the University Medical Centre Groningen (UMCG, the Netherlands) has a special feature: the face-to-face day 2 case-audit.

The A-team of the UMCG has an unique element: the face-to-face day 2 case-audit. The aim of the case-audit is to streamline therapy as early as possible. 48 hours after start of antimicrobial therapy the hospital pharmacist sends an automatic e-mail alert to all stewardship members. Subsequently a stewardship member visits the ward to discuss the patient's therapy with the bed-side physician. Together they decide on further treatment, for example IV-oral switch and dosage, based on available diagnostics and local guidelines. They discuss the therapy again after 30 days of treatment. The face-to-face consultations create effective learning moments.

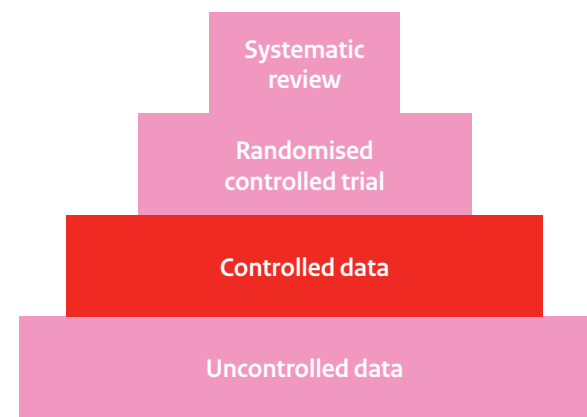
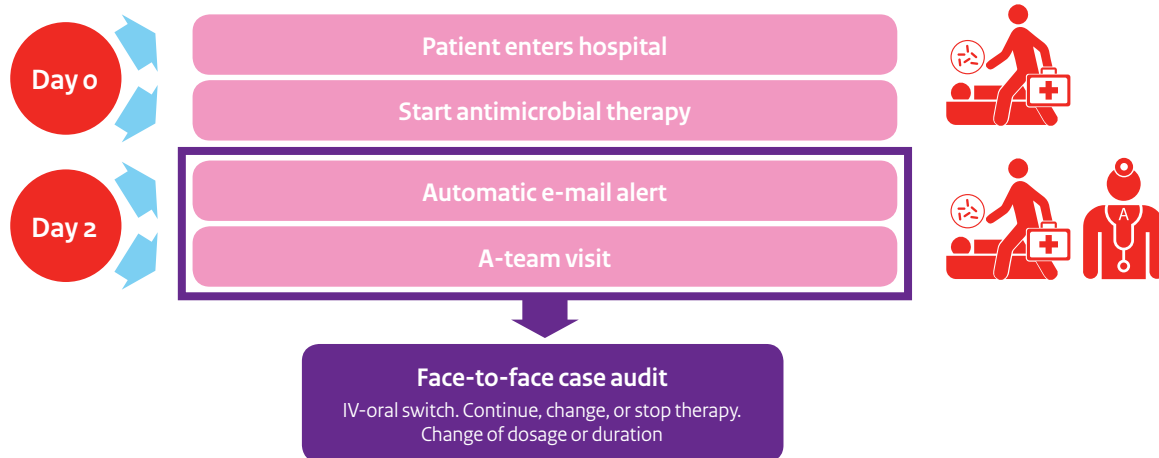
the sustainability of healthcare, given that both antimicrobial use and length of stay predict quality of care.

A yearly cost-saving of €40,000

The researchers also studied the cost-effectiveness of the A-team. They compared the hospital costs from patients in the effectiveness study with a historical cohort from the same urology ward. They divided the hospital costs into pre-intervention costs (stewardship meetings and the development of the pharmacy e-alert programme: €17,000) and intervention costs (case-audits, stewardship meetings, and maintenance of the pharmacy e-alert programme:

Attractive ROI

Antimicrobial stewardship provides practitioners with tools to prevent inappropriate use of antimicrobials and to control the spread of antimicrobial resistance. Besides, the stewardship has an attractive return on investment.



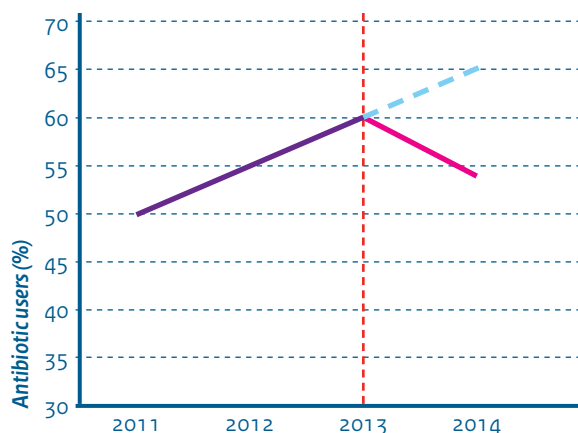
Evidence for the business case

The face-to-face day 2 case-audit

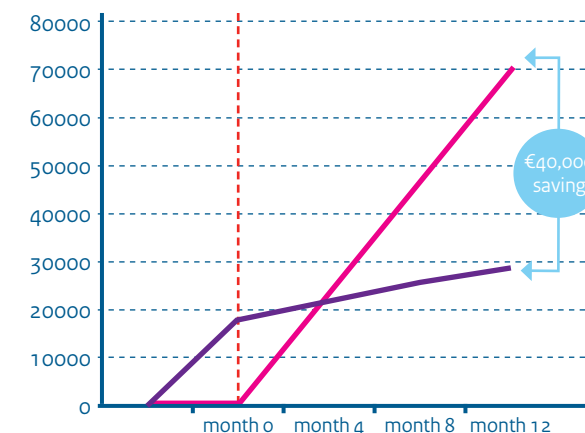
Considerably Fewer Antimicrobial Prescriptions

Alex Friedrich, Bhanu Sinha and colleagues from the UMCG studied the effectiveness of their A-team on a urology ward. They observed a significant reduction in the number of antimicrobial prescriptions. Also, the average length of hospital stay was reduced by more than one day. It should however be emphasised that these results only hold for patients without severe underlying co-morbidity. Nevertheless, the A-team seems to have a major impact on

€10,000 per year). Patients treated by the A-team switched significantly earlier from IV to oral therapy, had a shorter length of hospital stay, and required less nursing time. In total, this accounted for almost €70,000 less hospital costs than the historical cohort, during a 12-month period after implementation. It took only a few months to reach a break-even point. This implies that the A-team leads to positive return on investments, even shortly after implementation.



Antimicrobial use on a urology department before and after implementation of the A-team



Costs and savings of the A-team

Antimicrobial stewardship

The definition of antimicrobial stewardship is 'the optimal selection, dosage, and duration of antimicrobial treatment that results in the best clinical outcome for treatment or infection prevention, with minimal toxicity and minimal impact on subsequent resistance'. The objective of antimicrobial stewardship is threefold. First, to help each patient to receive the most appropriate antimicrobial with the correct dose and duration. Second, to prevent antimicrobial overuse, misuse, and abuse. Third, to minimise the development of antimicrobial resistance.

Successful A-team

- A successful antimicrobial stewardship team has four key elements:
- The stewardship team performs active surveillance by monitoring antimicrobial use and resistance hospital-wide.
 - The stewardship team provides tailored feedback on antimicrobial therapy. The recommendations are based on clinical guidelines and patient diagnostics. The feedback is provided both face-to-face and by a pharmacy e-mail alert system.
 - The stewardship team provides continuous education and training to healthcare professionals about appropriate antimicrobial use.
 - The stewardship team is multidisciplinary, preferably consisting of clinical microbiologists, infectious disease physicians, hospital pharmacists, and a quality assurance professional.

More evidence

The key elements of the A-Team of the Canisius-Wilhelmina Hospital Nijmegen (CWZ, The Netherlands) are antimicrobial vigilance alerts (daily monitoring of antimicrobial use), audit-feedback, and an IV-oral switch programme. The CWZ A-team consists of an internist-infectiologist, a microbiologist, a pharmacist and an IT-specialist. Internist-infectiologist Tom Sprong and colleagues showed that antimicrobial vigilance alerts and audit-feedback modified more than 50% of all antimicrobial prescriptions. In addition, considerably less restricted antimicrobials were prescribed. The A-team also resulted in a one day earlier IV-oral switch. According to their estimation the hospital-wide cost-saving over a 12-month period was €40,000.

Good animal husbandry and therapeutic practice

The Slovak Republic supports all the activities aimed at reduction of antimicrobial resistance as the world's biggest threat to animal and human health. Also the country has entered a lot of European programmes focused on control and reduction of antibiotic consumption, for example the antimicrobial consumption reduction programme in hog (pig) breeding organised by European Medical Agency (EMA).

The system of official distribution control, application (use) and monitoring of medical products has been implemented, which is being regularly evaluated according to the risk analysis and action programme which is being prepared. In order to reduce the consumption of antibiotics, measures for welfare of bred animals, animal nutrition, application (use) of the biologically active substances (minerals and vitamins), implementation of breeding farms' biosecurity, including vaccination programmes, have been taken in the Slovak Republic.

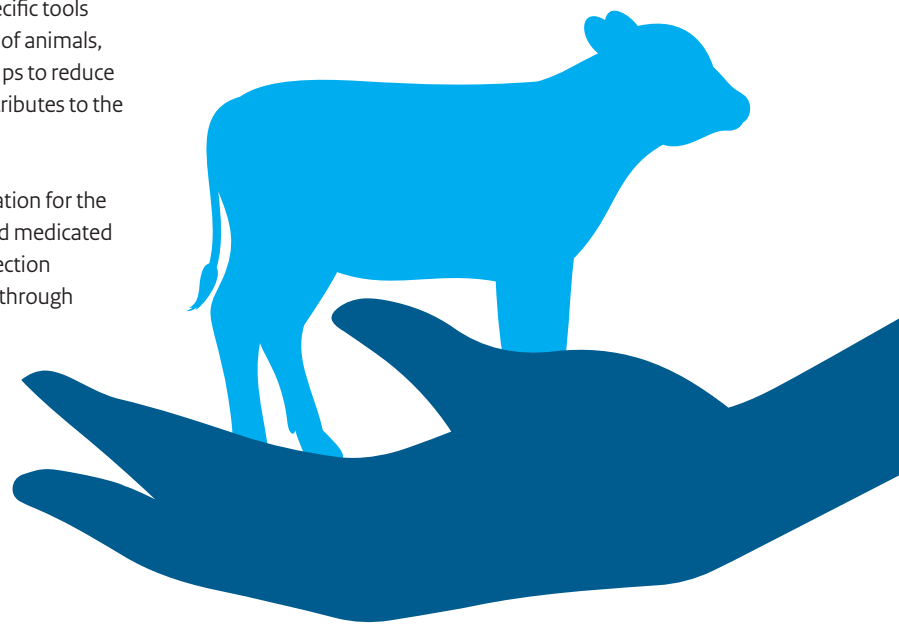
Legislative requirements

The basic principle of reducing Antimicrobial Resistance in animals is the application of good animal husbandry and therapeutic practice. Principles for reducing Antimicrobial Resistance are based on the legislative requirements for purchasing, distribution, prescribing and antibiotic use in animals. The organisation and frequency of official control of drug policy is governed by the legal regulations in addition to the risk analysis when using antibiotics especially in food-producing animals.

Law on veterinary care

Another legislative act to reduce antibiotics in animal husbandry practices is the law on veterinary care. This law defines the conditions of animal welfare, animal nutrition and good farming conditions. All these non-specific tools contribute to improving the health and welfare of animals, thereby reducing morbidity, which generally helps to reduce the need for antibiotic use and secondarily contributes to the elimination of Antimicrobial Resistance.

The Slovak Republic meets the change of legislation for the use of veterinarian medical products (drugs) and medicated feed, expecting a higher guarantee for the protection of consumers against Antimicrobial Resistance through veterinary products used in the food chain.



Antibiotic Awareness Day

The Antibiotic Awareness Day is celebrated each year on 18th November to raise awareness for the threat posed by antibiotic resistance, as well the need for prudent use of antibiotics. The campaign is organised as one of the actions of the National Programme of Antibiotic Protection established by the Polish Ministry of Health.

Different institutions are engaged in the campaign: scientific societies, outpatient clinics, hospitals, schools, government bodies, public transport, television, radio, the press. Some information about antibiotic resistance and the use of antibiotics are disseminated in the form of posters, leaflets, articles in scientific journals, educational materials for schools, radio broadcasts, advertising spots on TV and short texts on webpages. Scientific conferences are also organised.

Behavioural change

Some years ago a questionnaire study was carried out to assess the level of knowledge of people regarding antibiotics. The study revealed that about 30% of the people who were informed about the rational use of antibiotics stated that their behaviour model regarding this group of medicines had been changed. The Antibiotic Awareness Day therefore is a proven way to change the behaviour of patients and health care workers. A change that contributes to a decreased use of antibiotics and thus reducing Antimicrobial Resistance.

30% of the people who were informed about the rational use of antibiotics changed their behaviour



Information passed on to the public

- Antibiotics kill only bacteria
- Antibiotics do not cure viral infections such as flu
- Use only antibiotics prescribed by a physician
- Do not stop using antibiotics when you feel better
- If you break the upper-mentioned rules, antibiotics may be not effective when you will need them
- The overuse and irrational use of antibiotics causes antibiotic resistance in bacteria

Questions to physicians

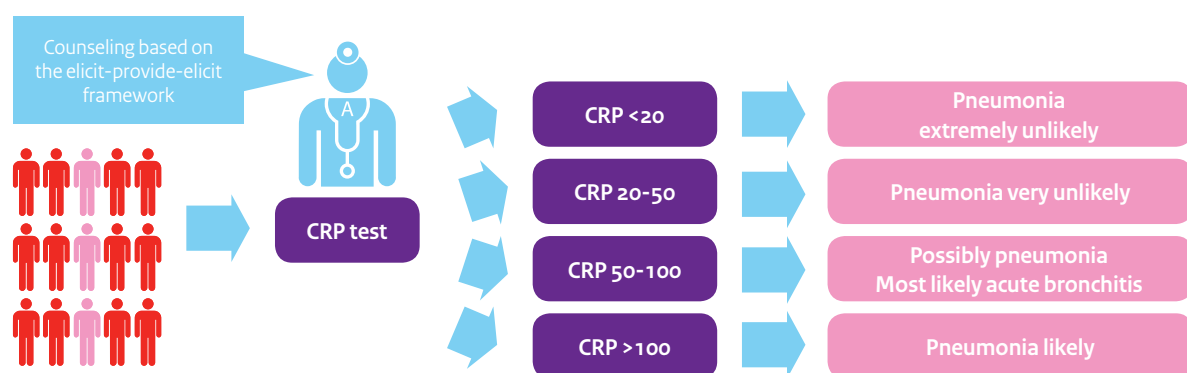
- Was a sample taken before description of an antibiotic?
- What is a proper antibiotic?
- Was an antibiotic used in empiric therapy chosen, taking into account antibiotic resistance patterns in your hospital?
- What is the proper time and dose of an antibiotic in therapy for this type of infection and this specific patient?
- Do the results of the sample culture and antibiogram indicate the need to change the antibiotic?
- Do you contact an expert in antibiotic therapy if the antibiotic is not effective?



Diagnostic certainty leads to €7 saving per treated patient

A rapid diagnostic tool to limit antimicrobial use for acute bronchitis

Does the patient suffer from acute bronchitis or pneumonia? A simple but highly accurate tool helping GPs to make the correct diagnosis could yield huge healthcare savings. And at the same time contribute enormously to the prevention antimicrobial resistance. For each year millions of people consult their GP with complaints of a lower respiratory tract infection. The majority suffers from acute bronchitis, which benefits little or not at all from antimicrobials. An accurate diagnostic tool could reassure GPs that other diagnostics and antimicrobial treatments are unnecessary. The C-reactive protein (CRP) Point of Care Test is such a tool. Jochen Cals and his colleagues (Maastricht University, the Netherlands) proved its cost-effectiveness.



Decisions based on the CRP Point of Care Test

The CRP Point of Care Test is a highly accurate diagnostic tool to differentiate between acute bronchitis and pneumonia. The CRP test can be done swiftly in everyday general practice by using a finger prick blood sample. The results are available after a few minutes. The figure shows graphically how the CRP test supports decisions about antimicrobial treatment.

Communication and expectations

Apart from diagnostic uncertainty, non-medical factors influence the decision about antimicrobial treatment. Examples are perceived patient pressure, patient satisfaction, and patient expectations. GPs often find it difficult to strike a balance between satisfying patient expectations and evidence-based prescribing. At the same time, inappropriate prescribing reinforces misconceptions and therefore affects future help seeking and expectations. A communication skills training can improve non-antimicrobial disease management.

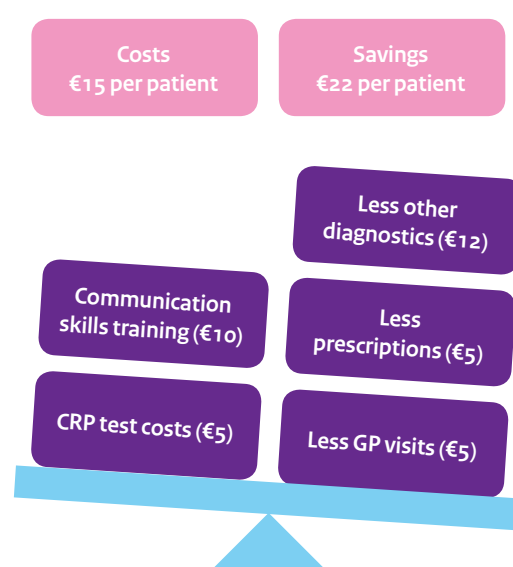
45% reduction in antimicrobial prescribing

Jochen Cals and his colleagues (Maastricht University) investigated the effectiveness of the CRP Point of Care Test, enhanced with communication skills training. The results were published in the British Medical Journal (2009). Their study was based on a large-scale pragmatic randomised trial with a one month follow-up period. The combined intervention resulted in a significant reduction in the number of antimicrobial prescriptions. The antimicrobial prescribing rate was 68% in the control group (usual care), compared to 23% in the combined intervention group. Despite the substantial reduction in antimicrobial prescribing, patients' recovery and satisfaction were similar in both study groups. The researchers claim that between 150,000 and 240,000 antimicrobial prescriptions could be saved annually, assuming nationwide implementation in the Netherlands.

Saving of €7 per patient

An economic analysis of the CRP Point of Care Test enhanced with communication skills training shows that the cost-savings are larger than the initial investments, after just one month of running the programme. Patients in the intervention group required less additional diagnostics, for example chest X-ray and spirometry. They used less antimicrobials and visited the GP less often than control group patients. This

accounts for a cost-saving of €22. The intervention costs are low, €15 per patient, and the CRP test requires only three minutes to perform. Therefore, the feasibility and financial investments cannot be hurdles for further implementation.



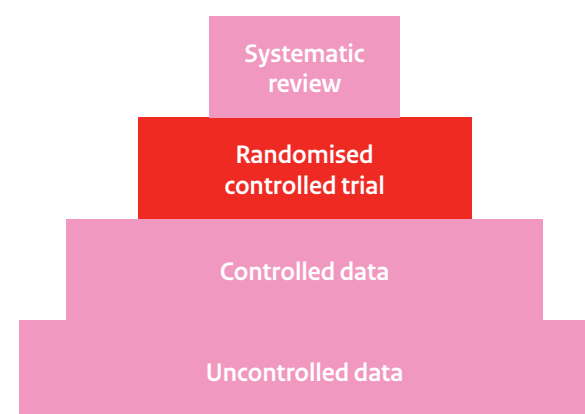
Costs and effects of the CRP Point of Care Test

EU-wide Transferability

A multi-national study was conducted to examine the transferability of the CRP Point of Care Test across languages, cultures, and health systems. Four additional EU countries participated: United Kingdom, Poland, Spain, and Belgium. GPs received online education to interpret CRP tests adequately and to communicate the results effectively. Although online training can be assumed to be less effective than face-to-face training, it has a wider reach and lower costs. The study proved transferability between very different primary care settings. The CRP Point of Care Test did not only show efficacy in countries with low prescribing rates, such as the Netherlands and the UK, but also in countries where prescribing rates are higher and thus interventions are needed most.

Major effect

GPs use of the CRP Point of Care Test combined with training in communication skills has a major effect on antimicrobial prescribing for lower respiratory tract infections, without affecting clinical recovery or patients' satisfaction. Taking into account the low intervention costs, the minor time investments, and the proven transferability, EU-wide implementation of the CRP Point of Care Test leads to huge healthcare savings, while having a positive effect on antimicrobial resistance.



Evidence for the business case

Facts & figures

17 million times a year someone somewhere in Europe visits his or her GP with complaints of a lower respiratory tract infection. It is one of the most common reasons to consult primary care. 80% suffers from an acute bronchitis. Evidence suggests that acute bronchitis benefits little or not at all from antimicrobials. Still, 8 in 10 people go home with a probably unnecessary prescription for antimicrobials. It might even harm their health, for example by putting them up with resistant bacteria. Limiting antimicrobial use in the treatment of lower respiratory tract infection is therefore a priority in the prevention of antimicrobial resistance.

Patient-centered communication strategies

Researchers from Maastricht and Cardiff universities developed a communication skills training. The training incorporates fundamental elements from patient-centered communication strategies, adapted to shared decision making about infection treatment. The main objective of the communication strategy is to elicit patients' expectations, provide evidence-based information on the natural course of common infections and the effect and side effects of antimicrobials, and elicit the patients' understanding. Thus facilitating non-prescribing decisions and increasing patients' self-care in the future, while relying less on antimicrobials.

More benefits?

The one month follow-up period was too short to capture all potential health and economic benefits. A model-based economic evaluation is needed to build a bridge between antimicrobial prescribing, antimicrobial resistance, and life-years saved. Nevertheless, the short-term effects on antimicrobial prescribing are considerable. These effects merit EU-wide implementation.



Broiler farmer in Brabant

Rely on the animal's natural resistance

Photo: Ellen Meinen, Agrio

The veterinary use of antibiotics was high on many Dutch livestock farms until 2009, when many vets and livestock farmers went into action. It turned out that on many farms it was possible to achieve unexpectedly significant improvements in animal health and a much lower antibiotic use by adopting a series of relatively simple and not particularly expensive management measures. These included checking the animal housing climate more often, giving animal behaviour more attention, improving the quality of the drinking water and applying hygiene measures.

This farm can accommodate 153,000 broilers, spread over 5 housing units. The production takes place in traditional housing and is aimed at the standard market. The farmer runs this farm on his own, but has external help to clean and disinfect the housing units and to deliver the animals.

Results

The farmer has managed to achieve an extremely low usage of antibiotics over the last few years (results from Avined). The farm obtains good technical results, which translate into above-average (high) gross margins. In spite of the greatly

Measures

The farmer has chosen to invest extra money in insulating the floors, walls and roofs and in increasing the volume of the animal housing in order to achieve a temperature that remains as constant as possible. He has also invested in his own equipment (e.g. a scoop) and personnel for delivering the animals – to prevent infection carry-over from outside. The estimated extra costs for insulation are around €10,000 per year, which is about 1 cent for every broiler delivered. The extra costs in the last few weeks involved for daily catching and loading the broilers oneself is also estimated to be 1 cent per broiler. To achieve a constant and healthy indoor climate for the animals, the housing unit is kept warm even when it is empty.

‘The general public claims to believe sustainability is very important but consumers buy the cheaper cuts of meat.’

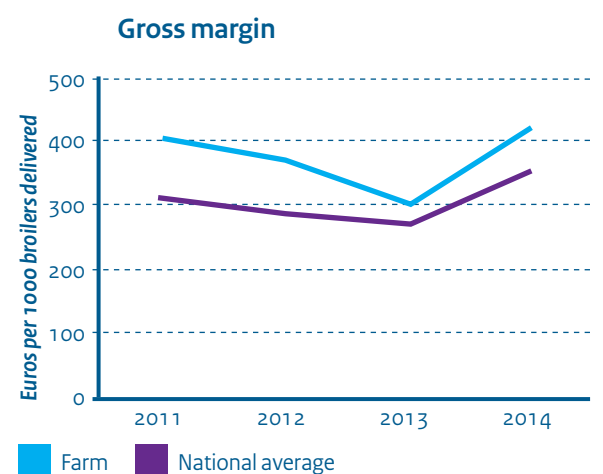
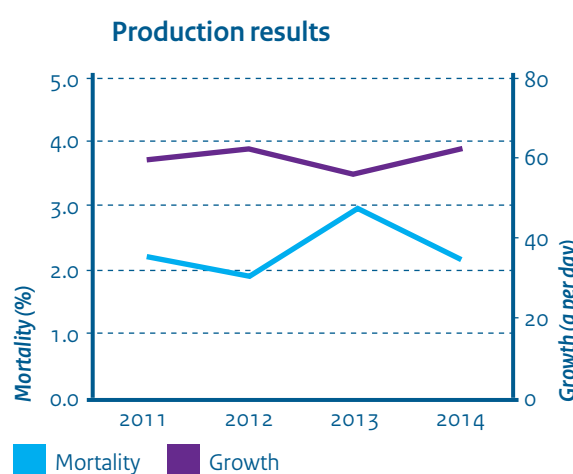
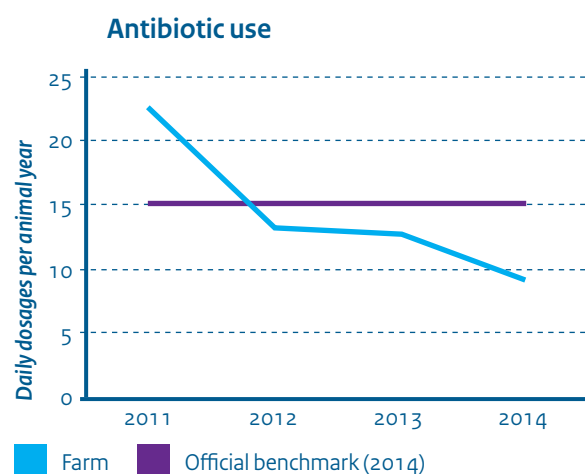
The farmer's vision

This farmer wants to earn a reasonable living and meet society's wish to limit the use of antibiotics in animal husbandry. His vision is to rely on the natural strength and resistance of the animal itself. In practice, therefore, he always aims to create an internal climate that is as stable and as healthy as possible for the animals. He wants to produce what the market demands. That is why he has had to decide to produce cheap meat.

reduced antibiotic use, there has been no worsening in the technical and economic results.

This broiler farmer does not expect that his antibiotic usage can always be zero; health problems do occur now and again. Animal welfare would then be too much at risk because of higher mortality, and this would also push the cost price up rapidly.

The initial temperature used for young animals is 2-3 degrees higher than normal. When delivering the animals, this is not done in one go, but spread out over several days; each day a small percentage of the animals is captured. In this way the farmer prevents agitation amongst the broilers, as well as temperature fluctuations. In addition, the functioning of the air conditioning is checked regularly, including at night.



Sources: Antibiotic use: Avined; Gross margin and Production results: FADN/LEI Wageningen UR. The official benchmark (2014) is laid down by the Netherlands Veterinary Medicines Authority (SDa).



Raising awareness for responsible use of antimicrobials among veterinarians

Each year, depending on the epidemiological situation, the Croatian Veterinary and Food Safety Directorate prepare an annual 'Order on measures to protect animals from infections and parasitic disease and the financing thereof'. Croatia notices that primary producers are more aware of prudent and rational use of antimicrobials and their role in the prevention of Antimicrobial Resistance. Veterinarians are also more aware of prudent use of antimicrobials and the consumption of antimicrobials has slightly dropped.

Since 2009 this Order determines annual measures and programmes for early detection, monitoring, surveillance and control of specific animal diseases. This includes programmes and measures aimed at the reduction of prevalence of zoonoses as well as programmes to monitor the antimicrobial resistance of *Salmonella* spp., *Campylobacter* spp., *Enterococcus* spp., *E.coli*, *E. faecium* and *E. faecalis* in primary produce and food production.

Valid license and prescription

According to national legislation only veterinarians with a valid license, registered with the Croatian Veterinary Chamber, may prescribe antimicrobials. A valid prescription is necessary to buy antimicrobials. National legislation also requires that veterinary organisations and farms keep records of prescribed and used antimicrobials. An annual veterinary check of holdings is used to raise the awareness of primary producers for responsible use of antimicrobials. The inspections carried out at farm level on the compliance with legislative requirements on VMP place an emphasis on prudent use of antimicrobials and properly kept records.

General results

Data on the use and consumption of antimicrobials before 2013 are not comparable with data from 2014 because the applied methodology is not the same. Therefore the first measurable results will be available in 2016. Nonetheless Croatia notices that primary producers are more aware of prudent and rational use of antimicrobials and their role in the prevention of Antimicrobial Resistance. Veterinarians are also more aware of prudent use of antimicrobials and the consumption of antimicrobials has slightly improved.

One Health

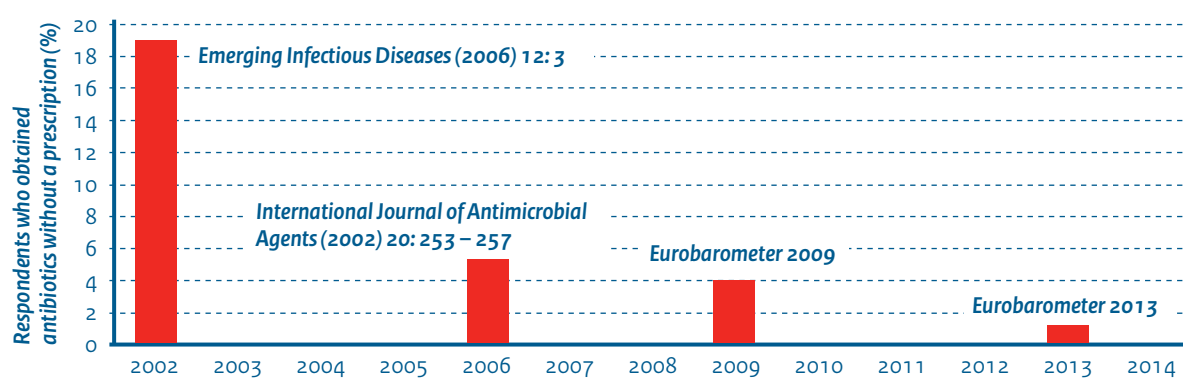
Since Antimicrobial Resistance is a global problem, according to Croatia all countries should follow the One Health approach. They should at least implement a minimum of recommendations in national strategies, as advised by leading human and veterinary medicine organisations such as OIE and WHO, as well as follow the guidelines from the EC.



Multi-pronged strategy in a Mediterranean climate

Public awareness and new dispensing practices

Malta encourages a more prudent use of antibiotics by reducing the use of non-prescribed antibiotics among the general population. The initiative was started in 2003 through a multi-pronged strategy, focusing on Maltese pharmacists and the general public. The Maltese success shows that, even in the Mediterranean, where antibiotic practices have historically posed a major challenge, it is possible to achieve significant improvement through well designed initiatives that take into account local culture and circumstances.



Proportion of Maltese respondents who stated that they had obtained antibiotics from a pharmacy or other sources without a doctor's prescription.

It started with an awareness campaign among the general public, pointing out that antibiotics are prescription-only medications and they are ineffective against colds, flu and sore throat. Concurrently the potential hazards of unnecessary antibiotic use were emphasised in terms of adverse effects and threat of resistance. This was undertaken through a variety of means including billboards within main roads, posters and leaflets in local councils and participation in discussion programmes on national media.

Encourage peer initiatives

The second pillar of the Maltese strategy was to encourage peer initiatives among pharmacists, especially through learned societies, highlighting the problem and supporting effective intervention. The last measure concerned a system change by increased regulatory reviews of dispensing practices in pharmacies, with specific focus on over-the-counter dispensing of antibiotics.

Local culture counts

Any initiative aimed at improving antibiotic practices, whether by prescribers or users, will need to take into account local issues, especially culture. There is now a solid amount of evidence supporting the role of cultural dimensions, especially uncertainty avoidance and power distance, as key drivers of antibiotic related behaviour. It would therefore be both presumptuous as well as inapt to advise other countries to follow the Maltese initiatives to the letter. However the overall strategy of addressing this challenge through a combination of education, motivational approaches as well as system change worked well.



Decrease antimicrobial consumption by adjusting the package size

The vast majority of authorised packages, especially those most recently approved, are appropriate to the duration of treatment (this aspect is part of the assessment made during the MAA). However, especially antibiotics that are authorised for many years, may have packages that have become obsolete due to the changes in clinical practice or change in antibiotic susceptibility patterns.

In September 2011, an expert working group was convened with the aim of reviewing the size of the package for oral antibiotics. This expert panel included a GP, a pediatrician, a pharmacist and government representatives. All oral antibiotic packages were reviewed and a proposal was made to adjust their size to the most common dosage and duration of treatment according to clinical practice.

Transitory period

In April 2012, Spain published an administrative decision

that all Marketing Authorisation Holders had to follow and apply in one month. From May 2012 to April 2014, there was a transitory period of coexistence of the 'old' and 'adjusted' packages. Over 900 packages were adjusted. According to the ECDC ESAC-Net surveillance data, this had a significant impact on the antibiotic consumption in terms of number of packages per 1,000 inhabitants and per day. Antibiotic consumption in terms of number of packages is probably the best surrogate for prescriptions. The conclusion is that less prescriptions were made due to the exact number of pills per package.

Country	2010	2011	2012	2013	2014	Trends in consumption of antibiotics, 2010 - 2014	Average annual change 2010 - 2014	Statistical significance
Spain	2.13 [†]	2.17 [†]	2.01 [†]	1.99 [†]	1.93 [†]		-0.06	significant
EU/EEA	3.03	3.14	3.15	3.18	3.05		-0.04	n.s.

Trends in consumption of antibiotics for systemic use in the community, EU/EEA countries, 2010-2014 (expressed in packages per 1,000 inhabitants per day)



Monitoring risk factors in assisted living facilities

HALT: healthcare-associated infections in long-term care facilities

Prevention of healthcare-associated infections (HAI) and the spread of resistant bacteria is a major patient safety issue. In addition, antibiotic stewardship helps decrease the development of antibiotic resistance. Both these core concepts rely on a loop of monitoring, feedback and improvement of local practices. The Swedish HALT project is an annual point prevalence survey that aims to support prevention of healthcare-associated infections and improve the use of antibiotics in assisted living facilities.

This national project is managed by the Public Health Agency of Sweden, but employees in each participating facility are responsible for entering survey data. They also extract the results of their own reporting, so that findings can be used for local evaluation and improvement purposes. Swedish HALT is a national adaptation of the ECDC HALT project (healthcare-associated infections in long-term care facilities). The original protocol has been adjusted to be more applicable to national conditions, for example regarding the included diagnoses, treatment alternatives and types of care facilities. Moreover, risk factors like wounds and urine and vascular catheters have been added to the monitoring. The national adaptation of the protocol has simplified reporting for participating facilities and thereby encouraged wider participation in the survey.

Web-based reporting

A web-based tool for data collection and feedback in Swedish HALT survey has been developed in the form of a module integrated in a nationwide quality register for health and social care, Senior alert. This collaboration has established a

link to all 290 regional authorities providing social care and assisted living in Sweden. Web-based reporting has made it easy for staff in each reporting unit to register infections, prescribed antibiotics and risk factors. It also makes it possible to evaluate prescribing of antibiotics in relation to various symptoms of HAI and how the presence of risk factors correlates to the prevalence of infections. Since data is easily extracted from the reporting module, all participating facilities can get instant feedback on their own results.

Antibiotic stewardship

From a handful of participating nursing homes in the ECDC HALT project 2010 and 2013, the national survey in Sweden included 110 municipalities and more than 1,000 reporting units in 2015. Participating facilities report that the survey results are important for identifying areas for targeted improvement and for raising awareness about risk factors. The results are also shared with regional groups for antibiotic stewardship, as a way to highlight the current use

of antibiotics and improve prescribing. Over time, the survey will be an important tool in benchmarking and follow-up of long-term efforts to promote patient safety and optimal use of antibiotics.

Local ownership

Careful consideration of indicators and an emphasis on local ownership has made it possible to engage various kinds of assisted living facilities in a nation-wide point prevalence survey.



Broiler farmer Van Harten in Fochteloo

Focus on quality of day-old broilers and yield

The veterinary use of antibiotics was high on many Dutch livestock farms until 2009, when many vets and livestock farmers went into action. It turned out that on many farms it was possible to achieve unexpectedly significant improvements in animal health and a much lower antibiotic use by adopting a series of relatively simple and not particularly expensive management measures. These included checking the animal housing climate more often, giving animal behaviour more attention, improving the quality of the drinking water and applying hygiene measures.

This farm is run by farmer Van Harten and his son. They have 180,000 broilers in a standard housing system in five units.

The farmer's vision

Van Harten aims to tailor his production to market demands and to do this, if possible, with fewer hours of work. Animal

During the last few months of 2014 there was a ban on transport because of avian flu (AI). The broilers were already heavy but could not be transported and had to remain in the housing units for a longer period. That caused health problems and more antibiotics were necessary. This influenced revenues negatively.

Clean drinking water

In addition to broiler quality the farmer believes it is essential that the animals are given clean drinking water and that there is a good internal climate in the housing units. That is why the drinking water system is regularly cleaned, as well as acidified periodically in order to reduce the pH and any bacterial risk. The temperature in the housing units in this farm is a couple of degrees higher than the norm. Van Harten: 'This type of broiler simply requires a higher temperature.' The day-old broilers are placed at 35°C, after which the temperature is gradually brought down to 20°C.

Higher level management

The investments in improvements have remained extremely limited. The most important investment was the early replacement of the drinking water system. The extra costs have been estimated at about €2,000 a year (0.2 cents per broiler delivered). The farmer has concluded that the management of the whole process needs to be raised to a higher level. This will not immediately cost more time but it will require extra alertness. During daily operations, Van Harten devotes most of his attention at the moment to 3 key points: broiler quality, drinking water and internal climate.

'We devote most of our attention to 3 key points: broiler quality, drinking water and internal climate.'

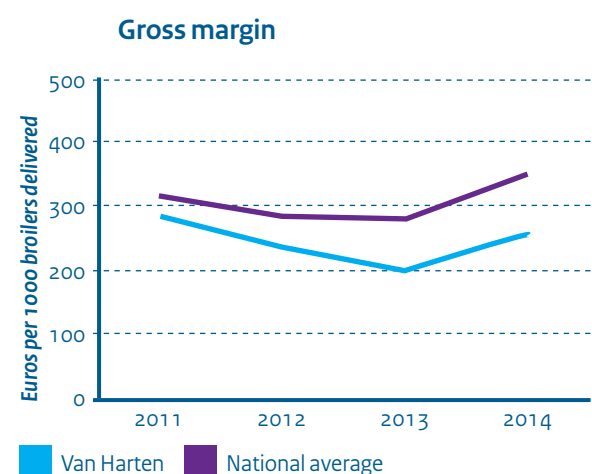
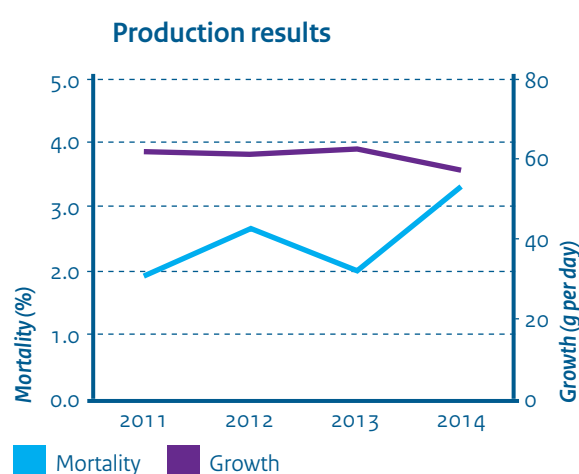
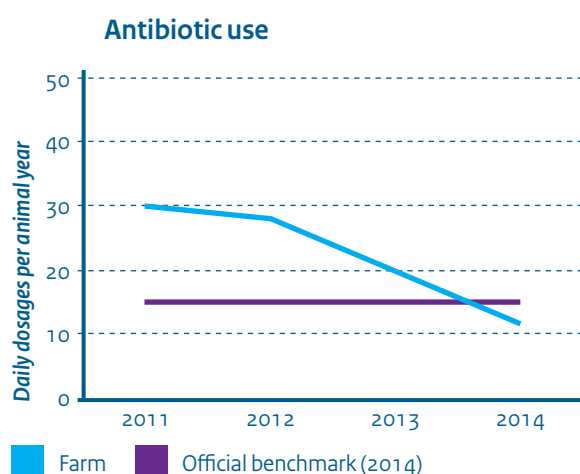
health laws are constantly reducing the numbers of animals that may be kept on one square metre. In order to maintain his revenue he would like to gradually increase his total area.

Results

Over the last few years Van Harten has achieved a 50% reduction in antibiotic use. In 2014 his use was lower than the national average and also lower than the targets laid down by the Veterinary Medicines Authority. The farm has achieved reasonable technical results and margins, which are a little lower than the national average but show comparable trends.

Alertness in hatchery choice

Van Harten believes the quality of the day-old broilers is particularly crucial for his results and his antibiotic use. During the last two years, he has been extra alert in checking the hatchery that supplied the broilers. In addition hatcheries have been monitoring breeders that supply eggs much more carefully as a result of welfare legislation which determines that mortality in broilers should not be higher than 3.5%. Van Harten does not have a permanent contract with his suppliers, so if the quality of the broilers is inadequate he can easily take his custom to another hatchery.



Sources: Antibiotic use: Avined; Gross margin and Production results: FADN/LEI Wageningen UR. The official benchmark (2014) is laid down by the Netherlands Veterinary Medicines Authority (SDa).



Biocheck.ugent®

A risk-based biosecurity scoring system

Biosecurity has been recognised as an increasingly important aspect of animal husbandry to prevent animals from becoming diseased and by doing so to avoid the need for antimicrobial use. To allow assessment and subsequent improvement of biosecurity levels in animal production, Ghent University has developed the Biocheck.ugent® risk-based biosecurity scoring system.

This is a freely available online tool that allows farmers and farm advisors to assess and quantify the biosecurity level of pig and broiler herds in an objective and neutral manner. The scoring system is based on a science-based questionnaire that can be filled in online and which provides immediate and detailed feedback. Furthermore, the website (www.biocheck.ugent.be) offers an extensive review of information concerning biosecurity and biosecurity measures on pig and poultry farms.

Benchmarking

Based upon the quantification of the biosecurity a biocheck.ugent report is generated which then can be used to identify strong and weak points in the current biosecurity and management status which then can be tackled and improved. Moreover, the scoring allows comparison of the herd biosecurity status with results of comparable farms (benchmarking) as well as with results of previous evaluations of the same herd (historic evaluation) to allow farmers to see what improvements are possible or have already been achieved.

Pigs and broilers

The biocheck.ugent pig scoring system was launched in 2009 and the broiler scoring system was launched in 2012. Currently the pig biocheck.ugent system is used in over 28 different countries throughout the world with no less than 1,250 different herd records already included in the anonymous dataset.

Quantifying the biosecurity level

The biocheck.ugent system is used increasingly by farmers, veterinarians and other herd advisors to assist in quantifying and subsequently improving the biosecurity level. The scoring system has also been used and is currently being used in several national and European research projects where the quantitative description of the biosecurity is used to be linked to production and health characteristics of the herds. This has already resulted in several scientific publications that describe the importance of biosecurity in animal production and that show the use of the improvement of biosecurity for a reduced antimicrobial consumption.

Free tool

Belgium advises all countries to make use of this freely available tool which can be used by different stakeholders and may help them in their improvement of the biosecurity state of their country and by doing so improving the general animal health situation and reducing antimicrobial usage.

www.biocheck.ugent.be

Reduced disease risk

A higher level of biosecurity results in a reduced risk of disease and less spread of disease within a herd and this subsequently results in healthier animals with a reduced need of antimicrobial treatment.



Knowledge centre AMCRA

Towards a durable policy of veterinary antimicrobial use

The Belgian government financially (70%) supports the knowledge centre 'AMCRA'. AMCRA is a sector organisation and its mission is to collect and analyse all data related to antimicrobial use and resistance in animals in Belgium and to communicate the outcomes in a neutral and objective manner, in order to safeguard both public and animal health and welfare, and to achieve a durable policy of veterinary antimicrobial use in Belgium.

AMCRA is operational since 2012 and has written different recommendations on antimicrobial use for indications per animal species, on data collection, on good farming practices, on prudent use of antimicrobials, on self-regulation, on stocks of medicines for farm animals and on zinc oxide. Notwithstanding the fact that an increase of the use of antibiotics was seen between 2013 and 2014, a general reduction on the sales of antibiotics of 11% has been achieved since AMCRA came into the picture.

Practical solutions

AMCRA has an influence on all stakeholders involved in the use of antibiotics, such as farmers keeping food-producing animals, veterinarians, pharma-industry and feed sector. All stakeholders are partner of AMCRA. The different recommendations have the broad support of the different partners. In this context, AMCRA serves as a driving force to stimulate actions by the stakeholders, not only by exposing the gaps in the current common practices, but also by offering practical solutions.

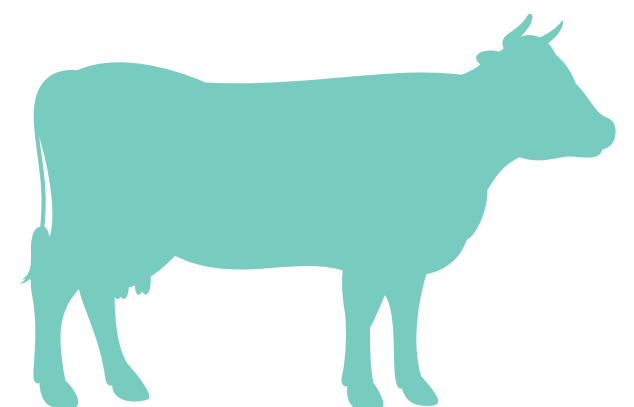
Worthwhile investment

As a starting point for an action plan to reduce the use of antibiotics, a knowledge centre, financially supported by the government, with all stakeholders as partners is a worthwhile investment. It helps the different sectors to find the gaps in their common practices and to sensitise their members. However, time has proven that this approach takes the reduction of the use of antibiotics only to a certain level. It is necessary to overcome the fear of economic consequences to get the use of antibiotics, and specifically of critical antibiotics, to an acceptable level. Therefore, in the second stage of an action plan, more pressure is needed, for example by setting official targets or laying down official measures.

Take action

Belgium advises to take action in the framework of the prevention of Antimicrobial Resistance and the prudent use of antibiotics, seeing it takes a great deal of time and energy to change people's way of thinking and acting.

Take action in the framework of the prevention of Antimicrobial Resistance and the prudent use of antibiotics



Pig farm Harbers in De Heurne

Keeping animals free from stress and infection

The veterinary use of antibiotics was high on many Dutch livestock farms until 2009, when many vets and livestock farmers went into action. It turned out that on many farms it was possible to achieve unexpectedly significant improvements in animal health and a much lower antibiotic use by adopting a series of relatively simple and not particularly expensive management measures. These included checking the animal housing climate more often, giving animal behaviour more attention, improving the quality of the drinking water and applying hygiene measures.

This farm has four housing units with a central corridor and a number of separate compartments. Each compartment has a half-latticed flooring, with the manure channel underneath. The feed is supplied by means of automatic feeders. Harbers has 1,750 fattening pigs on his farm. His aim is to produce quality pigs rather than to obtain maximum growth.

The farmer's vision

Harbers aims for an antibiotic usage of 0.1 Animal Daily Doses per animal per year. He is trying to achieve this by preventing as far as possible any infections entering the farm from outside. In addition he makes sure the conditions in which the young pigs are kept remain stable and free of stress moments, for the whole of their life cycle from breeding to finish.

'I believe the relationship and contact with the pig supplier is important. Then I know exactly what type of pigs I'm getting and how I can pamper them to give them a good start.'

Results

This farm achieves a gross margin somewhat above average, with a relatively low growth rate and little mortality. The national average for growth is about 760 grams a day and the average mortality is around 2.7%. The use of antibiotics here is very low, far below the target laid down by the Veterinary Medicines Authority.

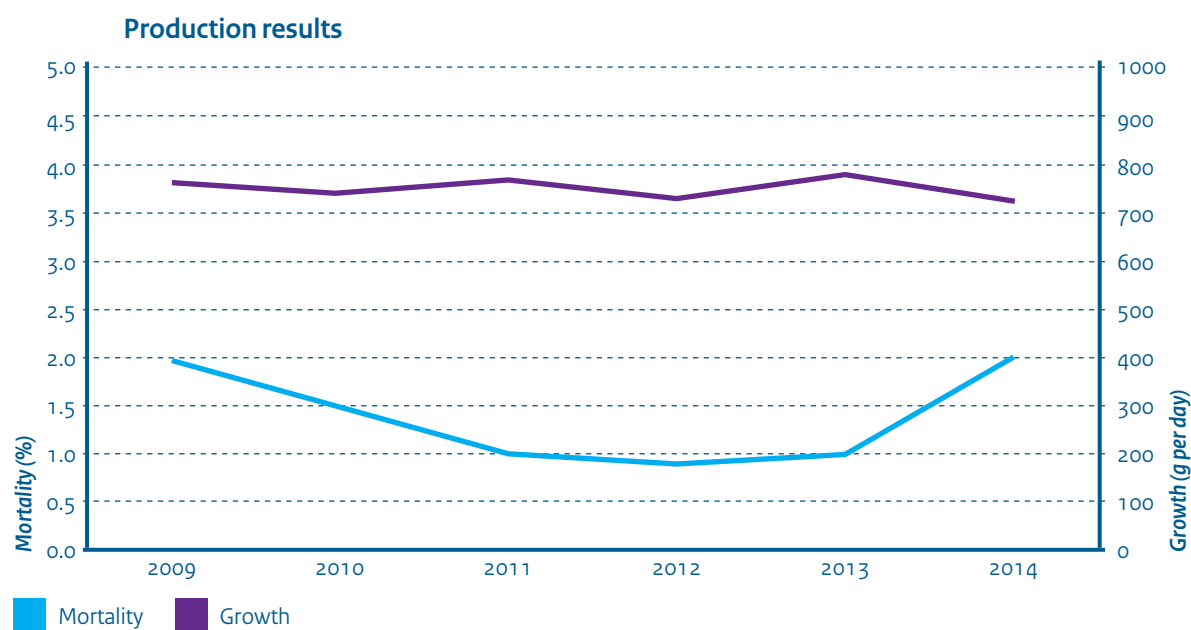
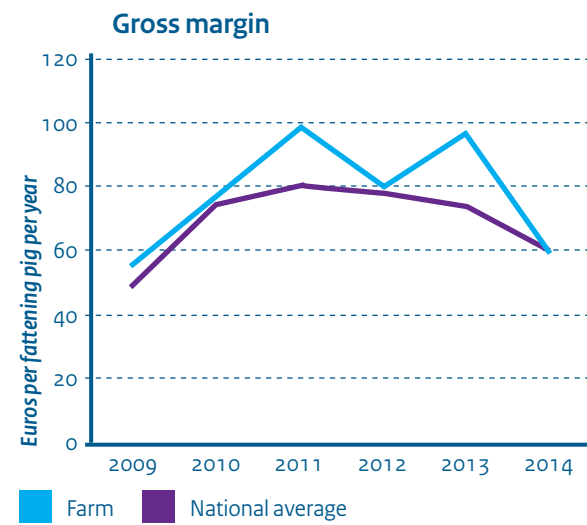
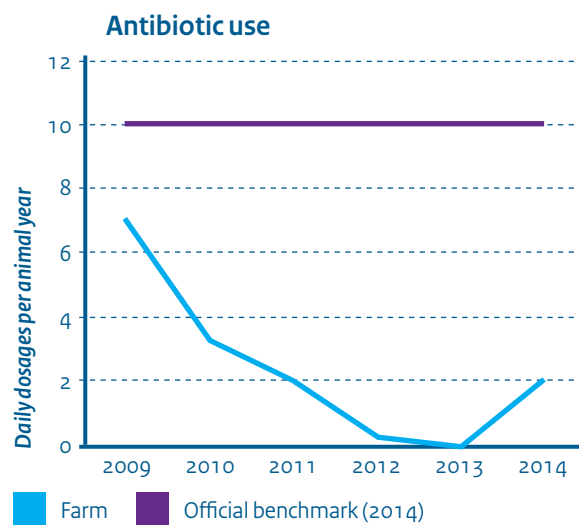
In 2014 both antibiotic usage and mortality percentages were slightly higher because of health problems at the breeding farms that supplied piglets. That is why vaccinations are now being given to increase resistance to, for example, respiratory diseases.

Free of infection

The farmer personally conveys the animals to and from his farm, using his own means of transport. In this way as few strangers and vehicles as possible enter his farm. The vet and feed supplier have both agreed to plan their visits to the farm directly after the weekend and are the first visitors of the day. The farmer also pays special attention to pest eradication. And as a final measure, the drinking water is acidified by adding whey.

Using one's own transport

Harbers uses his own vehicles and labour when transporting piglets and fattened pigs. The breeder and the slaughterhouse are situated nearby. Furthermore, Harbers has set aside enough time to carry out this work himself. The annual costs



Sources: Antibiotic use, Gross margin and Production results: FADN. Official benchmark (2014) was determined by the Netherlands Veterinary Medicines Authority (SDa).

of his own transport including the cost of extra labour are about 20% above the average standard costs of nearly 1 euro per piglet and 2 euros per fattened pig. It also provides him with extra benefits because he can deliver 99% of the pigs in the right weight class for the slaughterhouse and because the extra biosecurity prevents infection carry-over from external sources. All this contributes to an average of €0.40 savings in health costs and 0.8% lower mortality for each average fattened pig. Harbers estimates his net benefit to be around €3,000 a year.

Stress-free

The transport time is short because the animals are picked up and delivered only a short distance away from his farm. The farmer actively ensures the animals get used to their new housing and feed system as soon as possible. For example, the animals are placed in a housing unit where the temperature is 2 degrees higher than at the breeders. During the first few days, the farmer also entices the piglets to the feed troughs by offering them the feed manually three times a day.



Strict adherence to hygiene and infection control guidelines saves lives and costs

To control and prevent a nursing home outbreak of multiresistant *Klebsiella pneumoniae*

In 2013, a multiresistant *Klebsiella pneumoniae* outbreak affected nursing home De Riethorst in the Netherlands. The outbreak led to *Klebsiella pneumoniae*-associated deaths. Controlling the outbreak took considerable effort and costs, the costs amounting to €250,000. De Riethorst formed a special outbreak management team to stop the spread of the bacterium. More important, the example of De Riethorst shows that isolated treatment of *Klebsiella pneumoniae* patients and strict adherence to hygiene and infection control guidelines saves lives and costs.

In 2013, a 69-year old patient came from a hospital's isolated intensive care unit to nursing home De Riethorst. A few weeks earlier, the patient was infected with a multiresistant *Klebsiella pneumoniae* bacterium on an intensive care unit in a Greek hospital. Although De Riethorst undertook strict contact precautions, five additional patients were infected with *Klebsiella pneumoniae*. The bacterium led to severe health risks and contributed to the death of one patient.

Outbreak management team

De Riethorst formed a closely collaborating outbreak management team to stop the spread of *Klebsiella pneumoniae*. The team consisted of five internal members: a location manager, a geriatrician, a member from the board of directors, a facility manager, and a communication specialist. Additional external members were a microbiologist and an infection control specialist. The outbreak management team took several control measures to prevent further spread:

- Transfer of infected patients to a separate location outside the nursing home;
- Isolated treatment for transferred patients;
- Disinfection of the wards where the infected patients were treated earlier;
- Intensive screening on *Klebsiella pneumoniae* for all residents at De Riethorst;
- Development of an improved hygiene and infection control plan;
- Infection control measure audits;
- Communication of the outbreak with residents, family, healthcare personnel, the municipality, other healthcare organisations, and the media (newspapers, internet, television, and radio).

Controlling an outbreak

Controlling an outbreak not only takes a considerable effort but it is also costly. The total expenditure was €250,000. The major cost drivers were additional microbiological screening on *Klebsiella pneumoniae* (€93,000), isolated treatment of infected patients (€57,000), and hiring of temporary personnel and staff (€42,000). It took three months to control the outbreak. For more than a year after the outbreak all residents were intensively screened.

Strict hygiene guidelines

Currently De Riethorst implements more stringent guidelines for hygiene and infection prevention. An infection prevention specialist is involved. The current expenses for infection prevention are €75,000 annually. This is mainly spent on the infection control specialist, disinfection materials, and diagnostic procedures. The expenses equal 0.15% of the total budget.

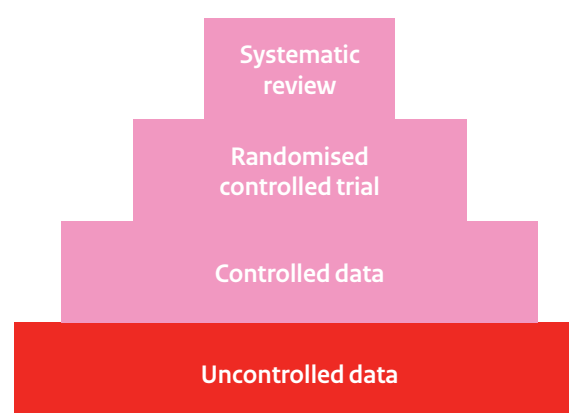
Importance of prevention

The substantial costs and severe health risks of a multiresistant *Klebsiella pneumoniae* outbreak underline the importance of prevention. At De Riethorst controlling the

Klebsiella pneumoniae outbreak took considerable effort and high costs. Their example shows that isolated treatment of *Klebsiella pneumoniae*-positive patients by highly trained personnel and strict adherence to hygiene and infection control guidelines are key to successful outbreak prevention management. Moreover, hospitals and nursing homes have to communicate carefully and effectively when transferring patients at risk to other healthcare institutions.



Costs associated with controlling the multiresistant *Klebsiella pneumoniae* outbreak



How does *Klebsiella pneumoniae* spread?

Exposure to the bacterium can cause an infection with *Klebsiella pneumoniae*. There are different types of healthcare-associated infections, including bloodstream, and wound and surgical infections. The bacterium is primarily spread through person-to-person contact. For instance, via hands of healthcare personnel or other persons. *Klebsiella pneumoniae* is not spread through the air. Infections with *Klebsiella pneumoniae* commonly occur among sick patients. Patients on breathing machines, having intravenous catheters, or having wounds caused by injury or surgery are particularly vulnerable. Given the presence of many vulnerable patients, a multiresistant *Klebsiella pneumoniae* outbreak concerns every nursing home. Infections with multiresistant *Klebsiella pneumoniae* are associated with increased costs, treatment failures, and death.

Hygiene guidelines

The nursing home staff must follow specific infection control guidelines to prevent the spread of *Klebsiella pneumoniae* infections between residents. The guidelines include strict adherence to hand hygiene and wearing gowns and gloves when entering rooms where patients with severe infections are housed. Healthcare facilities must also follow strict cleaning procedures. Moreover, residents have to clean their hands very often. For instance, before preparing food, after using the bathroom, after blowing their nose or sneezing, and before touching their eyes, nose or mouth. Healthcare professionals have the responsibility to encourage this.

Hygiene improvement programme

Nursing home Proteion enhanced the adherence to infection control guidelines among healthcare personnel with a hygiene improvement programme. The key elements of the programme were continuous education and feedback on adherence to hygiene guidelines. For example not wearing rings, watches, bracelets, nail decoration, and long sleeves. Proteion monitored the nursing home staff twice a year unannounced. Subsequently, they received tailored feedback on their adherence to hygiene guidelines. An infection control specialist (0.4 fte) was responsible for the programme. The specialist showed that education and monitoring-feedback is effective among nursing home staff. During the first unannounced assessment in April 2013, 60% of the nursing home staff were adhering to the hygiene guidelines. After two years and four feedback sessions, adherence had improved to 90%.



Reduction of the use of antimicrobials in animal husbandry

Denmark reduced the antimicrobial use in pigs and cattle by 17% between 2009 and 2014, and aims at another 15% reduction in 2018 compared to 2014. For critical important antimicrobials, the pig industry voluntarily introduced a ban on the use of 3rd/4th generation cephalosporins in 2010. The cattle industry introduced a similar ban in 2014.

In Denmark all antimicrobials used in both food producing animals and pets are prescription-only medicines. Dispensing of medicines by veterinarians was limited to non-profit sales in 1996. The DANMAP report, covering use of antimicrobial agents and occurrence of Antimicrobial Resistance from food animals, food and humans in Denmark, has been compiled since 1995. In the same year the Veterinary Advisory Service Contracts in herds of cattle and pigs came into force. In 2010 the contracts became mandatory for large herds of cattle, pigs and mink. The contracts establish a 1:1 relationship between farmer and veterinarian.

Yellow card system

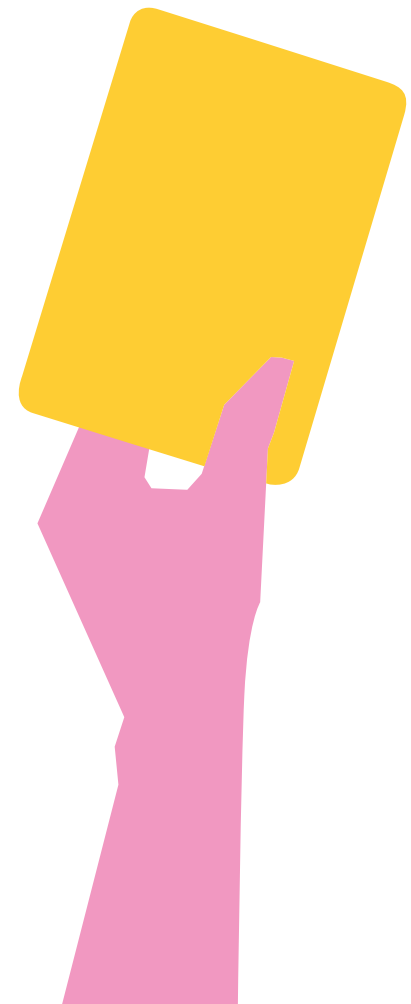
All antimicrobial consumption in production animals must also be reported to the medicine database VetStat on herd, animal species and age-group level since 2000. In 2010 a yellow card system was introduced to target actions to those having the highest use. Age-group dependent benchmark values are set from VetStat data for pigs and cattle. Furthermore legislation on treatment of groups of pigs was enforced in June 2014.

Taxes on antimicrobial agents

Differentiated taxes on antimicrobial agents for veterinary use and no taxes on vaccines have been enforced in 2013. The initiative strengthens the incentive to choose alternatives to antimicrobial treatment (e.g. vaccines) or to choose the most responsible antimicrobial treatment from a One Health perspective. The use of fluoroquinolones for food-production animals was restricted in 2002. The use of broad-spectrum antibiotics for treatment of mastitis in cattle was restricted in 2010.

Effective measures

The surveillance of the use of antimicrobials on herd, species and age-group level combined with the yellow card system setting benchmark values has been a very effective measure. The Danish experience with policy initiatives that focus both on reducing the crude use of antimicrobials and tackling the One Health challenge by creating incentive to change the constitution of the use has proven effective. Also sector specific policy initiatives combined with overall targets for the veterinary sector make the Danish policy successful.



Reducing antibiotic treatments by improving animal health

In July 2014, a mandatory strategy aiming at minimising the use of antibiotics in fattening livestock was implemented in Germany. It operates with an index for therapy frequency, which has to be determined individually for each species and age group on each farm twice a year. For the calculation of this index, the farmer has to report the number of animals kept, the number of antibiotic treatments and the number of treated animals for the past six months each year in the beginning of January and July.

In order to benchmark, two thresholds are defined for the whole of Germany. The first threshold is the median, the second threshold the third quartile of all farm-related indices. Farmers above the first threshold have to consult their veterinarian and identify the causes for the antibiotic treatments in order to eliminate them. If the second threshold is exceeded, the farmers have to hand in a written action plan to the competent authority containing measures to reduce antibiotic treatments. The competent authority has been given a range of actions to be taken if necessary to reduce the application of antibiotics. These actions include housing conditions, feed hygiene and animal density. As ultima ratio the animal husbandry can be suspended for a defined period.

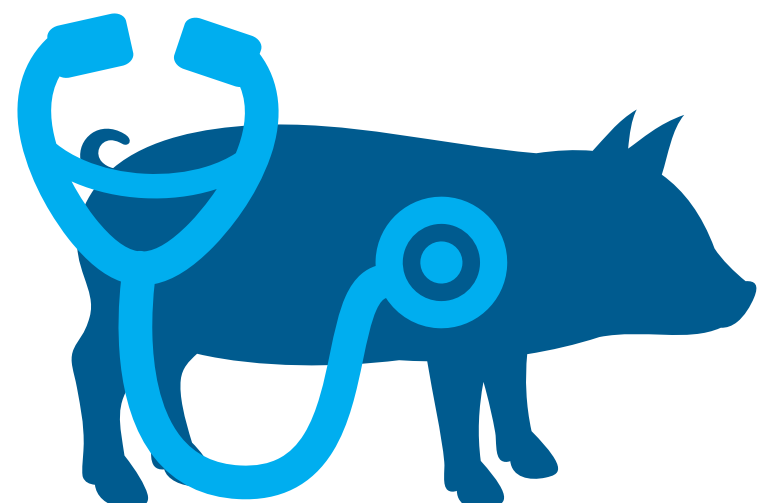
Increased awareness

The strategy started in July 2014. After two reporting periods, the implementation of this new system is well advanced. The

technical difficulties were within the expected range common to new systems. It is yet too early for the observation of effects of this new system. Nonetheless, sales of antimicrobials for veterinary use have decreased by 27% between 2011 and 2014. This reduction cannot be attributed to this system but to the increased awareness due to the broad discussion of antimicrobial use in animals.

Treatment index

Germany believes that every Member State should take measures to reduce the antimicrobial use in animals which do not impair animal health and animal welfare. Using a treatment index allows for measuring antimicrobial treatment regardless of differences in dosing regime and potency of the antimicrobial substance. The measures aimed at reducing the number of antimicrobial treatments should be augmented by rules for the prudent use of antimicrobials in animals.



EU Antimicrobial Resistance One Health ministerial conference 2016

Programme 9 & 10 February

Tuesday 9 February (evening)

17.00h-19.00h: Welcome drink and visit Micropia Museum

- Arrival of the participants, welcome drink at ARTIS Zoo and possibility to visit Micropia Museum via a guided tour.

Visit Micropia!

Micropia, the first museum of its kind, is located in Natura Artis Magistra's historical 'Ledenlokalen' (1870). It adds an important new chapter to our tradition of collecting, displaying and experiencing the natural world. It is impossible to fully understand the interconnectivity of the natural world without knowledge of the most powerful, most successful and, at the same time, smallest organisms. Microbiology can help solve global problems, from water purification to developing new ways to cure infectious diseases. It can produce energy, food and bio-plastics. There is no end to its uses.

The museum also focuses on antibiotic resistance, offering an overview of microbial warfare throughout the years. It is well worth a visit!

19.00h-19.30h: Transfer to the dinner location

- Transfer by boat through the canals of Amsterdam to the dinner location

19.30h-21.30h: Conference dinner

- Dinner in the Winter Garden of the NH Collection Grand Hotel Krasnapolsky.

Interpretation will be available during the conference in English, French, German, Spanish and Italian. Please note that there will be no interpretation provided during lunch.

Wednesday 10 February

08.00h-09.00h: Arrival at the Europa Building

- Welcome and registration

9.00h-10.00h: Opening

- Opening by Ms. Edith Schippers, Dutch Minister of Health and Mr. Martijn van Dam, Dutch Minister for Agriculture
- European Commission – The European Action Plan against AMR and its ongoing evaluation. Commissioner Dr. Vytenis Andriukaitis, DG Health and Food Safety
- Dr. Margareth Chan, DG World Health Organisation
- Dr. José Graziano da Silva, DG Food and Agriculture Organization (tbc)
- Dr. Monique Eloit, DG World Organisation for Animal Health (tbc)

10.00h-10.30h: Coffee break

10.30h-13.00h: Scenario-based policy discussion

- Interactive part with scenario films that form the basis for a deep discussion. In these scenario-based policy discussion the outcome of the conference will be discussed
- We end with an open question ('what is the added value of the EU'), this open question should be addressed during the lunch

13.00h-14.30h: Group picture and Lunch

- Closed lunch for Ministers only (this includes DG's of observing organisations and the EU Commissioner.
- Buffet lunch for other delegates

14.30h-16.15h: Next steps

- Interactive discussion with all delegates to reach political consensus on actions needed to fight AMR on national, EU and international level.

16.15h-17.15h: Finalisation outcome document and conclusions (with refreshments)

17.15h-17.30h: Closure of the conference



Co-funded by the European Union

Colophon

AMR Next was created using the input of the following countries: Belgium, Croatia, Denmark, Finland, France, Germany, Greece, Italy, Lithuania, Malta, Poland, Portugal, Slovakia, Spain, Sweden, the Netherlands and United Kingdom

More good practices and background documentation can be found at:

<http://english.eu2016.nl/latest/events/2016/02/10/ministerial-conference-on-amr>

This newspaper was compiled by the Dutch Ministry of Health, Welfare and Sport and the Dutch Ministry of Agriculture

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