KCE REPORT 311Cs

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
Belgian Health Care Knowledge Centre

SHORT REPORT

PROPOSALS FOR A MORE EFFECTIVE ANTIBIOTIC POLICY IN BELGIUM

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ROOS LEROY, WENDY CHRISTIAENS, CHARLINE MAERTENS DE NOORDHOUT, GERMAINE HANQUET

FOREWORD

The prescription and use of antibiotics are typical examples of the association between individual and collective responsibility. Every decision to prescribe a medicine is primarily taken to provide relief and cure for the individual patient. But with antibiotics, the potential indirect effects go beyond the health of a single patient. We know that the non-prudent use of antibiotics increases antibacterial resistance. The more the weapon is used, the stronger the shield becomes, and the less effective the weapon. Everyone, the prescriber as well as the patient, must therefore take his individual responsibility, so that antibiotics remain effective for the entire community.

In addition to the tension between individual and collective responsibility, there is also the issue of the benefits in the short term compared to those in the longer term. We do not always want to make clear choices in this, especially when our health is concerned. The problem of antibacterial resistance also confronts us with the limits of medicine. We have to learn again to rely on the self-healing ability of the body. And at the same time we must resist pressure from the performance-driven society which dictates invincibility and productivity.

Since health of humans, animals and environment are intertwined, a 'One Health' approach, with a collaboration between the various disciplines, is a necessary condition for the fight against antibacterial resistance. KCE already gave an initial impetus by - for the first time - actively involving the veterinary sector in this report. The way animals are kept and bred today is governed by productivity. The uninitiated reader will be surprised to discover how great the role of antibiotics is in livestock. However, scientific evidence illustrates that antibiotic use can be limited considerably if more attention is given to bio-safety and animal welfare, without jeopardizing the production results.

As usual, this KCE report was realised in close collaboration with a large group of external experts. We herewith want to thank them once again for their input and for the interesting discussions we had with them.

Marijke EYSSEN
Deputy general director a.i.

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General director a.i.

KEY MESSAGES

- Belgium was one of the first European countries to install in 1999 a national antibiotic policy coordinating commission, which was called BAPCOC. BAPCOC is seated within the Directorate Health Care of the Federal Public Service Health, Food Chain Safety and Environment; its activities mostly focus on the human health sector.
- Since 1999, numerous initiatives have been taken to improve the prudent prescription and use of antibiotics in Belgium, e.g. policy measures, sensitisation campaigns, the set-up of antimicrobial stewardship teams in hospitals, guidelines for the human and veterinary sector, the monitoring of antibiotic use in the hospital and veterinary sector. They were all performed separately in the human and the veterinary sector, with a focus on knowledge and awareness raising. Their impact on antibiotic use has rarely been evaluated. Areas that were insufficiently tackled are the nursing homes and the ambulatory sector, while in the latter the bulk of antibiotics are prescribed.
- For the ambulatory sector, Belgium is among the top 9 highest antibiotic prescribers with 21.1 DDD per 1000 inhabitants per day in 2017. For the hospital sector, Belgium is (with 1.64 DDD per 1000 inhabitants per day) situated just below the EU/EEA average. Belgian nursing home residents are also taking more antibiotics than their European peers. Likewise, there is room for improvement in the veterinary sector where the sales of veterinary antimicrobial agents equalled in 2016 140.1 mg/population correction unit (PCU), thus higher than the European mean (124.6 mg/PCU) and more than double the European median (57.0 mg/PCU).
- Determinants that play a role in the prescription and use of antibiotics are situated at the individual level (i.e. the prescriber and patient/user), the organisational level (e.g. hospitals, nursing homes) and the policy level. At all three levels barriers hamper the prudent prescription and use of antibiotics. These barriers are psychological (e.g. risk avoidance, feelings of uncertainty), social (e.g. relationship prescriber-patient) and institutional (e.g. peer practice norms, time pressure) in nature.
- The competences with regard to the prescription and use of antibiotics and AMR are shared between the federal state, the communities and the regions, which results in an intricate situation. Moreover, until very recently there was barely structural concertation between the many partners involved (e.g. BAPCOC, the federal public services, the agencies of the federated entities, Sciensano, RIZIV – INAMI, FAGG – AFMPS, FAVV – AFSCA, AMCRA). In addition, until very recently the One Health approach remained a dead letter.
- Based on the review of (inter-)national peer-reviewed and grey literature, the analysis of reimbursement data and a broad consultation of stakeholders, 21 recommendations are proposed to improve the current situation.

SHORT REPORT

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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AMCRA	Belgian Centre of Expertise on Antimicrobial Consumption and Resistance in Animals
AMR	Antimicrobial Resistance
AMT	Antimicrobial Management Team
ATC	Anatomical Therapeutic Chemical (classification)
BAPCOC	Belgian Antibiotic Policy Coordination Committee
BeH-SAC	Belgian Hospitals - Surveillance of Antimicrobial Consumption
BelVet-Sac	Belgian Veterinary Surveillance of Antimicrobial Consumption
BFA	Belgian Feed Association
CRP	C-Reactive Protein
DALY	Disability-Adjusted Life Year
DANMAP	Danish Integrated Antimicrobial Resistance Monitoring and Research Programme
DCDvet	Defined Course Dose for Animals
DDD	Defined Daily Dose
DID	Defined Daily Dose (DDD) per 1000 Inhabitants per Day
EBP	Evidence Based Practice
EC	European Commission
ECDC	European Centre for Disease Prevention and Control
EEA	European Economic Area
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EMR	Electronic Medical Record
ESAC	European Surveillance of Antimicrobial Consumption
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
FAGG – AFMPS	Federal Agency for Medicines and Health Products (‘Federaal Agentschap voor Geneesmiddelen en Gezondheidsproducten’/’ Agence Fédérale des Médicaments et Produits de Santé’)

FAVV – AFSCA	Federal Agency for the Safety of the Food Chain (‘Federaal Agentschap voor de veiligheid van de voedselketen’ – ’Agence Fédérale pour la Sécurité de la Chaîne Alimentaire’)
FOD VVVL – SPF SPSCAE	Federal Public Service Health, Food Chain Safety and Environment (‘Federale overheidsdienst Volksgezondheid, Veiligheid van de Voedselketen en Leefmilieu’ – ’Service public fédéral Santé publique, Sécurité de la Chaîne Alimentaire et Environnement’)
GP	General practitioner
HALT	Healthcare-Associated Infections in Long-Term Care Facilities
IGGI	Guideline on the prevention and treatment of infectious diseases (‘Infectiologiegids’/’Guide d'Infectiologie’)
KCE	Belgian Health Care Knowledge Centre (‘Federaal Kenniscentrum voor de Gezondheidszorg’ – ’Centre Fédéral d’Expertise des Soins de Santé’)
LOK – GLEM	Local quality circle (‘Lokale Kwaliteitsgroep’/‘Groupe Local d’évaluation Médicale’)
OECD	Organisation for Economic Co-operation and Development
OIE	World Organisation for Animal Health (‘Office International des Epizooties’)
PCU	Population Correction Unit
PPP	Purchasing Power Parity
PPS	Point Prevalence Survey
RD	Royal Decree
RIZIV – INAMI	National Institute for Health and Disability Insurance (‘Rijksinstituut voor Ziekte- en Invaliditeitsverzekering’ – ’Institut National d’Assurance Maladie-Invalidité’)
SANITEL-MED	Belgian registry for antibiotic use in animals
SDa	The Netherlands veterinary medicines institute (‘Stichting Autoriteit Diergeneesmiddelen’)
USD	US dollar
VIP^2	Quality improvement project in Flemish acute care hospitals (‘Vlaams Indicatorenproject voor Patiënten en Professionals’)
WHO	World Health Organization
ZnO	Zinc oxide

1. BACKGROUND

1.1. Rationale, research questions & scope

Since the discovery of penicillin in 1928 the use of antibiotics has made major contributions to public health.[1] Yet, **systematic misuse and overuse of antimicrobials** in human medicine and animal husbandry have **accelerated** the **development of antimicrobial resistance** (AMR), undermining many of the advances that were realised thanks to antimicrobial therapy. The direct consequences of infection with resistant microorganisms can be severe, including longer illnesses, increased mortality, prolonged hospital stays, lower protection for patients undergoing surgery and other medical procedures, and increased costs.[2] The Organisation for Economic Co-operation and Development (OECD) estimated that between 2015 and 2050 AMR will cause on average 33 000 deaths in the European Union/ European Economic Area (EU/EEA) countries per year; of these around 533 in Belgium. The OECD further expects that in Belgium AMR will result each year in on average 76 586 extra hospital days, around USD Purchasing power parity[a] 27 727 390 health care costs, and on average 13 149 disability-adjusted life years (DALYs[b]) lost.[4]

Any use of antimicrobials can result in AMR, but this risk increases if antimicrobials are used in a non-prudent way, e.g. unnecessarily prescribed/used, at sub-therapeutic doses, suboptimal spectrum, for inappropriate periods of time, in an untargeted manner through mass medication (e.g. in livestock) or use against non-susceptible microorganisms.[5, 6] Therefore, the **prudent use** of antimicrobials in both human and veterinary medicine is one of the main axes in tackling AMR. Prudent use of antimicrobials should lead to more rational and targeted use, thereby maximising the therapeutic effect and minimising the development of AMR.[5]

Given the interconnectivity between human health, animal health and the environment, the **One Health approach**, which encourages the collaborative efforts of multiple disciplines, is a condition sine qua non in the battle against antibiotic resistance.

In response to the high antibiotic use in the nineties, the Belgian Antibiotic Policy Coordination Committee (**BAPCOC**) was established in 1999. The overall objective of BAPCOC is to promote, according to the One Health approach, the prudent use of antibiotics in humans and animals and to promote infection control and hospital hygiene, with the overall aim to reduce antibiotic resistance.[7] During those 20 years, BAPCOC facilitated a substantial number of interventions that showed a positive impact on antibiotic use in Belgium. However, in the last years no further improvement was achieved. The present research topic was submitted to KCE by the Federal Public Service Health, Food Chain Safety and Environment (FOD VVVL – SPF SPSCAE), on behalf of BAPCOC.

The study has **four major research questions**:

1. Which initiatives with respect to prudent antibiotic prescribing and the push back of antibacterial resistance have been taken since the establishment of BAPCOC in 1999, in the human and veterinary sector? Was their impact on reducing AMR evaluated?
2. What is the current situation of antibiotic use in Belgium?
3. What are the main drivers of these current patterns of antibiotic use?
4. Which strategies can improve the prudent use of antibiotics in Belgium?

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a The purchasing power of a currency refers to the quantity of the currency needed to purchase a given unit of a good, or common basket of goods and services. Purchasing power is clearly determined by the relative cost of living and inflation rates in different countries. Purchasing power parity means equalising the purchasing power of two currencies by taking into account these cost of living and inflation differences. (https://www.economicsonline.co.uk/)

b The metric disability-adjusted life year(s) (DALY) quantifies the burden of a disease as the number of healthy years of life lost to morbidity and mortality.[3] DALYs for a disease or health condition are calculated as the sum of the Years of Life Lost (YLL) due to premature mortality in the population and the Years Lost due to Disability (YLD) for people living with the health condition or its consequences.

The ultimate objective of the study is to formulate proposals and recommendations to promote the prudent use of antibiotics in the human and veterinary sector, to effectively reduce antibacterial resistance.

The focus of the present study is **limited to antibiotics** (ATC[c] group J01); other antimicrobials like antifungals, antivirals and antiparasitics were not considered. Although infection control measures such as hospital hygiene and vaccination against non-susceptible pathogens play an important role in the overall reduction of antibiotic resistance, these topics were not included in the scope of the present study due to time constraints. Likewise, the development of new antibiotics, clinical trials and the research and development aspects, were not covered either. Our report covers the **human as well as the veterinary sector**. Environmental issues were not considered either.

1.2. Methodology

To answer the aforesaid research questions, the following research methods were applied, involving both the human and the veterinary sectors:

- A review of the international literature, policy documents, national and international reports;
- The consultation of stakeholders, through face-to-face interviews, stakeholder workshops and a stakeholder meeting (see Colophon);
- The analysis of the use of antibiotics in the ambulatory and hospital sector in Belgium in 2014-2016 based on reimbursement data;

As is the case for all KCE reports, the scientific report on which this short report is based, is reviewed by three independent scientific experts (see Colophon, external validators).

This study has several limitations. One of them is that, due to time and manpower constraints, dentists, pharmacists, nurses and veterinarians for companion animals were hardly consulted. In addition, we did not address the issues of specific antibiotics (e.g. last resort antibiotics) and specific resistance problems, such as hospital acquired infections.

[c] The Anatomical Therapeutic Chemical (ATC) Classification System is used for the classification of active substances of drugs according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties.

2. WHICH INITIATIVES HAVE BEEN TAKEN SINCE 1999?

Belgium was one of the first European countries to implement a national antibiotic policy coordinating commission, which was called BAPCOC. Its current governance is composed of a steering committee, working groups (covering ambulatory practice, hospital medicine, veterinary medicine, awareness raising and the federal hospital hygiene platform) and the general assembly. BAPCOC issued a **policy paper for the 2014-2019 term**, outlining policies to enhance the prudent use of antibiotics in the hospital, outpatient and animal sector.[8] It pays attention to among other things quality measures and audits, training, monitoring of antibiotic stewardship[d] in hospitals. In addition, the policy paper also includes targets for the various sectors, e.g. in the human sector, a decrease of the total antibiotic use in the ambulatory sector from more than 800 prescriptions per 1000 inhabitants per year in 2014 to 600 prescriptions by 2020 and 400 prescriptions by 2025, the increase of the amoxicillin versus amoxicilline-clavulanate ratio from about 50/50 in 2014 to 80/20 by 2018, the indication for antibiotic therapy recorded in at least 90% of hospital patient files. The interested reader can find more information on BAPCOC in the scientific report, section 3.4.2.2.

So far, the bulk of interventions with respect to prudent antibiotic prescribing and the push back of antibacterial resistance in Belgium have been performed separately in the human and in the veterinary sector.

2.1. Human sector

The National Institute for Health and Disability Insurance (RIZIV-INAMI), the Federal Agency for Medicines and Health Products (FAGG – AFMPS) and the Federal Public Service Health, Food Chain Safety and Environment (FOD VVVL – SPF SPSCAE), in collaboration with BAPCOC, are involved in the management and control with regard to the prudent use of antibiotics in the human sector. Sciensano plays a crucial role in **monitoring the prescription and use of antibiotics** in the hospital sector ('Belgian Hospitals - Surveillance of Antimicrobial Consumption' (BeH-SAC)), while antibiotic use data for the ambulatory sector are collected in the RIZIV – INAMI database Farmanet – Pharmanet. More information on the actors involved in antibiotic policy in Belgium is available in section 3.4.2 of the scientific report; section 4.2.1 covers the monitoring of antibiotic use in Belgium.

Over the years, the government has taken several **policy measures** which were suggested as initiatives to improve the prudent use of antibiotics and/or to save on the budget for medicines. For instance in the ambulatory sector, antibiotics intended for oral administration and delivered by pharmacies open to the public have moved since May 2017 from reimbursement category B to category C[e], which doubled the patient's co-payment.[9] From May 2018 onwards, the reimbursement of quinolones for oral administration and delivered by pharmacies open to the public, has been limited to certain infections or circumstances as they are now included in 'Chapter IV' of the list of reimbursable medicines.[10] These (and other examples of) measures are further elaborated in section 3.3.1.3 of the scientific report.

Since BAPCOC's foundation in 1999, **more than 30 different interventions** have been or are conducted in Belgium to promote the prudent use of antibiotics in the human sector, in addition to numerous guidelines on antibiotic prescribing. About half of these target the **hospital sector** and include various antibiotic stewardship activities conducted by the mandatory antimicrobial management teams of each hospital, as well as training in

[d] Antibiotic stewardship refers to a set of coordinated strategies to improve the prudent use of antibiotics with the goal of enhancing patient health outcomes, reducing resistance to antibiotics, and decreasing unnecessary costs.

[e] Category B and C are the reimbursement categories for therapeutically important pharmaceutical specialties and for drugs intended for symptomatic treatment, respectively. The patients' share for drugs of category C is exactly double that for drugs of category C.

antibiotic management, feedback to prescribers on antibiotic use and financial incentives. A dozen interventions target the prescribers of the **ambulatory sector**, mostly general practitioners (GPs), and involve feedback to prescribers, training, peer education, information campaigns, and availability of point-of-care testing in a limited number of GPs. Roughly six interventions target the **general public** and cover mostly information activities. A few limited (e.g. in scope) interventions address the prudent use of antibiotics in nursing homes.

A number of these interventions have been evaluated in Belgium, but the evaluations covered mostly the implementation aspects (process and output indicators), not their impact. The **impact of these interventions is difficult to assess with routine data**, as any improvement in antibiotic use and human health over time may not be attributed to a single intervention. The lack of a decline of the overall antibiotic use in Belgium in the last decade, in both ambulatory and hospital sectors (see scientific report, chapter 4), does not suggest an overall positive impact. A few studies, including three trials, assessed focused interventions using more specific outcomes and/or an appropriate comparison group, but **only few** of them identified a **positive impact**. More precisely, in the ambulatory sector, a significantly positive impact was observed in GPs who were trained in enhanced communication skills or had access to point-of-care testing; the combination of both interventions turned out to be the most effective.[11, 12] At hospital level, the temporary implementation (1997-2006) of a fixed lump sum for antibiotic prophylaxis by surgical procedure resulted in a more prudent use of antibiotic prophylaxis,[13] and a sharp decline in antibiotic expenses.[14] Lessons learned from other countries confirm the positive impact of these interventions and indicate that some other interventions had a significant effect. Among others, multifaceted interventions at both hospital and ambulatory level, the use of computer-assisted decision tools, post-antibiotic prescription review and point-of-care testing at hospital level.[15-18]

As described above, numerous initiatives have been taken with a focus on knowledge and awareness raising (e.g. media campaigns for both prescribers and patients, peer education, training, feedback on prescriptions). However, this approach tends to overlook that knowledge does not automatically translate in behaviour change because of a number of cultural, psychological, social and institutional determinants, which are much more difficult to change than an individuals' stock of knowledge.[19] The role of knowledge in behaviour change is by far overestimated. In addition, a huge number of potential drivers of behaviour change are left unexplored in the search for effective ways to improve antibiotic prescription and use, such as beliefs about capabilities, environmental context and resources, social influences.

More details on the above described initiatives can be found in the scientific report, section 6.1; the determinants for antibiotic description and use in the human sector are described in section 5.1. In section 6.3 other aspects to consider in developing interventions aiming to change prescription behaviour are discussed.

2.2. Veterinary sector

Since its foundation in 2012, the Centre of Expertise on Antimicrobial Consumption and Resistance in Animals (**AMCRA**) has been a key player in the coordination of activities with regard to the prudent use of antibiotics in the veterinary sector. AMCRA has organised roadshows and national **sensitization** campaigns (e.g. TV spots, posters) to raise awareness on AMR.[20] From 2013 onwards AMCRA has published **guidelines** for prudent antibiotic use in animals; they are free of charge available on www.e-vademecum.be. In these guidelines, antimicrobial active substances are given a colour label reflecting their importance for human and animal health based on the prioritisation attributed by the World Health Organization (WHO) and the World Organisation for Animal Health (OIE), respectively. AMCRA recommends, for instance, to avoid the use of the 'red group' of products, comprising the 3rd and 4th generation cephalosporins and the fluoroquinolones, in veterinary medicine.[21]

Importantly, in June 2016, **3 AMCRA 2020 goals** (i.e. a 50% reduction of antibiotic use by 2020, a 75% reduction of the most critical antibiotics by 2020, and a 50% reduction of feed medicated with antibiotics by 2017, see also section 3.4.3.2 of the scientific report) were **ratified** by an agreement between the Belgian Federal Government and the stakeholders; this increased the leverage for change.[22]

In addition, the Federal Agency for Medicines and Health Products (FAGG – AFMPS), the Federal Agency for the Safety of the Food Chain (FAVV – AFSCA) and the Federal Public Service Public Health, Food Chain Safety and Environment (FOD VVVL – SPF SPSCAE), in collaboration with AMCRA and BAPCOC, co-regulate initiatives with regard to the prudent use of antibiotics and the decrease of AMR (e.g. regulations relating to food standards /food chain safety, **monitoring of antibiotic use** through the BelVet-SAC and SANITEL-MED data registries – for more details see scientific report, section 4.2.2). Based on the SANITEL-MED register, AMCRA produces twice a year feedback reports (incl. benchmarking) which are sent to the individual farms. The BelVet-SAC database comprises antibiotic use data for both food-producing and companion animals; an annual report is publicly available on the website of FAGG – AFMPS.

For more information on the actors involved in antibiotic policy in the Belgian veterinary sector, the reader is referred to section 3.4.3 of the scientific report.

Over the last decade(s), several **policy measures** have been taken to restrict the use of veterinary antibiotics. At the Belgian level for instance, there was the covenant on the use of zinc oxide[f] and medicated feed (January 2013), the tax on veterinary antibiotics (June 2014), the covenant on the decrease of antibiotic use in animals (June 2016), legal conditions for the use of certain critically important antimicrobials (July 2016), and the compulsory registration of antibiotic use in the SANITEL-MED database (February 2017). At the European level, the use of antibiotics as growth promotors has been banned since 2006.[24] In addition, European legislation was issued on animal welfare (e.g. minimum weaning age for pigs, maximum stocking density for animals, minimum rules for the protection of chickens kept for meat production), which should lead to reduced infection pressure and by consequence decreased antibiotic use.[25] There is also the Animal Health Law, which is part of a package of measures proposed by the European Commission in May 2013 to strengthen the enforcement of health and safety standards for the whole agri-food chain.[26]

So far, most initiatives on the prudent use of antibiotics have been taken specifically for the sector of food producing animals, and only few in the sector of the companion animals. In the former, **economic interests** play an important role and are regarded as an important leverage for change.

The majority of the interventions undertaken in the veterinary sector have **not been evaluated** so far. Yet, there is scientific evidence that the optimization of herd management, improvement of the biosecurity and guidance on prudent antibiotic use are **promising routes of action**, without jeopardizing production results.[27-32]

For more information on the initiatives with respect to prudent antibiotic prescribing and the push back of antibacterial resistance in the veterinary sector, the reader is referred to the scientific report, section 6.2.

[f] Zinc oxide (ZnO) is administered to prevent post weaning diarrhoea in piglets. According to European legislation, Belgium is obliged to delete all authorizations of veterinary medicinal products based on ZnO for oral administration to food-producing animals by 26 June 2022. This decision was taken upon the advice of the Committee for Medicinal Products for Veterinary Use, which concluded unanimously that the overall risk-benefit balance of veterinary medicines containing ZnO is negative.[23]

3. WHAT IS THE CURRENT SITUATION OF ANTIBIOTIC USE IN BELGIUM?

The potential relationship between the use of antimicrobials by humans and animals and the occurrence of antimicrobial resistance is evaluated by the European Medicines Agency (EMA), together with the European Food Safety Authority (EFSA) and the European Centre for Disease Prevention and Control (ECDC). The most recent data (i.e. 2014) indicate that in Belgium the **overall use of antimicrobials in the human and food-producing animal sectors** were **comparable**: 153.4 mg/kg in humans and 158.3 mg/kg in animals.[33]

3.1. Human sector

3.1.1. Ambulatory sector

In 2017, the total use of antibiotics for systemic use in the Belgian ambulatory sector equalled **21.1 DID** (Defined Daily Doses (DDD[g]) per 1000 inhabitants per day or DID), which is higher than the EU/EEA population-weighted mean of 18.4 DID.[36] Among the 28 countries that transferred data to the ECDC, Belgium was in the **top 9 highest** antibiotic prescribers.[36]

In depth analyses of the RIZIV – INAMI data further revealed that a higher proportion of elderly residing in nursing homes received in 2016 at least one course of antibiotics compared to citizens aged ≥75 years staying at home (62.2 vs. 44.4%). The proportion of citizens that received that year at least one package of antibiotics was lowest in Brussels Capital Region and highest in Hainaut (35.3% vs. 45.2%).

The majority of antibiotics used in the Belgian ambulatory sector in 2016 were **broad-spectrum:** the ratio broad vs. narrow spectrum[h] equalled **2.26**. Likewise, still too often amoxicillin-clavulanate[i] is prescribed. The same year, the amoxicillin to amoxicillin-clavulanate ratio was 1:1, far below BAPCOC's objective of 4:1 by 2018.[8]

In 2016, **fluoroquinolones** comprised **10.7%** of the total DDD delivered by pharmacies open to the public. The target defined in the BAPCOC Policy paper for the 2014-2019 term with regard to quinolones (i.e. a decrease in quinolone use, from about 10% of the total antibiotic use today to 5% by 2018) is obviously not within reach.[8]

Not surprisingly, general practitioners prescribed the bulk of antibiotics in the ambulatory sector (76.6% of the total DDD), followed by the dentists (5.1%) and the dermatologists (3.5%). When taking the number of respective health providers into account, general practitioners (557 041 DDDs per 100 health practitioners), dermatologists (438 286 DDDs per 100 health practitioners) and pneumologists (207 775 DDDs per 100 health practitioners) ranked highest.

3.1.2. Hospital sector

In 2017, the total use of antibiotics for systemic use in the Belgian hospital sector was **1.64 DID** (based on the total population), just below the EU/EEA population-weighted mean of 1.8. When the 23 countries which transferred data to ESAC-Net were ranked from lowest to highest users, Belgium ranked **9th**.[36]

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g The data were analysed applying the ATC Index with DDDs 2019.[34] The DDDs 2019 better reflect the doses used in clinical practice than those listed in the ATC Index with DDDs 2018.[35]

h For the ambulatory sector the ratio broad to narrow spectrum antibiotics was calculated as follows: broad-spectrum penicillins, cephalosporins, macrolides and fluoroquinolones (J01(CR+DC+DD+(F-FA01)+MA)) to narrow-spectrum penicillins, cephalosporins and macrolides (J01(CA+CE+CF+DB+FA01).[33]

i Clavulanate is an example of a β-lactamase inhibitor. The combination of a β-lactamase inhibitor with amoxicillin extends the antibacterial spectrum of amoxicillin to some β-lactamase-producing microorganisms. The combination amoxicillin-clavulanate should not be recommended in the first line, but only when the risk of β-lactamase-producing microorganisms is clearly increased.[37]

The ECDC point prevalence survey (PPS[j]) held in 2016-2017 revealed that on the day of the survey **28.1%** of patients admitted in Belgian hospitals received **at least one antimicrobial**. About half of all antimicrobials used in Belgian hospitals (51.4%), were prescribed for a community-acquired infection.[39, 40] For hospital-acquired infections, combinations of penicillins and beta-lactamase inhibitors, and fluoroquinolones are more often prescribed in Belgium than in the EU/EEA (25.1% vs. 19.8% and 13.0% vs. 9.4%), while the use of carbapenems in these situations is lower (6.7% vs. 9.9%). First-generation cephalosporins, as is stipulated in the guidelines, are given as surgical prophylaxis to 70.5% of the patients in Belgium.[39, 40] The reason for antimicrobial use was documented in the patient's medical record for 80.8% of all antimicrobials, which is comparable to EU/EEA results (i.e., 80.2%),[39, 40] but still below the BAPCOC target of 90%.[8]

In line with the expectations, the analyses of the RIZIV – INAMI 2014 - 2016 data based on all hospitals (except psychiatric hospitals) revealed that antibiotics were prescribed most frequently in the intensive care units (536 DDDs per 1000 patient-days) and burn unit (358 DDDs per 1000 patient-days). The elderly (i.e. ≥65 years) were more exposed to antibiotics than the age group 15 to 65 years[k] (191 DDDs per 1000 patient-days and ≥65: 207 DDDs per 1000 patient-days). In the hospital sector the minority of antibiotics used were broad-spectrum[l] (e.g. in 2016, 29.9% of the total DDD). Intensive care wards and burn units used the highest proportion of broad-spectrum antibiotics (in 2016 44.5% and 39.8% of the total DDD, respectively).

It is important to note that although the bulk of antibiotics are prescribed in the ambulatory sector, the AMR risks are concentrated in hospitals, which are an environment that favours the emergence and spread of resistant bacteria.[6] The proportion of patients exposed to antibiotic treatment is also higher in hospitals:[41] as said before, the 2016-2017 PPS in Belgian hospitals showed that 28% hospitalised patients in Belgium were taking at least one antibiotic on that day.[40] Even though we do not have a similar measure for the ambulatory sector, a rough estimate of the prevalence of antibiotic use can be derived from the 2016 DID described above (21.1 per 1000). This indicates that in 2016, an equivalent 2.1% of the population on average took an antibiotic on a certain day in the ambulatory sector.[m 42]

3.1.3. Nursing homes

Also in the nursing homes, data on the prevalence of antimicrobial use on one day are collected through ECDC-coordinated PPS[j] (i.e. Healthcare-Associated Infections in Long-Term Care Facilities (HALT)). In Belgium, the most recent surveys were performed between September and November 2016.[43] They revealed that on the day of the survey, 5.9% of Belgian **nursing home** residents received at least one antimicrobial agent, which was higher than the EU/EEA crude, pooled prevalence of 4.9%. The urinary tract was the most common site for which antimicrobials were prescribed (50.4% in Belgium and 46.1% in EU/EEA), followed by the respiratory tract (31.5% and 29.4%, respectively) and skin or wound (8.8% and 12.6%, respectively).[43, 44]

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j A point prevalence survey is a count of the number of patients with a particular condition/treatment (in this case either a healthcare-associated infection or an antimicrobial agent) at a particular time (in this case a day), as a proportion of the total number of patients who are hospitalised at that particular time. A point prevalence survey only counts the condition/treatment if present at the time (on the day) of the survey, but does not count if it is present at other times during the patient stay in the hospital.[38]

k Comparison with children 0 to 14 years of age is difficult as DDD have been defined for an adult weight only and thus underestimate antibiotic use in children.

l For the hospital sector, the following antibiotics were considered broad-spectrum: piperacillin in combination with a beta-lactamase inhibitor (J01CR05), third- and fourth-generation cephalosporins (J01DD and J01DE), monobactams (J01DF), carbapenems (J01DH), fluoroquinolones (J01MA), glycopeptides (J01XA), polymyxins (J01XB), daptomycin (J01XX09) and oxazolidinones, linezolid (J01XX08) and tedizolid (J01XX11).[33]

m According to WHO, The DDD per 1000 inhabitants per day may be used to derive a rough estimate of the prevalence of use in the population being studied. For instance, 20 DDDs per 1000 inhabitants per day indicates that 2% of the population on average might receive a certain drug or group of drugs on a certain day.[42]

3.1.4. Self-medication with antibiotics and knowledge on antibiotics

In the 2016 Eurobarometer survey, 95% of Belgian respondents reported that they obtained their last course of antibiotics from their healthcare provider[n]. In the same survey, half of the Belgian respondents (54%) was aware that antibiotics are ineffective against viruses[o], which is higher than the EU-28 average (43%).[45]

In sections 4.3.1 and section 4.4 of the scientific report, more details are available on the use of antibiotics in the Belgian human sector; in section 4.2.1 the monitoring of antibiotic prescription and use in Belgium and Europe is described.

3.2. Veterinary sector

In the last decade a positive evolution with regard to the prescription and use of antibiotics in the Belgian veterinary sector has been noticed: compared to 2011 (i.e. the reference year for the AMCRA 2020 goals, see scientific report section 3.4.3.2), a total reduction of 25.9% (mg active substance/kg biomass) in antibiotic use was achieved in 2017. Yet, in order to reach the AMCRA 2020 goal (i.e. a 50% reduction by 2020), an annual reduction of 8% is needed in the coming years.[21]

In veterinary medicine, antibiotics are either administered as pharmaceuticals or in premixes (medicated feed). By 2017, a cumulative decrease of 66.6% was achieved for antibacterial premixes, hence the AMCRA objective (i.e. a 50% reduction by 2020) has been largely achieved on time. For the pharmaceuticals the picture is not that rosy: by 2017 a cumulative reduction of only 16.4% was achieved.[21] For this indicator, no target was set by AMCRA (as it is included in the general target of 50% reduction).

The decrease in antibiotic use is observed for the majority of subclasses. Importantly, from 2011 to 2017, a cumulative reduction in the use of the red group of antimicrobials (i.e. 3rd and 4th generation cephalosporins and fluoroquinolones, see also section 2.2) of 84.4% has been realised, in other words, another AMCRA objective (i.e. a 75% reduction by 2020) has been achieved, even 3 years before the set deadline.[21]

The most recent report of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) puts the Belgian data in a European perspective: the Belgian sales of veterinary antimicrobial agents equalled in 2016 140.1 mg/population correction unit[p] (PCU), thus higher than the European mean (124.6 mg/PCU) and more than double the European median (57.0 mg/PCU).[46] Hence, also in the veterinary sector, there is ample room for improvement.

More information on the use of antibiotics in the Belgian veterinary sector can be found in section 4.3.2 of the scientific report; in section 4.2.2 the monitoring of antibiotic prescription and use in Belgium and Europe are elaborated.

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n Question posed in the Eurobarometer survey: 'How did you obtain the last course of antibiotics that you used?'[45]

o Question posed in the Eurobarometer survey: 'Tell whether you think it is true or false. Antibiotics kill viruses.'[45]

p The population correction unit (PCU) is a proxy for the size of the food-producing animal population (including horses).

4. WHY DO THE PRESCRIPTION AND USE OF ANTIBIOTICS STAY AT A HIGH LEVEL IN BELGIUM?

4.1. At the level of the individual prescribers and users

Evidence suggests that physicians are well aware of the threat of antibiotic resistance, but for many this theoretical awareness is difficult to translate in actual prudent prescribing behaviour.[19, 47] This means that a number of other determinants are decisive in the decision to prescribe: e.g. perceived clinical risks, the relationship with the patient, the perceived patient demand for antibiotics (while research indicates that this demand is overrated),[48-53] uncertainty avoidance, diagnostic uncertainty, time pressure, the idea that over-using antibiotics presents fewer risks than limiting its use ('it's better to prescribe too much than too few'), the importance attached to therapeutic freedom and clinical autonomy, the lack of confidence in existing guidelines and even the opposition to evidence-based medicine ('each patient being unique').[49, 50, 52, 54-56] From the perspective of the patient and the general public at large, qualitative and quantitative research indicates that the demand for quick fixes, difficulties with accepting to manage self-limiting infections with simple rest and symptomatic treatment, the societal pressure to be healthy and performing, and presenteeism are into play.[48, 53, 57] In section 5.1 of the scientific report the determinants that influence the prescription of antibiotics for human use are described in detail.

Many of the factors described above, apply also in the veterinary sector. To name only some: risk and uncertainty avoidance, the belief in the professional obligation to alleviate suffering, fear of complications, client pressure and expectations all drive antibiotic prescribing.[58-61] But unlike in human medicine, veterinarians do not only prescribe medicines, they are also allowed to deliver (sell) the medication they prescribe. Although profit margins on antibacterial products are small, this situation may result in a certain conflict of interest. In the food producing field, veterinarians are working closely with farmers, among whom many still perceive that antibacterial products as a cure are cheaper than means to prevent infections.[62] An infection not in time and well diagnosed and treated, may have severe economic impact for the farmer, leading to farmers asking or expecting antibiotic prescription. The fear for being blamed and/or litigation should an antimicrobial not be prescribed and later be proven to have been indicated, drives antimicrobial prescription.[60] In addition, easier administration, shorter withdrawal period for slaughter or milk delivery, price or other economic factors and previous treatment failure, may stimulate veterinarians not to follow guidelines on the prudent use of antibiotics.[63] Last but not least, farmers are often reluctant to invest in biosecurity. They fear additional costs, while in fact small measures (e.g. changes in attitudes, work habits, stable hygiene) can make a difference.[58, 61] In section 5.2 of the scientific report more details are provided on the determinants that influence the prescription and use of antibiotics in the veterinary sector.

4.2. At the level of healthcare institutions and animal farms

Several strategies have been installed to curb antibiotic prescription, but from the intensive consultation of stakeholders in the field we understood that there is ample room for improvement (for a full description, see chapter 7 of the scientific report). For example, since 2007, multidisciplinary antibiotic management teams (AMT) are mandatory in all acute care **hospitals** and large (i.e. 150 beds or more) chronic care hospitals. Yet, the legislation only stipulates the installation of antibiotic management teams, the funding (in 2018: € 4 433 298) and the yearly delivery of an activity report.[64-66] It does not define the minimal human resources that should be allocated to the antibiotic management teams, the targets to reach, the consequences in case hospitals do not perform well, nor does it demand hospital managers to give account for the AMT funds they receive. In addition, according to several stakeholders, in several hospitals the antibiotic management teams lack support from the hospital management and as a result, their authority and ability to make improvements are limited. It is however clear that antibiotic management teams can only have an impact on the prudent use of antibiotics if they have sufficient resources (time and staff) to do their work properly, have the full support of the hospital management and if they are lent visibility and credibility from all involved.

Notwithstanding the substantial problem of antimicrobial resistance in **nursing homes**, the majority of these facilities currently lack structured antibiotic stewardship initiatives. The legislation describing the role of nursing homes' 'coordinating and advising physicians' ('coördinerend raadgevend arts' (CRA) – 'médecin coordinateur et conseiller' (MCC)), does not specify a precise task in terms of antibiotic policy.[67] Their input and impact varies considerably among nursing homes and is complicated by the

fact that every nursing home resident can choose his own GP, leading to many GPs taking care of the residents within a single nursing home.[68]

But also the **ambulatory sector** is denied of any structural antibiotic stewardship initiative, with the exception of some infrequent feedback on antibiotic prescription, while the bulk of antibiotics is prescribed there.[35] What is more, currently the greater part of BAPCOC's financial resources are allocated to actions in the hospital sector (see scientific report, section 3.4.2.2.). (FOD VVVL – SPF SPSCAE, *personal communication*) So far, dentists, who are prescribing 5% of the total DDDs, have not been involved.

Also in the **veterinary sector** antibiotic stewardship needs further development. Currently, veterinarians' advisory role is quite limited, in the sense that many veterinarians have the impression that most farmers are not willing to pay for veterinary counselling.[69] This may in part be explained (at least in pig farming) by the strong position of feed mill companies, which provide "free" veterinary advice.[70] But there is also considerable competition between veterinarians, which may counteract antibiotic stewardship.[61]

4.3. At the policy level

Our research also pointed to some important shortcomings at the policy level, which hamper the prudent prescription and use of antibiotics. For instance, the quality of the academic training on the prudent prescription and use of antibiotics presents gaps due to the fragmentation of the infectiology teaching base over different subdisciplines, taught by different experts which impedes consistency. Currently, there is no system of mandatory continuous education on antibiotic prescription and AMR for prescribers either. Although most stakeholders we met are convinced that clinicians with appropriate expertise and training about antibiotics and AMR are required in the battle against AMR, this medical specialty, which is mentioned in the royal decree of 2008 stipulating the composition of the antibiotic management teams in hospitals, is still not approved yet anno 2019.[66] Packages of antibiotics available on the Belgian market are often larger than what is needed for one treatment, which increases the risk of keeping leftovers at home and of subsequent self-medication (see scientific report, chapter 8). As importantly, access to the right antibacterial product is sometimes hindered by the fact that the (old) antibiotic is not (longer) available on the market, that it is temporarily unavailable or that a formulation of an antibiotic suitable for children is not available in the correct dosage (see scientific report, chapter 8).

In the veterinary sector, the matter of prudent prescription and use of antibiotics and the battle against AMR in companion animals has only received little attention. In this field, the prescription and use of antibiotics are currently not monitored. In the food producing field, large economic interests (among others competition with other countries) and the intensification of the industrialisation of husbandry jeopardize animal living conditions, health and well-being, which may lead to an increased need for antibiotics. Just like in human medicine, antibiotic package sizes do not always correspond with the volume needed, leading to left-overs and self-medication. Farmers' training programs do not include information about the advantages of healthy animals, the importance of biosecurity to keep them healthy, and the use of antibiotics only as last resort.

In addition, as competences with regard to the prescription and use of antibiotics and AMR are shared between the federal state (e.g. regulation and financing of the compulsory health insurance, legislation on professionals qualifications, registration and price control of pharmaceuticals, health workforce planning and forecasting, health of food producing animals), the communities (e.g. training of physicians, dentists, veterinarians, quality control in acute hospitals, coordination in primary healthcare, health promotion and disease prevention, long-term care) and the regions (e.g. agriculture, the environment, health of wildlife, animal welfare), the actors involved are working in a three-level structure, an intricate situation. Moreover, many partners are involved: e.g. BAPCOC, the federal public services, the agencies of the federated entities, Sciensano, RIZIV – INAMI, FAGG – AFMPS, FAVV – AFSCA, AMCRA. In all these entities, dedicated experts are working on (some aspects of) the antibiotic use/AMR issue, some entities have also appointed a Single Point of Contact, yet, until very recently there was barely structural concertation between them. Until very recently, the concept of a One Health approach was a dead letter. BAPCOC was installed as a coordinating body, but it misses the authority to build a national strategy and action plan, stipulate a mission, reflect on the governing purposes, and decide on resource allocation between the different actors involved. It is crystal clear: tackling the threat of AMR requires an international multi-disciplinary, multi-stakeholder and multisector approach.

5. HOW CAN THE SITUATION BE IMPROVED?

Based on what we learnt from the international literature, the policy documents, the national and international reports, the analysis of reimbursement data and the broad consultation of stakeholders, we recommend the following in order to promote the prudent use of antibiotics in the Belgian human and veterinary sector, so that antibacterial resistance can be reduced. We opted not to give any priority ranking to the various recommendations as the future impact of each strategy is currently unknown. Only for the convenience of the reader, we numbered the recommendations:

5.1. Develop a national One Health AMR action plan

Belgium was one of the first European countries to implement a national antibiotic policy coordinating commission. The work and dedication demonstrated so far by the Belgian Antibiotic Policy Coordination Commission (BAPCOC) are considerable.

A national One Health AMR action plan countering AMR should be developed, together with all involved parties, i.e. according to the One Health approach. The action plan should be evaluated on a regular basis, so that gaps or deficiencies can be identified and so that it can be adjusted where indicated. Effective leadership should facilitate the inclusive participation and engagement of relevant stakeholders including national and regional ministries/public services, the medical and veterinary professions, the pharmacists, research and academic institutions (including the social and behavioural sciences), agricultural organisations, and the food and pharmaceutical industries.[71] Collaboration with other partners at the European and international level should be ensured on AMR issues that go beyond the national context.

The ECDC country visit team (see scientific report, chapter 9) already suggested the development of a national action plan on AMR. According to the ECDC team, it should be implemented in a **multi-disciplinary way**, it should include a strong infection prevention and control component and a tangible presence from the relevant ministries. Its activities should not be limited to antibiotic policy alone.

Tackling the threat of AMR requires a **multisector approach,** referred to as One Health.[72] In the One Health AMR action plan it should be ensured that the human, veterinary and environmental **sectors collaborate intensively**, for instance to avoid the current situation where the sectors are working in parallel (see the systems map, which clearly illustrate the human and veterinary clusters having little or no variables in common (scientific report, chapter 7). Currently, the **various responsibilities with regard to prudent antibiotic use and AMR are shared out** to (several persons working within) several institutions (see scientific report, chapter 3). It is thus very important to ensure the **coordination of the actions** taken by the many involved partners (e.g. BAPCOC, the federal public services, the agencies of the federated entities, Sciensano, RIZIV – INAMI, FAGG – AFMPS, FAVV – AFSCA, AMCRA, academic institutions).

To effectively curb AMR, **strong leadership** is essential.[73] **High level experts** (incl. medical doctors with expertise in infectious diseases and veterinary doctors) should be involved because a core group of scientists is needed to address all the AMR tasks and to support the implementation of the activities stipulated in the One Health AMR action plan. They should ensure a strong technical expertise and should receive an appropriate remuneration for their work. The current situation with everybody involved participating on a voluntary basis (with the exception of the support team), adversely affects the persistence and continuity of BAPCOC's activities (see scientific report, chapter 7).

Sufficient and stable resources are needed to ensure that initiatives can be taken in all sectors but also between the different sectors. These resources must be readily available and should be provided **collectively** by the human, veterinary and environmental sectors.

The One Health AMR action plan should also address the development, implementation and evaluation of **interventions** that promote the prudent use of antibiotics and tackle AMR. An inventory of all implemented antibiotic use/AMR interventions should be made and kept up-to-date; the inventory should be made accessible to all so that actors involved can learn from each other (by analogy with the POP database[q]).

In addition, in the action plan it should be defined which data are requisite for decision making, who should compile them and how they should be shared. A **One Health antibiotic use and AMR report**, comprising data from all involved sectors should be published on a yearly basis; the DANMAP report can be used as a source of inspiration (https://www.danmap.org/).[74] In the other recommendations (5.2-5.21) more items are described that should be included in the action plan.

5.2. Strengthen antibiotic stewardship in acute care hospitals

Since 2007, multidisciplinary antibiotic management teams (AMT) are mandatory in all acute care hospitals and large (i.e. 150 beds or more) chronic care hospitals. Their legal framework and funding (in 2018: € 4 433 298) have been established in Royal decrees.[64-66]

As said before, the legislation on the antibiotic management teams has some important shortcomings (e.g. **minimal human resources** nor targets defined). Moreover, hospitals not performing well, are not forced to improve the situation; there are no consequences whether or not improvements are realised. But also, the general public is not aware which hospital performs well and which not.[75] The One Health AMR action plan should include initiatives (among others at the **legislative level**) to improve that situation. Last but not least, hospital managers should **give account for the AMT funds** they receive. At present, there are no data on the actual use of the AMT funding within hospitals.[41]

Initiatives in certain hospitals that **increase the authority of the antibiotic management teams** and that facilitate that hospital policies are **implemented at the ward level** (e.g. Post-Antibiotic Prescription Review, Automatic stop order) should be further evaluated. If proven effective, it should be assessed how they can be adopted in other hospitals. Stakeholders indicated that antibiotic management teams could benefit from more support from the national level (currently BAPCOC) in terms of concrete projects (e.g. sharing of 'success stories') and quality improvement initiatives (see scientific report, chapter 7).

According to the stakeholders, the prudent use of antibiotics in the wards can be improved substantially by increasing the involvement of specialists **in infectiology/medical microbiology in the wards**, so that they can give technical advice on specific cases. Yet, this requires a system to remunerate this advice (see scientific report, chapter 7). Likewise, the role of hospital pharmacists in the wards regarding the prudent use of antibiotics should be reinforced, by analogy with the model of nurses of the infection control teams who are on the job and who give concrete advice to the specialists in the various hospital wards. Sufficient resources should be made available to also realise that in smaller hospitals.

To preserve last-line antibiotics, **barriers should be reinforced** in the hospitals' prescription system (e.g. reinforce the system that prescription of certain broad-spectrum antibiotics are restricted to specific medical specialties or for specific indications).

The **quality improvement projects** that are implemented in hospitals (e.g. Pay for Performance, VIP², external quality accreditation; see scientific report, chapter 6) should systematically include a number of indicators related to the prudent use of antibiotics.

[q] The EUnetHTA Planned and Ongoing Projects (POP) database allows HTA agencies to share information with each other on planned, ongoing or recently published projects conducted at the individual agency. The aim of the database is to reduce duplication and facilitate collaboration among HTA agencies. (https://www.eunethta.eu/pop-database/)

5.3. Roll out local antibiotic stewardship teams in the ambulatory sector

Currently, the bulk of antibiotics in Belgium are prescribed in ambulatory care, as is the case in many high-income countries.[71] Available AMR data reflect mostly the hospital sector. Yet there are only limited antibiotic stewardship initiatives in this sector. In addition, the greater part of BAPCOC's financial resources are allocated to actions in the hospital sector (see scientific report, chapter 3).

Local antibiotic stewardship teams for ambulatory care should be developed and rolled out over the whole country (e.g. within the current structure and organisation of the Lokale Kwaliteitsgroeps (LOKs) and Groupe Local d'Évaluation Médicale (GLEMs)). The stewardship teams could be moderated by local general practitioners (GPs) who are regularly updated (e.g. yearly) in antibiotic stewardship. The local antibiotic stewardship teams should not only include GPs, but also **pharmacists** and specialists **in infectiology/medical microbiology from the local hospitals** (in order to ensure exchange of information and expertise). In the One Health AMR action plan the overall strategy should be defined.

The local antibiotic stewardship teams should have access to anonymised prescription data of the GPs working in their catchment area and with a minimal delay so that they can be reviewed among peers. They should also have access to the AMR data that reflect the local epidemiology at ambulatory level (community acquired infections).

The local antibiotic stewardship teams should invite the local GPs on a regular basis, to **provide continuous education** (e.g. on the recent AMR situation), to discuss their **prescription behaviour** and possible interventions, to improve their **communication skills** with patients, and to share experiences, lessons learnt etc. encountered in their daily practice. This could be encouraged by including it in the current accreditation system.

The members of the local antibiotic stewardship teams should be available and able to provide ad-hoc advice to their peers in case they need rapid advice on e.g. the type, dose and/or duration of an antibiotic for a specific patient; this could be organised through e.g. an on-call system or a mobile messenger service adapted to health care services (e.g. Pandalab (https://www.pandalab.fr/) in France). In addition, peer **support** and support from specialists in infectiology/medical microbiology from the local hospitals should be provided.

The activities of the local antibiotic stewardship teams and referent specialists should be **funded**.

Similar initiatives could be taken for medical specialists working in the ambulatory sector (e.g. dermatologists, pneumologists, ENT specialists, paediatricians) as well as for dentists.

Close collaboration between the stewardship initiatives taken in the hospitals, ambulatory care and nursing homes (cf. infra) of the same area should ensure an integrated approach in the three sectors. Inspiration can be found in Sweden, where different health care professionals from general practice, hospital medicine and long-term care are collaborating closely in local STRAMA (Swedish program to combat AMR) groups. The STRAMA groups facilitate coordination and knowledge transfer between all levels of care locally whilst coordinating with the national STRAMA steering group and the Swedish public health agency. In this way they are acting as a mechanism to adapt national initiatives to local settings.[71]

5.4. Develop antibiotic stewardship in nursing homes

There is a substantial problem of antimicrobial resistance in nursing homes. In addition, there are currently several barriers to antibiotic stewardship in nursing homes: the legislation describing the role of nursing homes' 'coordinating and advising physicians', does not specify a precise task in terms of antibiotic policy,[67] and many GPs take care of the residents within a single nursing home as every nursing home resident can choose his own GP.[68]

In order to improve the prudent use of antibiotics and to address the problem of AMR in nursing homes, antibiotic stewardship should be further developed in these facilities. This recommendation is in line with the European guidelines for the prudent use of antimicrobials in human medicine, issued in 2017 by the European Commission.[76]

The role of the coordinating and advising physician needs to be adjusted for that purpose. The data on the prescription behaviour of GPs caring for nursing home residents and on AMR in nursing homes can contribute to develop locally relevant activities leading to a more prudent use of antibiotics. In addition, the results of the pilot project in four nursing home

consortia, the set of recommendations developed by a 2018 FOD VVVL – SPF SPSCAE report and the results of the ECDC-coordinated point prevalence surveys[j] in nursing homes (the so-called HALT surveys, see also 3.1.3) could be used as a basis for developing stewardship action plans for nursing homes.[77]

The antibiotic stewardship initiatives in the nursing homes should be taken in **close collaboration with the antibiotic stewardship teams of the local or regional hospitals** (e.g. to set up initiatives to prevent the spread of resistant bacteria when nursing home residents' illness requires hospital admission) and in close collaboration with the **local ambulatory antibiotic stewardship teams** (e.g. to set up initiatives to prevent the spread of resistant bacteria from nursing home residents and their relatives and friends) to obtain an integrated approach. In addition, peer support and support from specialists in infectiology/medical microbiology from the local hospitals should be provided.

5.5. Improve the professional education on prudent antibiotic prescription and use, and develop and implement interventions targeting psychological, social and institutional determinants of behavioural change

*According to the stakeholders, the **academic training** on the prudent prescription and use of antibiotics presents gaps due to the fragmentation of the infectiology teaching base over different subdisciplines, which prevents consistency. This is a result of the fact that infectiology is not recognised yet as a separate discipline (cf. infra). Currently, there is no system of mandatory **continuous education** on antibiotic prescription and AMR for prescribers. There is no requirement that quality circles (LOK – GLEM) focus on the topic of prudent antibiotic prescription nor that practitioners attend these sessions.*

In order to improve the prudent use of antibiotics and to address the problem of AMR in all sectors, the quality of the training on prudent antibiotic prescription and use should be improved. It was also reported to the ECDC country visit team (see scientific report, chapter 9) that many GPs and other clinicians lack knowledge on the mode of action of different antibiotics, their indication and use. For example, the ECDC country visit team recorded anecdotal evidence that doctors overprescribe quinolones for acute, uncomplicated urinary tract infections, amoxicillin-clavulanate for simple skin infections, amoxicillin rather than penicillin V for tonsillitis, or combinations of oral and topical antibiotics simultaneously.[73]

In order to improve the knowledge on the prudent prescription of antibiotics and AMR, the continuous education should include a **mandatory yearly or biannual** module on these topics, as recommended by the ECDC country visit team.[73] The observation that physicians partly maintain antibiotic prescribing habits of the past as they age[78] is an additional argument for the mandatory continuous training in these topics.

Last but not least, training sessions should be regarded as an excellent opportunity for knowledge exchange between the veterinary and human sectors.

Knowledge on itself (realised through among others training, peer education, guidelines, and awareness campaigns) is an essential, yet insufficient condition for behavioural change. It is no coincidence that knowledge is also the easiest to influence and/or to adjust.[19]

The One Health AMR action plan should thus include interventions targeting psychological, social and institutional determinants of behavioural change as well. Improvement strategies only have a chance of success when all types of barriers are targeted.[79] For this purpose, collaboration with the Evidence Based Practice (EBP)[r] implementation cell should be envisaged.

[r] The EBP Network, initiated by the minister of Social Affairs and Public Health in 2016, aims at coordinating all federal initiatives related to Evidence Based Practice (EBP) in Belgium. In this network, Ebpracticenet (www.ebpnet.be) disseminates guidelines and other EBP products by offering a central, unique and dedicated distribution platform for the spreading of EBP information in Belgium. Ebpracticenet also takes up the role of implementation cell. The goal of the implementation cell is to stimulate the real practice use of guidelines and other EBP products, and to change the behaviour of healthcare professionals and patients. Currently this network focuses on primary care, but extension to secondary care will be considered in the future.

5.6. Recognise medical microbiology and infectiology as medical specialty and provide remuneration for their advice

Specialists with appropriate expertise and training about antibiotics and AMR, such as those in infectious diseases and medical microbiology, as well as laboratories of medical microbiology, are essential to ensure appropriate treatment of infections, appropriate use of antibiotics and support for antibiotic stewardship programmes.[73] These medical specialties are mentioned in the royal decree (RD) of 2008 stipulating the composition of the antibiotic management teams in hospitals, and the vast majority of EU countries have already recognised them officially as medical specialty. Yet the approval of infectiology and medical microbiology as medical specialty in Belgium is still outstanding anno 2019.[66]

As was also suggested by the ECDC country visit team (see scientific report, chapter 9), infectious disease specialisation should be **legally recognised** and their advice should be eligible for **remuneration**.[73] These specialists should not only be involved in the antibiotic stewardship programmes in the hospitals, the ambulatory sector and the nursing homes, but also in the training and continuous medical education of medical doctors and dentists. They should be available in the hospital wards for onsite consultation as well.

5.7. Improve the availability of old/narrow spectrum antibiotics

A vital component in the battle against AMR is access to the right antibacterial product. Yet, sometimes (old, narrow spectrum) antibiotics are not (longer) available on the market, or temporarily unavailable or not available in the correct dosage or formulation suitable for children (see scientific report, chapter 8). The inadequate availability of certain antibiotics has a serious impact on antibiotic prescribing: prescribers may be forced to replace them by less optimal, often broad-spectrum antibiotics. The alternatives may be less effective, may have more adverse effects, and may be more prone to drive the selection of resistance.[80] Hence, the lack of availability of certain antibiotics is a threat to antibiotic stewardship.

The One Health AMR action plan should include an appropriate approach for this problem. One should identify key antibiotics vulnerable to shortages and price increases and investigate together with FAGG – AFMPS how the **availability of old/narrow spectrum antibiotics on the Belgian market can be improved** and how therapeutic alternatives can be made available when certain antibiotics are removed from the market. As this problem is not confined to Belgium and the actors involved (among others pharmaceutical companies) are operating in an international context, a European approach will be indicated (e.g. through a multidisciplinary international taskforce, as is suggested by others).[81] Negotiations should also ensure high quality of medicines, continued production, a reasonable stock policy, and avoid dependence on a single supplier.[81]

In addition, the One Health AMR action plan should describe how prescribers can be informed pro-actively that a temporary supply problem occurs, but also when it has been solved; this should be done in close collaboration with FAGG – AFMPS.

5.8. Put into practice the delivery of the exact number of antibiotic tablets in pharmacies open to the public

Packages of antibiotics available on the Belgian market are often larger than what is needed for one treatment, which increases the risk of keeping leftovers at home and of subsequent self-medication (see scientific report, chapter 8). Self-medication with antibiotics is inappropriate because of the possibility of an unnecessary therapy, incorrect choice of antibiotics, of insufficient dosages, or of inappropriate duration.[82] But even when leftover antibiotics are discarded, they add to the problem of environmental pollution. Therefore, unlike most other drugs that in case of incorrect use may simply pose a risk to the particular patient, the inappropriate use of antibiotics adds to the global risk of increased antibacterial resistance.[83]

An effective way of **preventing self-medication with antibiotics** is the prevention of leftovers from prescribed courses. This can easily be implemented by the **dispensation of the exact number of antibiotic tablets in pharmacies through fractionation**, as is already the case in the UK, the Netherlands, US, Japan, Israel and the Czech Republic.[82-84]

Since 2006, pharmacists working in pharmacies open to the public are **authorized** to fractionate medicine packages, provided that certain conditions are met, one of them perfectly addressing the problem outlined above: 'there is no adequate primary package size of the medicinal product, licensed and marketed in Belgium, for the duration of the treatment for which it is prescribed'.[85]

Upon inquiry with FAGG – AFMPS it appeared that there are still barriers to be cleared in order to extend the current fractionation activities to e.g. antibiotics: prices and reimbursement rules have to be adopted (these are set now per package and not per unit), computer systems used by pharmacists have to be adapted (which currently only record the delivery of a box of medicines to one patient and not to several) and prescribers have to be informed. With regard to the financial aspects, the billing rule for nursing home residents issued in 2015 can be a source of inspiration (see scientific report, chapter 8). In the interest of the patient, the price should be defined per unit. If fractionation of medicines is indeed extended to e.g. antibiotics, FAGG – AFMPS will also have to adapt its supervision (e.g. the expiry date, the patient leaflet). (FAGG – AFMPS, *personal communication*)

5.9. Improve the compliance with evidence-based prescription guidelines

The prudent prescription of antibiotics starts with evidence-based guidelines, which clearly mention for each indication a first and second choice antibacterial agent, dose, posology and duration. Yet, some stakeholders reported that the visibility, the regular updates and the alignment of the different guidelines could be improved and thus enhance compliance. For instance, BAPCOC has published a guideline on the prudent use of antibiotics in the ambulatory sector (last version 2012, update expected in 2019), but in summer 2017 RIZIV – INAMI spread the report of a consensus meeting (held in June 2016) on the use of antibiotics in children in ambulatory care, which leads to confusion in the sector (and among stakeholders). Anno 2019, there is still no guideline on the prudent use of antibiotics for dentists. In addition, the impact of the antibiotic guidelines alone is limited in daily practice by a number of factors described earlier. In particular, their dissemination and their subsequent availability at the point of care is too often limited, they meet opposition and distrust from the clinician side, and in hospital care they need to be adapted to the local health care settings, drug formularies and resistance patterns.[51, 86]

In the One Health AMR action plan it should be stipulated how the **development and update** of guidelines should be coordinated for the various sectors involved and hot it can be ensured that they are adapted to the different target groups of professionals. These guidelines should be used in the curriculum and continuous training of physicians, dentists, pharmacists and nurses. Access and visibility must be improved, and free access to electronic versions should be ensured (through e.g. funding of the IGGI guide[s]). In that respect, the current digitization of health care ('e-health') brings about important opportunities: e.g. accessibility to **decision-making tools** for therapies in accordance with national guidance or warnings in the event of inappropriate prescription, **e-prescribing** can be linked to national guidelines (through e.g. pop-up windows reminding the clinician what the first choice antibiotic is and why).

5.10. Make use of the (future) mandatory implementation of e-prescribing to improve the prudent prescription of antibiotics

E-prescription will become mandatory on 1 January 2020.[87] *It presents many opportunities to improve prudent prescription and to inform prescribers on their prescription behaviour*.

Information on the **indication** (type of infection) for each antibiotic prescription should be incorporated in the e-prescription module, so that criteria for prudent use can be assessed, allowing to improve monitoring and feedback on the prescription of antibiotics. In this way, incentives for prudent prescribers can be envisaged.

[s] IGGI: 'Infectiologiegids - Guide d'Infectiologie', developed by the Belgian Society for Infectiology and Clinical Microbiology (BVIKM – SBIMC) with partial support from BAPCOC. Hospitals that want to register for this guideline have to pay in proportion to their size (i.e. € 2 420/year for hospitals up to 400 beds, €4 235/year for hospitals from 401 to 800 beds and € 6 050/year for hospitals with more than 800 beds).

In addition, **decision-making tools** for therapies (including the prudent use of antibiotics), should provide warnings in the event of inappropriate prescription, and be made accessible, e.g. through a linkage between e-prescribing and national guidelines or through a linkage of decision-making tools with the Electronic Medical Record (EMR) as foreseen in the EBP network. Likewise, linkage to regulations and forms (e.g. prescription of fluoroquinolones under Chapter IV) should be included.

The One Health AMR action plan should address how e-prescription may lead to faster feedback of prescribing practices to GPs and other prescribers; this should be done in close collaboration with the respective departments of RIZIV – INAMI.

5.11. Consider taking structural measures to improve the prudent prescription and use of antibiotics

The international literature and the consulted experts suggested several structural measures which may improve the prudent prescription and use of antibiotics.[50,52,88,89-91]

The One Health AMR action plan should comprise an approach to evaluate which structural measures can improve the prescription and use of antibiotics in **the Belgian context**, based on scientific evidence. This should be done based on scientific evidence and in close collaboration with the stakeholders.

5.12. Perform a health technology assessment on point-of-care testing for the diagnosis of infectious diseases in the Belgian ambulatory care context

In the ambulatory sector the treatment of infectious diseases (e.g. upper respiratory tract infections) is most often empirical (i.e. based on a case history, clinical examination and previous experience of the healthcare provider), which is of poor accuracy in identifying the likely aetiology and thus when antibiotics are required.[92] *However, most respiratory tract infections in the ambulatory sector are from viral origin. Usual laboratory-based tests, which are sensitive, result in too long delays to guide the immediate prescription. Point-of-care testing, such as C-reactive protein (CRP) test or procalcitonin, may assist the clinician to assess the likelihood of a serious bacterial infection versus a less severe bacterial or viral infection, and the results may be obtained in a few minutes. In clinical trials in other settings, the use of CRP and procalcitonin lowered significantly the rate of antibiotic prescribing.*[93]

The One Health AMR action plan should comprise a cost-effectiveness evaluation on point-of-care testing in the diagnosis of infectious diseases in ambulatory care in Belgium and an assessment whether it is desirable to reimburse them.

5.13. Stimulate behavioural change among the general public as well as the prescribers towards more prudent use of antibiotics

So far, the national public awareness campaigns on the prudent use of antibiotics included different communication strategies such as posters, advertising in media, brochures, TV spots, bags for pharmacies, and direct mailing (see scientific report, chapter 6). However, as said above awareness alone is not sufficient to change behaviour.[19] *In addition, despite high amounts of resources invested in awareness campaigns, only a limited impact of the last campaigns has been observed.*[94] *In addition, the international literature shows that formal education, guidelines and concerns about emerging resistance seem to have minor influence on antibiotic prescribing.*[95, 96]

Sensitisation campaigns should be better targeted and should follow the **One Health approach**, e.g. informing pet owners on the transmission of (resistant) bacteria from their pet to themselves (and the other way around) and their relatives in case of (too) close contact. Sickness funds and patient associations can play a supporting role in these campaigns.

The campaigns should also be **directed to groups that need adapted messages**: e.g. nursing home residents and staff, lower socio-economic groups and citizens who do not master the national languages (see the scientific report, chapter 5). Differences in terms of health literacy should be taken into account when targeting various groups. Communication teams with special expertise in contacting these groups should therefore be consulted.

Cultural barriers with regard to the prescription and use of antibiotics should be taken into account when organising sensitisation campaigns: e.g.

uncertainty avoidance, paternalism, attitude towards self-healing mechanisms.

In order to improve the awareness on AMR and the importance of the prudent use of antibiotics as early as possible, school children should be further targeted as well and **various communication channels** should be used: e.g. social media, local radio stations, popular TV shows not only on the national TV channels, but also on commercial channels and TV channels frequently watched by citizens from non-Belgian origin.

5.14. Strengthen veterinarians' counselling role

Veterinarians earn their income through consultations (farm visits) and the sale of medication; the latter is an important part of the veterinarian's income.[69] Currently, veterinarians' advisory role is quite limited, in the sense that veterinarians have the impression that most farmers are not willing to pay for veterinary counselling.[69] This may in part be explained (at least in pig farming) by the strong position of feed mill companies, which provide "free" veterinary advice.[70]

In order to make the improvement of biosecurity (cf. infra) at farms a priority, **veterinarians' counselling role should be strengthened**. Counselling on herd management strategies should be an important part of their professional role, contributing to their revenues. This is only realistic if farmers are willing to **pay for counselling**. This could e.g. be realised through training cheques (e.g. 'opleidingscheques'/'chèque-formation') or be part of the innovation wallet of small and medium-sized enterprises (e.g. 'KMO portefeuille'). Alternatively, a number of (pre-)paid veterinary visits could be made mandatory in the context of a herd health plan. In this way, the one-to-one relationship between a contracted herd veterinarian and the farmer can be enhanced. In the One Health AMR action plan it should be assessed whether incentives should be given to encourage farmers who take up a stewardship relationship with a veterinarian or advisor, who define a herd health plan and who set targets related to antibiotics use in an action plan together with a veterinarian or advisor.

Veterinarians' counselling role and the **one-to-one relationship between contracted herd veterinarians and farmers** should also be enhanced through legislative work: in the legislation on farm guidance, a health plan and plan of action (with targets regarding antibiotics use) could be added as a condition for farm guidance. This is also recommended by AMCRA.[25] In addition, the prescription and delivery of antibiotics could be made an exception in the description of the role of the substitute veterinarian in the RD of 10/04/2000 on farm guidance,[97] in this way the herd veterinarian can keep the overview on the total use of antimicrobials as he provides all antimicrobials for an animal group, with the exception of emergency cases.

5.15. Change prescribing behaviour of high antibiotic prescribers

With the introduction of SANITEL-MED in 2017 the monitoring of antibiotic prescription and use in food producing animals has been installed. The SANITEL-MED register is developed to measure antibiotic use at farm level. Importantly, this comprises individual feedback (including benchmarking) to the farms in the format of two reports a year for every Belgian farm. SANITEL-MED allows the identification of high prescribers. There is currently no monitoring of antibiotic use, nor prescription in the sector of companion animals. Hence, among small animal veterinary practices high prescribers cannot be identified so far.

The One Health AMR action plan should comprise a strategy to identify and monitor high antibiotic prescribers in order to change their prescribing behaviour. Yet, **feedback and benchmarking** are essential but not sufficient: additional **support** and **supervision to change prescribing behaviour** should be provided as well. If this does not help, sanctioning of high antibiotic prescribers (e.g. by the withdrawal of their right to dispense antibiotics) should be considered.

Especially in the pet sector, there are more initiatives needed to realise this. Registration of the prescription and use of antibiotics, should also include information on the indication (e.g. type of infection) and the case-mix of the veterinarian's clientele. A registration system for antibiotic use in companion animals is challenging because the exact number of companion animals (which is the denominator) is unknown. However, pilots could be considered for specific animal species (e.g. dogs and horses for which identification and registration is mandatory) or specific contexts (e.g. kennels and nurseries of small animals) for which exact numbers are known.[98, 99]

5.16. Monitor and stimulate research on antibiotic use and AMR in the sector of companion animals

From the Household budget survey 2013 we learn that in Belgium about 20% of the households take care of at least one dog, 27% keeps at least one cat and 3% has at least one horse.[100] Yet, so far the matter of prudent prescription and use of antibiotics and the battle against AMR in companion animals has received little attention in the international scientific literature.

In recent years, AMCRA developed guidelines (e-vademecum) on the prudent use of antibiotics in dogs, cats and horses. But it is unclear to what extent the e-vademecum is actually used by veterinarians.

Within the frame of the One Health AMR action plan it should be investigated how the monitoring of antibiotic use and the surveillance of AMR in companion animals can be realised. Inspiration for this initiative can be found in Denmark, where all prescriptions of antibiotics in livestock and companion animals are recorded in the national database VetStat.[74]

In addition, in the One Health AMR action plan it should be stipulated that research projects investigating different aspects of antibiotic prescription and use in companion animals (e.g. determinants of antibiotic prescription, barriers to prudent antibiotic use, and transmission of AMR between pets and humans and vice versa) should be stimulated. Last but not least, it should also be investigated how the use of the e-vademecum can be incentivised.

5.17. Stimulate biosecurity improvements as an alternative to antibiotic use

Improved biosecurity (e.g. changes in attitudes, work habits, infrastructure) is beneficial to animal health and welfare, antibiotic reduction and production results.[29, 30, 101, 102] For example, in an intervention study it was observed that the implementation of optimization of herd management, biosecurity status, and vaccination strategy as a team effort of the farmer together with experts resulted in significant reductions in antibiotic use, while they also had a positive impact on the production results.[29]

For the decrease in antibiotic use a mind shift among farmers is essential: antibiotics should be perceived as a therapeutic solution in case of clinical symptoms of an infection.[25] Therefore farmers should be well informed about ways to keep animals healthy. Biosecurity measures are often very cheap. They are often more about **attitude and small procedure changes**. Farmers need to be **informed and/or trained** (e.g. during farmers' training programs) about the advantages and importance of healthy animals, the importance of biosecurity to keep them healthy, and the use of antibiotics only as last resort, coupled to the threat of antimicrobial resistance. This could be done by means of a kind of accreditation system.

In addition, **a licence to administer antibiotic products should be developed**, not one-off, but with mandatory regular updates (e.g. every 5 years) to keep farmers' knowledge up to date (similar to the phyto licence[t]). The idea is that a stock of antibiotic products at the farm should be a right that farmers acquire through training, through the presence of a health plan, etc.

Last but not least, **additional support, coaching and supervision** by veterinarians and independent experts to change farmers' behaviour **should be financed**, especially in farms with high antibiotic use. In addition, it is important to support local groups of farmers and veterinarians meeting regularly to exchange information and experience, and where critical success and failure factors are identified and further disseminated so that good practices can be established.

[t] A phyto licence is a certificate from the federal government that indicates that a professional user, distributor or information officer can deal correctly with plant protection products and additives. Through the obligatory continuous licensees remain informed of the developments concerning crop protection. (see also https://fytoweb.be/nl/fytolicentie/gids)

5.18. Enforce compliance with the legislation on animal welfare

Quite some legislative work has been done in recent years to protect animal welfare. Yet, out of economic interest, exceptions have become the rule, jeopardizing animal health and leading to an increased need for antibiotics. For example, the Council Directive of 18 December 2008 lays down minimum standards for the protection of pigs. More precisely, it imposes a minimum weaning age of 28 days, except for farms with specialised housing which are allowed to wean piglets at 21 days.[103] Because the sow can be inseminated earlier resulting in more piglets per year, the exception in the law has now become common practice in Belgium, while in a natural setting weaning is a gradual process and the average weaning age is about 17 weeks.[104, 105] Abrupt weaning at 4 weeks or earlier causes considerable stress for piglets (separation from the sow, change in diet, moving to an unfamiliar barn mixed with unfamiliar pen mates),[105] leading to growth depression and diarrhoea due to a reduced feed intake and an impaired intestinal tract.[62, 106] Antibiotics are often used to control post-weaning diarrhoea.[107] Last but not least, at this young age piglets are also prone to infections because of immaturity of the intestinal immune system,[108] leading again to the need for antibiotics. Likewise, legislation stipulates maximum stocking density per animal species (e.g. the Council Directive 2008/120/EC of 18 December 2008 for pigs[103] and the Council Directive 2007/43/EC laying down minimum rules for the protection of chickens kept for meat production[109]) as there is an important association between stocking density and the animals' health and wellbeing. [110] A too high stocking density has a deleterious effect on animal health, resulting in infection pressure and by consequence antibiotic use.[25]

It is clear from the examples above that when animal welfare is taken seriously, animal health will benefit and antibiotics are less needed. Therefore **strict observance of legislation on animal welfare** (e.g. regarding the legal minimum weaning age for piglets, minimum age for transport, maximum stocking density) is very important.

In addition, **alternatives** to infeed antibiotics should be sought, other weaning systems developed (e.g. gradual weaning) and feeding programs and nutritional strategies further optimised as a means for controlling problems associated with the weaning transition without using antibiotics.[104, 105, 108]

5.19. Make the use of antibiotics as means to intensify animal production superfluous

Some farmers still consider antibiotics as an essential link in the chain of production optimisation (e.g. metaphylactic[u] use of antibiotics to prevent disease in the whole herd, antibiotics to treat diarrhoea in weaned piglets because they are weaned too early). However, recent studies indicated that it is feasible to reduce antibiotic usage without jeopardizing production parameters.[27, 29, 30]

In order to have a durable husbandry, **structural measures** should be taken to stop this race to the bottom. In essence, the consumer price for animal products is too low for animal husbandry to be profitable. As long as consumers are not prepared to pay more for animal products, we keep flogging a dead horse. Measures should be taken to make sure farmers get a decent price for their products.

In addition, the One Health AMR action plan should address how one can push for a level playing field in the international market of animal products. European/international rules for minimum hygiene and biosecurity standards are needed in case of export. This could avoid the competition with farmers from abroad who can sell at lower prices because they do not have to obey the same constraining rules.

[u] Metaphylactic treatment is the administration of a medicinal product to a group of animals after a diagnosis of clinical disease in part of the group has been established, with the aim of treating the clinically sick animals and controlling the spread of the disease to animals in close contact and at risk and which may already be subclinically infected.

5.20. Avoid self-medication by minimizing stocks at farms and by adjusting package sizes

Veterinarians can leave a stock of veterinary medicines for follow-up treatment of up to three weeks at farms that do not have a contract for farm guidance and even up to two months at farms with such a contract (see scientific report, chapter 3).[97, 111] This stock of medicines includes antibiotics. Yet, there is no antibiotic treatment that takes as long as two months in the veterinary setting. As is sufficiently known, leftovers of antibiotics give way to self-medication.

Small package sizes (sometimes licenced) and uni-doses of antibiotics are seldom commercially available. Hence, veterinarians are often not able to provide the exact volume necessary for the treatment because of packages being too large and because of the legal restrictions on and practical difficulties with fractionation (e.g. availability of a package leaflet together with each fraction).

In order to avoid leftovers of antibiotics at farms, the legislation with regard to the maximum stock veterinarians can deliver at farms for follow-up treatment by the farmer should be adapted, by making an exception for antibiotics.[97, 111] The **maximum stock of antibiotics should be limited to the duration of the treatment** as defined in the product specifications. In addition, a stock of antibiotics at farms should be made conditional to e.g. the presence of a health plan, coupled to a minimum number of (remunerated) meetings with the herd veterinarian (e.g. 4 times a year).

Alternatively, the size of the antibiotic stocks at farms could be made proportional to the number of animals. This is already the case in the Netherlands, where the stock of first-choice antibiotics is limited to maximum 15% of the present and potentially susceptible animals on the farm. For second-choice antibiotics the conditions are more strict (e.g. farmers can only administer second-choice antibiotics after contacting a veterinarian) and linked to the farm's health plan.[112]

Within the frame of the One Health AMR action plan it should be investigated how fractionation of antibiotic products can be realised in a safe way and/or whether it is possible to make small antibiotic packages or uni-doses commercially available. As this problem is not confined to Belgium and the actors involved (i.e. the pharma) are operating in an international context, collaboration with other European countries will be indicated.

5.21. Define new goals regarding antibiotics in the veterinary sector

Since 2006, European legislation banned the use of antibiotics as growth promotors.24 Over the years, it resulted in a decreased use of feed medicated with antibiotics. The 2018 BelVet-SAC report (with 2017 data) demonstrated a cumulative reduction of the use of antibiotic premixes of 66.6% and of the use of the 'red' group of antimicrobials (i.e. 3rd and 4th generation cephalosporins and fluoroquinolones, see also section 2.2) with 84.4% since the reference year 2011. In other words, for both indicators the AMCRA objective (i.e. a 50% reduction in the use of antibiotic premixes by 2017 and a 75% reduction of the use of the 'red' group of antimicrobials by 2020), ratified by the Belgian government in 2016 has already been achieved.21

In order to avoid a standstill, the One Health AMR action plan should include new goals, which should be defined together with the stakeholders.

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