

Use of antibiotics in Austria

Antibiotikaeinsatz in Österreich

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Summary

In 2015, 119.2 t of active ingredients of antibiotics were used in Austria in human medicine (70.4 t; 59.1%), for food animals (48.8 t; 40.9%) and in plant production (0.002 t; < 0.1%). During the last five years, consumption of antibiotics increased in human medicine by 3.8% (2011: 67.8 t; 2015: 70.4 t). In hospitals, it increased by 17.3%, from 19.7 t in 2011 to 23.1 t active ingredients in 2015. In the community, measured in kg active ingredient, it increased by 0.3% from 2011 to 2015. Consumption in defined daily dose (DDD) per 100,000 inhabitants per year decreased by 3.6%. Our numbers for the community (2015: 17.0 DDD) contradict AURES reports and a recent ECDC report, which claim a consumption of 14.0 DDD/1000 inhabitants per day in primary care in Austria, based on the social insurance company's sales data. Declining pharmacy sales prices due to an increase in market shares for cheap generic drugs as well as increase in deductibles for insured people falsely suggest low consumption. In food animals, the antibiotic consumption decreased by 8.7%, from 53.4 t to 48.8 t. In plant production, the annual usage fluctuated considerably and decreased by 95.3%, from 47.2 kg in 2010 to 2.2 kg in 2015.

Keywords: antibiotic consumption, Austria, human medicine, food animals, plant production

Zusammenfassung

Im Jahr 2015 wurden in Österreich insgesamt 119,2 t antimikrobielle Wirkstoffe abgesetzt: In der Humanmedizin (70,4 t; 59,1 %), in der tierischen Lebensmittelproduktion (48,8 t; 40,9 %) und in der Pflanzenproduktion (0,002 t; < 0,1 %). In den letzten fünf Jahren ist der Gesamtverbrauch in der Humanmedizin um 3,8 % angestiegen (2011: 67,8 t; 2015: 70,4 t), im stationären Bereich sogar um 17,3 % (von 19,7 t im Jahr 2011 auf 23,1 t im Jahr 2015). Im niedergelassenen Bereich stieg der Verbrauch (in kg Wirksubstanz) um 0,3 %. Der Verbrauch in definierter Tagesdosis (DDD) pro 100.000 Einwohner und Jahr sank um 3,6 %. Unsere Zahlen für den niedergelassenen Bereich (2015: 17,0 DDD pro 1000 Einwohner und Tag) stehen im Widerspruch zu AURES-Berichten und einem rezenten ECDC-Report, die – basierend auf österreichischen Sozialversicherungsdaten – für 2015 einen Antibiotikaverbrauch von 14,0 DDD postulieren. Aufgrund sinkender Abgabepreise (bedingt durch steigende Marktanteile von Generika) und steigender Selbstbehalte (Rezeptgebühren) spiegeln Sozialversicherungsausgaben den Verbrauch nicht korrekt wider. Der Verbrauch in der tierischen Lebensmittelproduktion ging um 8,7 % zurück, von 53,4 t im Jahr 2011 auf 48,8 t im Jahr 2015. Der jährliche Verbrauch von Antibiotika im Pflanzenschutz schwankte stark und sank in diesem Zeitraum um 95,3 %, von 47,2 kg im Jahr 2010 auf 2,2 kg im Jahr 2015.

Schlagworte: Antibiotikaverbrauch, Österreich, Humanmedizin, tierische Lebensmittelproduktion, Pflanzenproduktion

1. Introduction

The use and overuse of antibiotics is one of the main factors responsible for the development and spread of antimicrobial resistance (AMR). This has become a serious threat to public health, notably because of the emergence and spread of highly resistant bacteria, and because there are very few novel antimicrobial agents in the research and development pipeline (ECDC, 2015). European countries increasingly implement actions to control AMR through the rational use of antimicrobials, including awareness campaigns on the prudent use of antibiotics, such as the European Antibiotic Awareness Day (Earnshaw et al., 2014). Direct consequences of the emergence of AMR for patients include delaying administration of appropriate antibiotic therapy, longer stays in hospitals, higher health-care costs and poor patient outcome (Cosgrove, 2006). On September 21st 2016, the General Assembly of the United Nations therefore adopted the resolution “Political Declaration of the High-level Meeting of the General Assembly on Antimicrobial Resistance”, which reads: “*Acknowledge that resistance of bacterial, viral, parasitic, and fungal micro-organisms to antimicrobial medicines that were previously effective for treatment of infections, is mainly due to inappropriate use of antimicrobial medicines in human, animal, food, agriculture and aquaculture sectors; lack of access to health services, including to diagnostics and laboratory capacity; as well as residues of antimicrobials into soil, crops and water. Within the broader context of AMR, resistance to antibiotics which are not like other medicines, including medicines for the treatment of tuberculosis, is the greatest and most urgent global risk that requires increased attention and coherence at the international, regional, and national levels*” (Mushtaq, 2016; UN General Assembly, 2016).

Antimicrobial resistance in humans is inter-linked with AMR in other populations, especially farm animals, and in the wider environment (Woegerbauer et al., 2015). The relatively few bacterial species that cause disease in humans, and are the targets of antibiotic treatment, constitute a tiny subset of the overall diversity of bacteria that includes the gut microbiota and vast numbers in the soil (Woolhouse et al., 2015) and plant-associated bacteria. However, resistance can pass between these different populations; and homologous resistance genes have been found in pathogens, normal flora and soil bacteria. Farm animals are an important component of this complex system: they are exposed to large quantities of antibiotics and act as another reservoir of resistance genes (Woolhouse et al., 2015). The

application of antibiotics in plant production can lead to a gradual increase in the prevalence of resistance in the environment, for example, to streptomycin-resistant plant pathogenic bacteria (Manulis et al., 1999; 2003; Russo et al., 2008; Door et al., 2013). There are also indications that streptomycin-resistant epiphytes like *Pantoea agglomerans* and *Pseudomonas* spp. increase under the selection pressure (Tancos et al., 2016). Of the steps that need to be taken to address AMR, reducing the overall use of antibiotics is the most important action needed to slow the development and spread of antibiotic-resistant bacteria.

An efficient surveillance system is needed to evaluate how local and global resistance situations respond to a change of antibacterial application. Hence, the Austrian Agency for Health and Food Safety (AGES) established a surveillance system to assess the antibiotic consumption in human medicine, food animals and plant production.

2. Materials and Methods

2.1 Use of antibiotics in human medicine

Since 2015, the Austrian Agency for Health and Food Safety (AGES) purchases antibiotic consumption data from IMS Health Marktforschung GmbH. The data obtained is based on sales figures of the pharmaceutical wholesale market and represents overall antibiotic consumption in Austria in hospitals as well as in outpatients. Data is recorded into the anatomical therapeutic chemical classification system (ATC codes) and defined daily dose (DDD). The ATC classification system is used to categorize drugs based on their site of action and chemical and pharmacological properties. A DDD is assigned to a specific substance and is internationally comparable due to its average daily dose, an arbitrarily defined standard dose for adults (WHO Collaborating Centre for Drug Statistics Methodology, 2015). For analysis, only systemically applied antibiotics were considered (ATC classification J01). The groups consisted of J01A tetracyclines, J01C beta-lactam antibacterials, penicillins, J01D other beta-lactam antibacterials, cephalosporins, J01E sulfonamide and trimethoprim, J01F macrolides, lincosamides and streptogramins, J01G aminoglycosides, J01M quinolone antibacterials and J01X other antibacterials (WHO Collaborating Centre for Drug Statistics Methodology, 2015). Consumption data (DDD) refers to 100,000 inhabitants per year for total consumption and for consumption of outpatients only. Hospital consumption data (DDD) refers to 100 inpatient

days per year (inpatient occupancy data is available online: http://www.kaz.bmgf.gv.at/fileadmin/user_upload/Aufenthalte/1_T_Aufenthalte_stat.pdf). Antibiotic consumption data is also presented in kg per active ingredient. Consumption data from IMS Health Marktforschung GmbH do not include colistin. All the registered colistin producing and colistin importing companies were directly contacted to collate data on colistin use in human medicine in 2015.

2.2 Use of antibiotics in food animals

Since 2010, AGES has collected data on the sale of veterinary antimicrobials in Austria in a standardized manner according to the recommendations of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project (European Medicines Agency, 2013). The ESVAC project collects information on how antimicrobial medicines are used in animals across the European Union (EU). The European Medicines Agency (EMA) started this project in April 2010 following a request from the European Commission for the Agency to develop a harmonized approach in collecting and reporting data on the use of antimicrobial agents in animals from EU and European Economic Area (EEA) member states (European Medicines Agency, 2013). The data obtained is based on pharmaceutical wholesale data for veterinary medicine provided by 18 companies. Wholesale data covers the overall antimicrobial consumption for livestock in Austria (not for pets and leisure animals). Since 2014, the pharmaceutical producers and wholesalers directly upload their data to a database via the homepage of the Austrian Medicines and Medical Devices Agency (<http://www.basg.gv.at/eservices/veterinaer-antibiotika-mengenstromanalyse/>). Overall antibiotic consumption data is presented in kg active ingredient and in ATC Vet codes (analog ATC-classification in human medicine) (WHO Collaborating Centre for Drug Statistics Methodology, www.whocc.no/atcvet/). EMA

(European Medicines Agency) provides conversion factors for those antibiotics activities that are licensed and quantified in international units (European Medicines Agency, 2013). Sales volumes cannot be assigned to species-specific livestock populations as the veterinary medicinal products containing antibacterial agents are authorized for multiple target species.

2.3 Use of antibiotics in plant protection

In Austria, antibiotics are only applied against *Erwinia amylovora*, the causing agent of fire blight, a highly infectious bacterial plant disease. Streptomycin has been used as a plant protection product against fire blight in Austria since 2006. The application of streptomycin for the control of fire blight in commercial pome fruit orchards is strictly regulated. The necessity of treatments (according to the risk assessment systems) is defined by the plant protection service. A certificate of eligibility given to the farmer by the authorities responsible (district administration) is required for use. Furthermore, written confirmation of receipt of plant protection products (including the quantity received and applied) must be submitted to the Federal Office for Food Safety, which provides the consumption data to AGES.

3. Results

In 2015, a total amount of 119.2 t active ingredients of antimicrobials were used in Austria in human medicine (70.4 t; 59.1%), for food animals (48.8 t; 40.9%) and in plant production (0.002 t; < 0.1%).

3.1 Use of antibiotics in human medicine

In 2015, the overall antibiotic consumption in human medicine was 70.4 t active ingredient, consisting of 47.3 t

Table 1. Antibiotic consumption (kg active ingredient) in human medicine in Austria 2010-2015; outpatients and hospitals
Tabelle 1. Aufteilung des Antibiotikaverbrauches in der Humanmedizin in Österreich von 2010-2015 nach niedergelassenem Bereich versus stationären Bereich in kg Wirksubstanz

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|--------------|--------|--------|--------|--------|--------|--------|
| total amount | 69,158 | 66,907 | 67,812 | 70,941 | 68,514 | 70,437 |
| outpatients | 48,585 | 47,182 | 47,049 | 49,575 | 46,977 | 47,332 |
| hospitals | 20,573 | 19,725 | 20,763 | 21,366 | 21,537 | 23,097 |

(67.2%) for outpatients and 23.1 t (32.8%) in hospitals (Table 1). Consumption details (DDD/100,000 inhabitants per year) for the years 2010 through 2015 are presented in Table 2. The most consumed antibiotics were β -lactam-antibacterials (ampicillin, amoxicillin, penicillin G, tazobactam, piperacillin, etc.), followed by other β -lactam-antibacterials or cephalosporins (cefazolin, cefuroxime, cefotaxime, cefepime, meropenem, aztreonam, etc.) and the group of macrolides and lincosamides (clindamycin, erythromycin, clarithromycin, azithromycin, etc.).

In 2015, antibiotic consumption in outpatients was highest for β -lactam-antibacterials (320,690 DDD/100,000 inhabitants per year), followed by the group of macrolides and lincosamides (123,963 DDD/100,000 inhabitants per year). In hospitals, the most consumed antimicrobials were β -lactam-antibacterials (39.55 DDD/100 inpatient days), followed by other β -lactam-antibacterials or cephalosporins (11.09 DDD/100 inpatient days).

Over the last five years, antibiotic consumption in kg active ingredient increased in hospitals by 17.3% (2011: 19.7 t; 2015: 23.1 t), in outpatients by 0.3% (2011: 47.2 t; 2015: 47.3 t). In the same period (2011 to 2015), the antibiotic consumption in DDD increased in hospitals by 3.5% (from 63.22 DDD/100 inpatient days in 2011 to 65.46 DDD/100 inpatient days in 2015) and decreased in the community by 3.4% (from 646,481.29 DDD/100,000 inhabitants to 624,193.40 DDD/100,000 inhabitants).

In 2015, the total consumption of colistin in human medicine amounted to 5 kg active ingredient.

An analysis of seasonal variation in the community's antibiotic consumption showed fluctuations. During the

colder months of the year (January-March and October-December), there was a higher antimicrobial consumption: beta-lactam-antibacterials (J01C; January 2015: 3,312 kg active ingredient; August 2015: 1,804 kg; December 2015: 2,626 kg), other beta-lactam-antibacterials or cephalosporins (J01D; January 2015: 482 kg active ingredient; August 2015: 294 kg; December 2015: 397 kg), of so called macrolides, lincosamides and streptogramins (J01F; January 2015: 876 kg active ingredient; August 2015: 378 kg; December 2015: 609 kg) and of quinolone antibacterials (J01M; January 2015: 339 kg active ingredient; August 2015: 251 kg; December 2015: 296 kg).

3.2 Use of antibiotics in food animals

In 2015, the overall antibiotic consumption in food animals was 48.8 t of active ingredients. The largest amount of veterinary antimicrobials was used for systemic application (45.7 t, 93.8%). Oral preparations – this group includes oral powders, oral solutions, tablets and oral paste – were the most widely used application form (39.5 t, 81.1%). Parenteral preparations were second (5.4 t, 11.2 %), followed by the so-called premix preparations (2.4 t, 5.0%). Intramammary preparations for lactating cows and for dry cow treatment had a total consumption of 1.2 t (2.4%) (Table 3). The antibiotic sales data for systemic use broken down into ATC Vet codes are given in Table 4. More than half of the antibiotics applied were tetracyclines, followed by penicillins with extended spectrum, sulfonamides and macrolides. Over the last five years, antimicrobial consumption decreased by 8.7%, from 53.4 t in 2011

Table 2. Antibiotic consumption according to ATC3 codes in Defined Daily Doses per 100,000 inhabitants and year in Austria, 2010-2015
Tabelle 2. Aufteilung des Antibiotikaverbrauches in Österreich von 2010-2015 in Tagesdosen pro 100.000 und Jahr Einwohner/innen

| | 2010 | 2011 | 2012 | 2013 | 2014 | 2015 |
|---|---------|---------|---------|---------|---------|---------|
| J01A tetracyclines | 50,233 | 49,949 | 44,622 | 47,185 | 43,423 | 44,267 |
| J01C beta-lactam-antibacterials, penicillins | 399,018 | 393,017 | 396,145 | 414,628 | 401,289 | 404,168 |
| J01D other beta-lactam-antibacterials, cephalosporins | 99,334 | 96,620 | 93,500 | 99,569 | 86,019 | 87,323 |
| J01E sulfonamide and trimethoprim | 24,682 | 23,470 | 22,151 | 21,574 | 20,851 | 20,163 |
| J01F macrolides, lincosamides and streptogramins | 153,700 | 144,581 | 138,496 | 141,651 | 130,424 | 132,609 |
| J01G aminoglycosides | 2,189 | 2,058 | 1,997 | 1,595 | 1,531 | 1,474 |
| J01M quinolone antibacterials | 72,672 | 68,025 | 66,042 | 65,683 | 64,598 | 66,453 |
| J01X other antibacterials | 8,533 | 6,654 | 6,673 | 6,464 | 6,835 | 6,663 |
| total | 810,361 | 784,374 | 769,626 | 798,348 | 754,969 | 763,121 |

Table 3. Antibiotic consumption (kg active ingredient) in food animals by mode of application

Tabelle 3. Antibiotikaverbrauch in der tierischen Lebensmittelproduktion aufgeteilt nach Applikationsart (kg active ingredient)

| | 2011 | 2012 | 2013 | 2014 | 2015 |
|--------------|--------|--------|--------|--------|--------|
| oral | 42,500 | 43,900 | 45,280 | 45,640 | 39,540 |
| parenteral | 5,410 | 5,360 | 5,260 | 4,620 | 5,440 |
| premix | 4,080 | 2,370 | 2,910 | 2,260 | 2,420 |
| intramammary | 1,250 | 1,330 | 1,280 | 990 | 1,190 |
| intrauterine | 200 | 260 | 240 | 160 | 190 |

to 48.8 t in 2015. The maximum antibiotic consumption (55.0 t) was documented for 2013. For colistin, a total amount of 1.6 t active ingredient was dispensed in 2015.

3.3 Use of antibiotics in plant protection

In 2015, a total amount of 2.2 kg streptomycin was used in plant protection products. Within the last 5 years, the use ranged from 0 to 24.3 kg active ingredient. The use of streptomycin from 2010 to 2015 was as follows: 47.2 kg in 2010; 5.8 kg in 2011; 18.0 kg in 2012; 24.3 kg in 2013; 0 kg in 2014; and 2.2 kg in 2015.

4. Discussion

The use of antimicrobial agents has contributed to a great extent towards improving health conditions. For decades, antibiotics have been used to treat and prevent infectious diseases and infections. However, the use of antibiotics also results in a growing prevalence of microorganisms that have become resistant to one or several of these agents. The resistance to antimicrobial agents is a threat to public health as it may result in longer periods of illness for patients, leads to higher health costs and has economic repercussions on the society (Allerberger et al., 2002). Approaches to solving the problem of antibiotic resistance must include efforts to reduce the overall use of antibiotics. Agricultural plant production is only of minor relevance concerning antibiotic consumption in Austria, amounting to less than 0.1% of the total antibiotic use in 2015. The use of antibiotic substances in plant protection is highly fluctuating since it is generally depending on weather conditions and infection risks. Fire blight management without antibiotics is a major goal in fruit production. A strategy to control this disease has been created by all relevant

stakeholders (<https://www.ages.at/themen/landwirtschaft/feuerbrand/strategie>). This management programme includes preventive measures and limited use of pesticides based on prognosis models and orchard sanitation during dormant and growing season. In Austria, antibiotics will be excluded from disease management as soon as a new efficient plant protection product is authorized for fire blight control, but at the latest in 2020.

In 2015, the antimicrobial use in food animals accounted for 40.9% of the total antimicrobial consumption of Austria. In Germany, 54.5% of the total consumption was used in food animals (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Paul-Ehrlich Gesellschaft für Chemotherapie e.V., Infektiologie Freiburg, 2016). In the United States, antimicrobial use in food animals is estimated to account for approximately 89% of the nation's annual antimicrobial consumption (Food and Drug Administration, 2015). Linking antimicrobial consumption in animals to drug-resistant infections of humans is inherently complex owing to the ecological nature of the selection pressure for drug resistant pathogens as well as the existence of indirect routes or transmission through the environment (van Boeckel et al., 2015). However, the widespread use of antimicrobials in livestock at least contributes to the emergence of antibiotic-resistant bacteria: antibiotic-resistant bacteria of animal origin can be transmitted to humans not only by direct contact (van Cleef et al., 2011; Smith et al., 2013) but also through the environment (Graham et al., 2009) and food products (Price et al., 2005). Antibiotics given to animals generate huge amounts of feces and urine that contain residual levels of these compounds. Manure sprayed on fields as fertilizer can contaminate vegetables and produce, and can even reach drinking water reservoirs (Sapotka et al., 2007). In 2014, Inreiter et al. studied the antibiotics in Austrian drinking water resources and detected antimicrobial agents

Table 4. Antibiotics (kg active ingredient) for systemic use in food animals according to ATCVet

Tabelle 4. Verbrauch systemisch verabreichter Antibiotika in der tierischen Lebensmittelproduktion nach ATCVet-Code in kg Wirksubstanz

| | 2011 | 2012 | 2013 | 2014 | 2015 |
|--|--------|--------|--------|--------|--------|
| QJ01AA tetracyclines | 31,640 | 29,730 | 30,590 | 29,640 | 26,390 |
| QJ01CA penicillins with extended spectrum | 3,100 | 5,540 | 6,370 | 6,160 | 5,990 |
| QJ01EQ sulfonamides | 5,750 | 5,950 | 5,600 | 6,080 | 4,280 |
| QJ01FA macrolides | 4,860 | 4,420 | 4,630 | 4,580 | 3,900 |
| QJ01GB aminoglycosides | 1,170 | 1,090 | 1,000 | 1,100 | 1,140 |
| QJ01CE beta-lactamase sensitive penicillins | 1,380 | 1,300 | 1,200 | 930 | 1,100 |
| QJ01EA trimethoprim and derivatives | 810 | 850 | 750 | 850 | 760 |
| QJ01MA fluoroquinolones | 580 | 500 | 570 | 460 | 510 |
| QJ01XQ pleuromutilins | 410 | 360 | 410 | 430 | 420 |
| QJ01XX other antibacterials | 400 | 390 | 450 | 170 | 400 |
| QJ01BA amphenicols | 320 | 280 | 310 | 300 | 360 |
| QJ01FF lincosamides | 320 | 310 | 370 | 120 | 350 |
| QJ01DD/QJ01DE third- and fourth-generations cephalosporins | 180 | 160 | 170 | 140 | 160 |

in ten (5%) of the 200 drinking water samples tested (Inreiter et al., 2016). A recent study from seven European countries (Norway, Sweden, Denmark, Austria, Switzerland, The Netherlands and Belgium) showed a strong correlation between consumption levels of eight classes of antimicrobials (Chantziaras et al., 2014) and the prevalence of antimicrobial-resistant commensal *Escherichia coli* in pigs, poultry, and cattle. According to a report by the European Medicines Agency and the European Surveillance of Veterinary Antimicrobial Consumption (2016), Austria was in a good middle position compared to other European countries (2014: 53.4 t, not including tablets; total amount as ascertained in our study: 53.67 t). The lowest consumption was seen in countries such as Norway (5.8 t), Sweden (9.3 t), Luxemburg (2.1 t), Slovenia (5.7 t) or Iceland (0.6 t). There was high antimicrobial consumption in Spain (2,963.9 t) (European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2016). In Germany, the amount of antibiotics dispensed for veterinary medicine decreased from 1,706 t in 2011 (first year of data collection) to 1,305.8 t in 2014 and 837 t in 2015 (Bundesinstitut für Risikobewertung, 2016). This reduction impressively shows the potential for reducing antibiotic use, provided that there is clear political commitment.

Although it is clear that resistance problems concerning animal food production are important, most of the problems with resistance in human medicine are related to the

use of antimicrobials by humans. In human medicine, the use of antibacterial agents for the treatment of viral infections, the unjustified use of substances with an extremely broad activity spectrum, and the prophylactic use of antibiotics over too long episodes prior to or after surgical interventions, as well as the use of antibiotics in the case of mere colonization (and not infection) of the patient are regarded as the main driver of the resistance problem (Allerberger et al., 2002).

In 2015, antibiotic consumption in human medicine amounted to 59.1% of the total antibiotic usage in Austria. In Germany, 45.5% of the total antibiotic use comes from human medicine (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Paul-Ehrlich Gesellschaft für Chemotherapie e.V., Infektiologie Freiburg, 2016). A causal relationship is evident between antibiotic consumption and the development of resistances in bacteria, both in practitioners' patients and hospital, acquired infections (Andersson and Hughes, 2010). Unlike Germany, the Netherlands and Scandinavian countries, Austria did not have the comprehensive antibiotic consumption data in human medicine available until now (Kern, 2016).

In hospitals, where approximately one third (32.8%) of the antibiotics used in Austrian human medicine are used, multi-resistant hospital germs are a problem faced every day, especially in intensive care units. In particular, the immune-suppressed patients, patients who have been given antibiotics for a long period, as well as the transfer of bac-

terial pathogens from patient to patient lead to infections caused by multi-resistant pathogens, which no longer respond to antibiotic treatment. In October 2015, the National Council (Nationalrat) encouraged the compilation and assessment of antibiotic consumption data in hospitals in Austria (Republik Österreich Nationalrat, 2015). In cooperation with the Austrian Society for Antimicrobial Chemotherapy (ÖGACH) and the German Robert Koch Institute (RKI), AGES recently established an antibiotic consumption surveillance system for hospitals. Following EU-wide specifications for reducing antibiotic resistance, this pilot project established an Austrian-wide, standardized antibiotic-reporting system for hospitals to provide a statistically secured basis for managing prudent use of antibiotics. Currently, nine hospitals are participating. The first ECDC/EFSA/EMA joint report on the integrated analysis of the consumption of antimicrobial agents and the occurrence of antimicrobial resistance in bacteria from humans and food-producing animals (2015) reports a total use of 37.5 t of antibiotics for practitioners' patients in 2014, amounting to 13.9 DDD/1,000 inhabitants per day (that is 507,350 DDD/100,000 inhabitants per year) and placing Austria among the most conservative antibiotic users in Europe. Recently, ECDC published similar data for 2015, claiming a consumption in the Austrian community of 14.0 DDD/1000 inhabitants per day (ECDC, 2016; Weist and Högberg, 2016). However, these data about antimicrobial consumption in Austrian outpatients are based on social insurance company's sales data (Bundesministerium für Gesundheit und Frauen, 2015). During the last few years, the declining pharmacy sales prices due to an increase in market shares for cheap generic drugs as well as an increase in deductibles for insured people (increasing prescription fee) falsely suggest a low level of antibiotic prescriptions in the Austrian primary care sector. Patients prefer to purchase their prescribed «cheap» antibiotic out of their own pockets, rather than pay a deductible costlier than the actual drug. We consider our findings of 47.3 t usage in the community sector, 618,681 DDD/100,000 inhabitants per year (that is 17.13 DDD/1,000 inhabitants per day), as well as 70.4 t total usage, 763,121 DDD/100,000 inhabitants per year (that is 21.2 DDD/1,000 inhabitants per day) as the correct numbers for antibiotic use in human medicine. The total Austrian usage of 70.4 t correlates well with the situation in Germany where the usage in human medicine totals 700 t. In 2015, the Austrian prescription volume in outpatients constituted 67.2% of

overall antimicrobial consumption in human medicine. In Germany, 85.7% of overall antimicrobial consumption in human medicine was used for outpatients in 2015 (600 t in community sector and 100 t in hospitals) (Bundesamt für Verbraucherschutz und Lebensmittelsicherheit, Paul-Ehrlich Gesellschaft für Chemotherapie e.V., Infektiologie Freiburg, 2016).

According to our findings, the antimicrobial consumption in the community, measured in kg active ingredient, increased by 0.3% from 2011 to 2015; consumption in DDD/100,000 inhabitants decreased by 3.6%. These numbers contradict the AURES reports, which claim a reduction of 45.2% in prescriptions per 100,000 inhabitants for the period 2011 (31.4 prescriptions per 100,000 inhabitants) till 2015 (17.2 prescriptions per 100,000 inhabitants) in Austria (Bundesministerium für Gesundheit und Frauen, 2012; 2016). These data rely on packages reimbursed by Austrian health insurance funds as a proxy for prescriptions (Bruyndonckx et al., 2014) and miss the antibiotics cheaper than the prescription fee. Already in 2007, Campos et al. have shown for Spain that antibiotic consumption as estimated from reimbursement data is substantially less than that from sales data (Campos et al., 2007); their sales data suggested that ~30% of the total antibiotic consumption was not registered by the reimbursement data of the National Health System. Using ECDC-data from 2014 (37.5 t), the underreporting of consumption in the community in Austria amounts to 20% (ECDC/EFSA/EMA, 2015).

Also, the seasonality of antibiotic use at the community level, as documented in our study, indicates the need for campaigns to reduce unnecessary antibiotic use. The higher consumption rate of antibiotics during winters reflects the antibiotic treatment of viral respiratory tract infections (Sun et al., 2012). In 2011, the European Surveillance of Antimicrobial Consumption (ESAC) study group surveyed the outpatient antibiotic use in 33 European countries and asked for a reduction in seasonal variation in antimicrobial consumption (Adriaenssens et al., 2011). Altiner et al. (2010) propagated the use of fluoroquinolone prescription surveillance as a quality indicator in the outpatient setting. In Austria, seasonal variation for beta-lactam-antibacterials amounts to 45%; that for other beta-lactam-antibacterials including cephalosporins 39%; the so-called macrolides, lincosamides and streptogramins show seasonal variation of 56%, and quinolones 25% (the differences between January and August taken as a measure). The Scottish Government successfully aimed to re-

duce the seasonal variation in quinolone consumption by < 5% (Health Protection Scotland, 2011).

In a survey performed by the European Commission (European Commission, 2016) in April 2016 in Austria, only 28% (EU-28: 43%) of the persons interviewed correctly answered that antibiotics cannot affect viruses; 63% (EU-28: 46%) falsely believed in the effectiveness of antibiotics against viruses; 9% did not provide an answer to this question. Patients with misconceptions on the mode of action of antibiotics contribute to inappropriate antimicrobial consumption by unjustified demand. It is important to educate the public not to expect antibiotic prescriptions for non-bacterial infections.

Antibiotic use for patients varies substantially among European countries (Mor et al., 2016). Countries such as the Netherlands or Switzerland show only a small consumption density (about 356,000 DDD/100,000 inhabitants) compared to other modern societies like Austria, which showed a consumption density of 763,121 DDD/100,000 inhabitants in 2015 (ECDC/EFSA/EMA, 2015). Reducing the amount of antimicrobial consumption does not result in quality loss (Hayashi and Paterson, 2011; Lidao et al., 2015; Scholze et al., 2015). However, this huge difference in the density of antibiotic use – the Netherlands and Switzerland using >50% DDD less than Austria – may be seen as indicating the potential magnitude of possible reduction of antibiotic use in human medicine. Concerning veterinary medicine, in August 2016, the European Medicines Agency (EMA) even asked member states to reduce their colistin consumption by 65% in the course of three to four years, due to the discovery of a new mobile resistance mechanism in enterobacteriaceae (European Medicines Agency, 2016). In Austria in 2015, food animals received 1,548 kg of colistin, which was 300 times more than the 5 kg amount used in human medicine.

In 2011, an action plan of the European Commission against the rising threats from antimicrobial resistance (AMR) set out key actions for a successful fight against AMR and requested the strengthening of surveillance systems on antimicrobial consumption in human medicine and in animal medicine (European Commission, 2011). The National Action Plan on Antimicrobial Resistance (Bundesministerium für Gesundheit und Frauen, 2014) of the Federal Ministry of Health and Women's Affairs instructed the hospitals to survey their antimicrobial consumption, an aim that was specifically endorsed by the health committee of the Austrian Parliament in October 2015 (Republik Österreich Nationalrat, 2015).

In 2015, the WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (WHO-AGISAR) provided a joint report on the integrated analysis of the global consumption of antimicrobial agents (WHO-AGISAR, 2015). Like the first joint ECDC-EFSA-EMA report on the occurrence of antimicrobial resistance in bacteria from humans and food-producing animals (ECDC/EFSA/EMA, 2015), they suggest actions at the global as well as regional levels to sharpen the system of integrated antimicrobial consumption surveillance. All these policies suggest curtailing unnecessary use of antibiotics in situations such as animal husbandry and human medicine (Opal and Pop-Vicas, 2015).

5. Conclusions

While there was already an 8.7% decrease in antimicrobial consumption in food animals from 2011 to 2015, the amount of active ingredients used in human medicine increased by 3.8% in the same time period (2011-2015). Agricultural plant production is only of minor relevance concerning antibiotic consumption in Austria, amounting to less than 0.1% of the total antibiotic use in 2015. To reduce the spread and development of multi-resistant bacteria, all fields are called upon to set measures and take responsibility. The global state of antimicrobial resistance has already placed us in a critical situation in which antibiotic consumption needs to be reduced aggressively beyond the current levels.

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