Quantification, Benchmarking and Stewardship of Veterinary Antimicrobial Usage

First International Conference

27-28 February 2018

ABSTRACTS BOOK

Oral presentations

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Herd level antimicrobial consumption in animals
Collect | Analyze | Benchmark | Communicate

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ON ANTIMICROBIAL RESISTANCE

Used Daily Dose vs. Defined Daily Dose – Advantages and disadvantages of different dosage assumptions for the benchmarking of antimicrobial usage in livestock

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Antimicrobial resistance is a serious threat for public health globally. Tackling the problem of rising resistances requires, amongst others, valid data, and also demands harmonized monitoring of antibiotic use and a benchmarking system on farm level.
Up to date, there is no harmonized monitoring of antibiotic use and no system to assess such data Europe-wide, thus hampering direct comparison between different European countries. Most of the monitoring systems are based on sales data. In order to assess the number of animals treated, defined daily doses (DDD) and estimated weights of the treated animals have to be applied. Only few monitoring systems obtain data that facilitate calculation of used daily doses (UDD).
Since 2011, data about the use of antibiotics in livestock in Germany are collected and evaluated in a sentinel of farms and veterinarians within the VetCAb project (Veterinary Consumption of Antibiotics; see www.vetcab-s.de). Compared to other antibiotic monitoring systems, the VetCAb database maintains detailed information on the number of animals treated, the treatment duration, the application route and also the indication. Therefore, calculation of the UDD is possible for every single treatment.
In this evaluation, we calculated the treatment frequency for each farm based on UDD and, in contrast, the treatment frequency based on DDDvet published by ESVAC in April 2016. Results show that there are differences between both outcomes, which may have serious implications for the benchmarking of farms. As an example, for broiler we calculated a false-positive rate of 40% by indicating the upper 25% of the distribution in comparing DDDvet- vs. UDD-calculation. Furthermore, it shows that the calculation procedure also has an impact on the comparison between populations which needs further reflection.
Results for pigs and poultry will be presented and advantages and disadvantages of these two calculation methods will be discussed.

Conclusion
Standardizing sales data based on the DDD and estimated standard weights has the great advantage of not needing additional information, but the treated species and the amount of active substance sold. But it carries the risk of under- or overestimating the real use due to the unknown number of animals treated, especially when the treated animals do not scale the standard weights. In addition, systematic shifts in the UDD in contrast to DDD may seriously bias the estimates of antibiotic use. Therefore, additional standardization in reporting as well as in calculation is crucial in order to facilitate comparison of results of monitoring systems.

Advancement of Dairying in Austria: Calculating Defined Course Doses (DCD_{vet}) for Antimicrobial Dry Cow Therapy on Conventional and Organic Farms

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In Austria, veterinarians are legally obliged to report all antimicrobials dispensed for use in food-producing animals, however, they do not need to report antibiotics administered themselves. The Advancement of Dairying in Austria (ADDA) project involved over 250 farms and 17 veterinary practices. The study collated antimicrobial use and dispensing data over one year from farms selected by their herd veterinarians and was, therefore, a more complete dataset than statutory reporting. Farmers, veterinarians and national milk recorders were also asked to complete online surveys.

A total of 211 farmers completed the management survey (84% response rate). Of these, 78% farmed conventionally, 20% organically and 2% were converting from conventional to organic methods (and were excluded from the analysis). Mean herd size was 20.5 (median 18.5) dairy cows in organic herds compared to 28.7 (median 22.0) cows on conventional farms. When asked whether they used antimicrobial dry cow therapy on all cows (i.e. blanket dry cow therapy, bDCT), 56.2% of conventional farmers and 16.7% of organic farmers answered "yes". Two conventional farmers (but none of the organic farmers) stated that they did not use antimicrobials at drying off. The remaining farmers administered DCT selectively (sDCT) to cows following a positive bacteriological culture (42.9% organic farmers; 14.8% conventional farmers) or clinical symptoms suggesting mastitis (40.4% and 29.0%, respectively). The difference between conventional and organic systems with respect to bDCT versus sDCT was statistically significant at the 5% level (Table 1, Chi^2 test statistic 20.85; p-value < 0.00001).

Table 1: 2x2 contingency table based on farmers' response to survey question

	Blanket DCT	Selective DCT	Total
Conventional farms	91	71	162
Organic farms	7	35	42
Total	98	106	204

When analysing the antimicrobial treatment data for dry cow therapy according to the European Medicines Agency's standardised course of 4 udder tubes being equivalent to 1 Defined Course Dose (DCD_{vet}), the mean number of DCD_{vet} administered per cow and year on conventional farms was found to be 0.48 (median 0.49), compared to 0.45 (median 0.35) on organic farms. The difference between production systems for antimicrobial dry cow therapy (aDCT) by DCD_{vet}/cow/year was not statistically significant at the 5% level (Mann Whitney U Test, Z score 0.14887, one-tailed p-value: 0.44038).

Conclusion
Despite the apparent differences in the decisions made by conventional and organic farmers determined from the survey responses, the overall level of aDCT calculated by DCD_{vet}/cow/year was not statistically different between the two production systems.

Antimicrobial use in medicated feeds on Irish pig farms in 2016: quantitative data and the consequences of using different treatment indicators.

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Background: In the Republic of Ireland, the development of a system to monitor antimicrobial use (AMU) in the pig industry has been identified as a priority in Ireland's National Action Plan (iNAP) for the Department of Agriculture, Food and the Marine in 2018. This study presents the first quantitative data on antimicrobial use in medicated feeds on pig farms in Ireland and examines the consequences of using various treatment indicators.

Methods: Data on antimicrobial use was obtained from a cross-sectional survey on biosecurity and management practices of 67 farrow to finish pig farms. Production data from the farms (Teagasc eProfit Monitor) were used to estimate the amounts of medicated feed used (numerator) and the population on each farm (denominator). Numerators were expressed in mg of active ingredient or in Defined Daily Doses. The ESVAC system (DDD_{vet}) and two systems derived from the SPC documents for antimicrobial products available in Ireland (DDD_{irl} and DDD_{irl_comb}) were used. Denominators were expressed in terms of kg liveweight sold, the population correction unit (PCU) or the average weight of biomass (kg) present. Twelve treatment indicators (TI) were calculated using each combination of numerator and denominator. A benchmark for each was set at its mean value. To assess the effect of each TI at farm level, the change in rank was determined for each farm relative to its rank when mg/PCU was used as the reference.

Results: A small effect of TI on the number of farms above the benchmark was observed. Eight farms (11.9% of 67) were above the benchmark for some TIs and below for others. When rankings among each TI were referenced against mg/PCU, 52.7% of ranks changed no more than one place; 86.4% by no more than five. Ranking was more sensitive to the numerator than denominator: the percentage of ranks changing by one or less places was 83.3% for TI's using the same numerator as the reference; 45.9% when using a different numerator. Six farms (8.9%) were affected by changes in rank of 10 or more places.

Conclusion: The numerator had a greater influence than the denominator in determining the effect of the treatment indicator. The choice of TI did not have an effect at population level. Important changes were observed at individual farm level which have potential consequences for the affected farms and may have implications for policy making.

Table 1. Mean antimicrobial consumption in medicated feeds on 67 Irish pig farms during 2016 expressed in the various treatment indicators (figure in parenthesis represents percentage of farms above the mean)

	numerator			
denominator	***mg***	***DDD_{vet}***	***DDD_{irl}***	***DDD_{irl_comb}***
Population Correction Unit (PCU)	123.7 (34.3%)	6.2 (32.8%)	9.5 (29.9%)	8.2 (31.3%)
Liveweight sold (kg)	85.1 (37.3%)	4.3 (32.8%)	6.6 (29.9%)	5.7 (31.3%)
Average weight of biomass (kg)	422.0 (31.3%)	21.4 (32.8%)	32.1 (29.9%)	27.4 (31.3%)

Farm-level antimicrobial use surveillance in a FoodNet Canada-CIPARS sentinel site; application of several antimicrobial use indicators to monitor industry interventions

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The objective of this surveillance project is to describe antimicrobial use (AMU) using different metrics for broiler chicken and turkey data collected from a FoodNet Canada (FNC) sentinel site located in the province of British Columbia. Since 2013, the Canadian Integrated Program for Antimicrobial Resistance Surveillance (CIPARS) has been collecting AMU and antimicrobial resistance (AMR) data from sentinel broiler chicken and turkey flocks in British Columbia as part of the national CIPARS/FNC farm program. A total of 78 broiler flocks (1,765,933 kg biomass) and 88 turkey flocks (5,147,396 kg biomass) were surveyed between 2013 and 2015. AMU data were collected via a questionnaire. Several AMU metrics were applied to the data: frequency of use (number of farms), total kg, mg/population correction unit (mg/PCU), number of Canadian defined daily doses (nDDDvetCA)/1,000 animal-days at risk (i.e., the treatment incidence) and nDDDvetCA/PCU. The application of denominators for the latter two metrics was necessary given the design of our surveillance framework (i.e., data collection from a single grow-out cycle per farm per year). Reasons for AMU were described in terms of frequency of use and mg/PCU. In both poultry species, greater than 94% of the quantity of antimicrobials (mg/PCU) was administered via feed and less than 4% via water and injections. In 2013 producers reported the use of in-ovo ceftiofur in both broiler chicken and turkey hatcheries to prevent diseases associated with avian pathogenic *E. coli.* In 2014 and 2015 the poultry industry implemented a voluntary intervention aimed at the elimination of the preventive use of antimicrobials deemed critically important to human medicine (primarily ceftiofur and enrofloxacin). Questionnaire data from those years indicated that there was no ceftiofur use in hatcheries. A corresponding decrease in the prevalence of ceftriaxone resistance was noted in chicken *E. coli* and *Salmonella* isolates over the same period. In terms of AMU frequency, the top 3 antimicrobials used in both species were bacitracin, virginiamycin and penicillin. These antimicrobials were administered in feed to prevent *Clostridium perfringens* infections (necrotic enteritis). The relative ranking changed for broilers when mg/PCU was used (bacitracin > penicillin > virginiamycin) but remained consistent using the nDDDvetCA metric with the 2 different denominators, 1,000 chicken-days at risk and PCU. In turkeys, the ranking remained consistent using the 3 quantitative metrics. The overall quantity of antimicrobials used in broiler chickens and turkeys remained relatively stable over the last three years; however, regardless of the metric used, when compared to chicken, AMU in turkeys was lower. The lower frequency of diseases diagnosed and the lower proportion of rations medicated during finishing stages of growth may explain the lower quantity of AMU in turkeys. Additionally, the longer duration of growing period in turkeys (mean days at risk of 90 days) compared to broilers (mean days at risk of 35 days) may explain the lower nDDDvetCA/1,000 days at risk.

Conclusion
The CIPARS/FNC sentinel-farm surveillance program identifies which antimicrobials are commonly used in broiler and turkey production, monitors trends in how/why they are used, and assesses the impact on associated AMR. These findings highlight the importance of ongoing AMU surveillance to monitor the impact of industry-wide interventions aimed at reducing AMU and AMR. Various metrics can be used to monitor the efficacy of AMU reduction initiatives (reduction / elimination of specific antimicrobials and reduction in the total quantity) and further inform antimicrobial stewardship practices at the farm level.

Enhancing Awareness of Antimicrobial Use in Danish Pig Farmers through the Yellow Card Initiative

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From 2001-2009 an increase of 45 % was seen in the consumption of antimicrobials in the Danish animal production – primarily in the pig production. Increasing antimicrobial consumption leads to increased risk of developing antimicrobial resistance in exposed bacteria. This may pose a risk to human and animal health due to the potential risk of treatment failures.

In order to raise awareness and reduce the antimicrobial consumption in the pig production, the Danish Veterinary and Food Administration (DVFA) established the yellow card initiative in 2010. The initiative addresses high use farms by setting thresholds for antimicrobial consumption. The thresholds were set for different age groups and are measured in animal daily dose per 100 animals per day over nine months. The yellow card addresses the pig farmer because he/she is in charge of the holding and thereby able to change feeding, biosecurity, management or implement other preventive measures under the oversight of the herd veterinarian in order to raise the health status and thereby minimizing the need for antimicrobial treatment.

In July 2016 the differentiated yellow card was implemented to promote a more responsible use. All classes of antimicrobials are assigned a factor. Antimicrobials which are critical important for human use such as fluoroquinolones are assigned a factor 10 while e.g. pleuromutilin is assigned factor 1. The use of antimicrobials with a higher factor will add more to the herd average in the yellow card, and the herd will reach the threshold sooner. The thresholds have been reduced gradually in 2013, 2014 and 2017 to achieve the national goals of reduction.

When a holding exceeds the threshold levels, the DVFA issues an order – **the yellow card** – compelling the owner of the holding to reduce the consumption. Also, the DVFA may carry out one or more inspection visits to the holding. If the consumption at the holding has not been reduced below the threshold after the nine month period, the DVFA may issue another order compelling the owner of the holding to follow expert advice from an impartial veterinarian.

Conclusion
The Yellow card initiative has raised the AMR awareness of pig farmers and veterinarians. The incentive has helped the pig sector to reduce consumptions of antimicrobials (kilo active compound) by 25 % from 2010 to 2016. The differentiation introduced in 2016 has proven very effective – lately by taking the consumption of colistin to a level close to zero.

Quantitative analysis of antimicrobial product usage in the UK sheep industry

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This study represents the first robust, quantitative estimate of the quantity and diversity of antimicrobial active ingredients used in commercial sheep production in the UK. Hitherto there was no published evidence on this subject pertaining to the UK and no reliable basis on which industry stakeholders could make decisions upon antibiotic reduction or refinement. The antibiotic prescription records from 207 sheep flocks over a 12 month period between Aug2015-July2016 were collated along with farm information on flock size, management system (Organic/Conventional) and topographical stratification (Hill, Upland, Lowland). Data were provided by eight veterinary practices in England, Scotland and Wales. The mean and median mg/PCU across all flocks was 11.38 and 5.95 respectively while mean and median ADDD was 1.47 and 0.74 respectively. These figures are low in comparison with the target of 50mg/PCU adopted for all UK livestock sectors. In this study 98% of flocks were below the 50mg/PCU target. The correlation between the two metrics was high ($R2 = 0.84$, $p<0.001$). In total 80% of all antibiotic usage occurred in the 39% of flocks where per animal usage was greater than 9.0 mg/PCU. Oxytetracycline was the most commonly prescribed antibiotic accounting for 57.4% of total by both metrics, followed by Penicillins (including extended spectrum) 23.6% and Aminoglycosides 10.7%. Parenteral antibiotics represented 82% of the total Mg/PCU. Antibiotic usage peaked in the late winter/early spring with 24% and 22% of all antibiotic usage in February and March respectively. Analysis of a subset of 24 flocks from one of the veterinary practice with more detailed prescription records revealed 65.5% of antibiotic use was prescribed for the treatment of lameness. Extrapolation of the treatment rate from Defined Course Doses (DCDvet) for each of the antibiotics prescribed for this purpose suggested a median treatment rate for lameness of 29.6 treatment courses per hundred breeding ewes with a range of 9.6-67. Oral antibiotics were prescribed in 47% of flocks with a median of 64% of predicted lamb crop treated per farm. Lowland flocks were prescribed significantly more antibiotics than hill flocks. Flock size and management system were not significantly associated with antibiotic usage. Variance partitioning apportioned 79% of variation in total antibiotic usage (mg/PCU) to the farm level and 21% to the veterinary practice indicating that veterinary practices have a substantial impact on overall antimicrobial usage. The results of this study indicate that significant progress in reducing antibiotic usage in the sheep sector should be possible with better understanding of the drivers of high usage in individual flocks and of veterinary prescribing practices.

A deeper analysis of correlations between antimicrobial usage, production output and disease prevalence was conducted on a subset of 36 flocks with sufficiently detailed recorded data and this work is now being extended to all 207 farms to examine relationships between usage and disease prevalence over successive years and correlations with preventative health measures such as vaccination.

Conclusion

We cannot assume that low antibiotic usage correlates with low disease or good welfare and there is a great danger in conflating the two measures. Low, targeted usage of antibiotics in all veterinary species is desirable but this must be balanced with concern for animal welfare and sustainable productivity. This study has demonstrated significant variation in antibiotic usage between farms and between veterinary practices. Further research is required to understand the biological, managemental and physiological drivers of antibiotic prescription and use among sheep farmers and their prescribing veterinary surgeons in order to achieve a sustainable reduction in antibiotic use.

SAVSNET: near real-time wide scale companion animal antimicrobial prescription surveillance, benchmarking and stewardship

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The Small Animal Veterinary Surveillance Network (SAVSNET) is a veterinary health informatics project that collects Electronic Health Records (EHRs) from in excess of 250 veterinary practices (3.5< million EHRs to date) and 7 diagnostic laboratories (70< million EHRs to date) in the United Kingdom. In partnership with the Veterinary Medicines Directorate, SAVSNET has developed an interest in antimicrobial prescription surveillance focusing on three key objectives:

(i) Monitoring
Using a semi-automated text-mining technique, SAVSNET routinely captures antimicrobial prescription occurrences from EHRs. Between 2014 and 2016, SAVSNET demonstrated a significant reduction in canine and feline antimicrobial prescription frequency. Veterinary practices which frequently prescribed to dogs also prescribed frequently to cats. Cats were prescribed 'highest priority critically important antimicrobials' significantly more frequently than dogs, and were also prescribed a significantly less diverse range of antimicrobials than dogs. We found that antimicrobials were commonly prescribed in combination with anti-inflammatory drugs.

(ii) Factors associated with antimicrobial prescription
SAVSNET collects a range of signalment data pertaining to each animal; this provides a novel opportunity to explore factors associated with antimicrobial prescription risk. At a practice-level, practices reporting a greater proportion of vaccinated, neutered or insured dogs prescribed antimicrobials significantly less frequently, as do Royal College of Veterinary Surgeons accredited practices. At a consultation-level, focusing on animals reported as presenting for investigation of clinical signs related to ill-health, certain presentations were at significantly greater risk of systemically-authorised antimicrobial prescription than others e.g. respiratory-related clinical signs, with risk also peaking in animals aged around 5 years old. Compared with crossbreed dogs, a number of genetically-similar breed groups were associated with increased risk of systemically-authorised antimicrobial prescription including sight hounds; ancient/spitz breeds and working dogs; breed-based associations were less clear in cats.

(iii) Benchmarking and stewardship
Practices taking part in SAVSNET can access an online, secure, anonymised platform that enables them to monitor the frequency and variety with which they prescribe antimicrobials, and benchmark against their peers. For veterinary practices not yet able to take part in SAVSNET, 'mySavsnet AMR' (https://www.liverpool.ac.uk/savsnet/my-savsnet-amr) enables any veterinary practice to submit antimicrobial prescription data for benchmarking against anonymised peers.

Conclusion
SAVSNET now has the capability to effectively monitor antimicrobial prescription and resistance in companion animals, and to identify important factors influencing antimicrobial prescription likelihood. Together with a novel benchmarking platform, these key findings can form a foundation for sustainable and effective antimicrobial stewardship programmes both in the UK and farther afield.

Global trends in antimicrobial use in food animals, an update.

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Purpose: Demand for animal protein for human consumption is rising globally at an unprecedented rate. Modern animal production practices are associated with regular use of antimicrobials, potentially increasing selection pressure on bacteria to become resistant. Despite the significant consequences for antimicrobial resistance, there has been no quantitative measurement of global antimicrobial consumption by food animals.

Method: We address this gap by employing multivariate models combining maps of animal densities, economic projections of demand for meat products and current estimates of antimicrobial consumption to map antimicrobial use in food animals for 2013 and 2030. Sales of veterinary antimicrobials were obtained via public records for 38 countries and estimated for 190 more.

Results: In 2013, the global consumption of all antimicrobials in food animals was estimated at 131,109 tons [95% confidence interval (CI) (100,812 to 190,492 tons)] and is projected to reach 200,235 tons [95% CI (150,848 to 297,034 tons)] by 2030. Up to a third of the increase in consumption in livestock between 2013 and 2030 will be imputable to shifting production practices in middle-income countries where extensive farming systems currently dominates.

Conclusion: The rise in antimicrobial consumption in food animals is likely to be driven by the growth in consumer demand for livestock products in middle-income countries and a shift to large-scale farms where antimicrobials are used routinely. Better understanding of the consequences of the uninhibited growth in veterinary antimicrobial consumption is needed to assess its potential effects on animal and human health. Our findings call for initiatives to preserve antibiotic effectiveness while simultaneously ensuring food security in low- and lower-middle income countries.

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Using medicine waste bins to validate on-farm medicine records and veterinary prescription data on UK dairy farms

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The use of prescription veterinary medicines (PVM) on dairy farms in the United Kingdom (UK) is currently not well understood, despite potential implications for the development and transmission of antimicrobial resistance and animal health. Currently in the UK, veterinary medicine use is measured at a national level, with measurement at the veterinary practice level likely to be instituted soon. Despite detailed on-farm medicine records being a requirement for dairy farmers, there is limited data available at the farm level.

Materials & Methods

26 dairy farms with a broad range of management systems, herd sizes and production goals were enrolled in September 2016. A full PVM inventory was taken along with a structured management survey. Medicine waste bins were placed on farms and participants were asked to dispose of all used medicine packaging into these bins. Farms were followed for a 12-month period. At the end of the study, farm medicine records and veterinary sales data were obtained.

Results

Medicines were recorded and stored in a variety of different ways. Critically important antimicrobials (fluoroquinolones, 3rd & 4th generation cephalosporins) were stored on 89% of farms; these accounted for between 0% and 30% of the total weight of antimicrobials. Expired antimicrobials were present on 74% of farms, and were used on 69%. On-farm medicine record quality varied widely between farms; some farmers kept very accurate and up-to-date records, while others kept no records at all. Veterinary sales data were accurate and easy to obtain, and correlated well with actual on-farm use, particularly when combined with a pre- and post-audit medicines inventory .

Conclusions

Veterinary sales data provide more granular data than current UK national estimates, however they are prone to overestimating the amount of medicine being administered and are subject to time lag. On-farm medicine records provide a more temporally accurate measure of use and generally provide information on dose rate, course length and the identity of the individual animal being treated. However, the quality of on-farm records varies widely, and the current format of these records is such that collating data is inefficient and time-consuming. Medicine waste bins provided the most accurate record of PVM use on many of the participating farms, capturing data on expired medicine use, off-license use and wasted medicines. Waste bins, however, were at risk of underestimating use where participants forgot to use them.

The question of the denominator: Estimating the live animal population

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The choice of both nominator and denominator is crucial in quantifying antimicrobial usage, when aiming at comparison of populations or evaluation of trends in antimicrobial usage. In particular, it is crucial that the measures are comparable between species or age groups, when summarizing data on different populations or sub-populations.
Preferably the denominator should represent the population at risk, i.e. the live population, taking into account the time at risk. This may be measured in kg-live biomass*days or live-animal*days. For both measures, the average live biomass of the animals must be estimated for each subpopulation as part of the calculation procedure: either for calculation of the biomass or for calculation of the standard animal daily dose (DDDanimal).
When census data are available, the live biomass of a population can be estimated directly, by multiplication with the average live biomass of one animal. However, valid census data are not available for many animal populations. Therefore, the live biomass must be estimated for each subpopulation from other available data on the population. The most valid data sources should be chosen for the estimation, rather than the most convenient data, eg. valid production data are better than census data with low validity.
In the DANMAP reports, the live biomass of the pig population in a given year is estimated from a combination of slaughter data, export data and productivity data of the growing pigs, together with census data on the sows, as valid census data are not available for the growing pigs. In DANMAP 2012, the biomass was also estimated for other species and production types, for which other sources and types of data are available, but the methods have not previously been published.
The aim here is to present the principles and different methods for estimating the live biomass of a population based on different data types, thus providing a comparable denominator across species and production types.

Conclusion
When quantifying antimicrobial usage, the denominator should represent the population at risk, i.e. the live population, taking into account the time at risk. In most countries, valid census data are available only for some populations, mainly the sow population and the dairy cow population, but not for growing pigs, calves, poultry and a number of other production types. Nevertheless, census data within specific age groups or populations can be estimated from the number of animals produced for slaughter together with different types of productivity data.

Selective dry cow therapy on Flemish herds based on a new infection-indicator at dry-off: preliminary results

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Selective dry cow therapy (SDCT), i.e. only administrating dry cow tubes that contain long-acting antimicrobials to cows with an existing intramammary infection (IMI), may be the solution to meet the justified public demands without endangering udder health. To apply SDCT, it is essential to be able to accurately differentiate between infected and uninfected cows at the time of dry-off. Therefore, a new infection indicator, using (test-day) SCC adjusted by cow- and herd-level information, was developed using data from a first field study and is applied in a second ongoing field study that started in April 2017.

In total, 448 cows from 12 herds were dried-off. Within each herd, cows were divided into 2 groups. The first group (n = 239) received blanket dry cow therapy (BDCT), the second group (n = 209) received SDCT based on the infection-indicator (Figure 1).

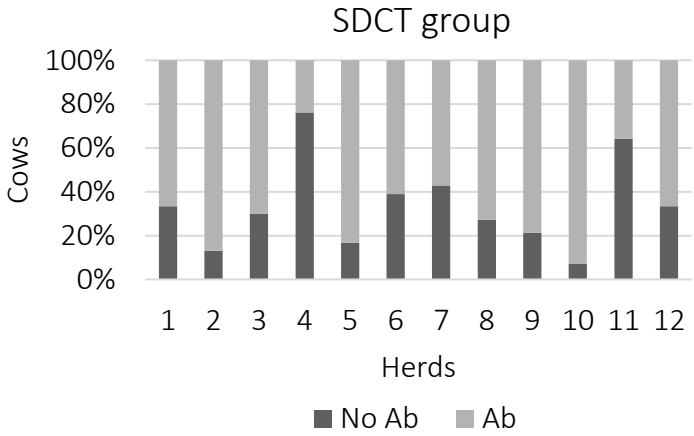

Figure 1: In the SDCT group, on average 33.5% (n = 70) of the cows did not receive long-acting antimicrobials (Ab) at dry-off, ranging from 7.1% to 76.2% of the cows within different herds.

So far, 47 new cases of clinical mastitis were detected within 100 days after calving in both groups, mostly (48.9%) caused by *Escherichia coli*. In the BDCT group, 20 new cases of clinical mastitis after calving were detected. In the SDCT group, 27 new cases were detected of which 7 did not receive long-acting antimicrobials at dry-off. In total, 12 cows were culled within 100 days after calving, of which only 2 with IMI as main cause and both of them were dried-off with antibiotics. 5 cows were part of the BDCT group, so 8 cows were culled in the SDCT group of which only 1 did not receive long-acting antimicrobials at dry-off. Analyses of the somatic cell counts and milk yield after calving in both groups are ongoing.

Conclusion

Application of SDCT based on a newly defined infection-indicator can reduce the use of the long-acting antimicrobials at dry-off up to about 75%, depending on the general udder health status of the cows and the associated herd health management. Comparing cows' performances between the SDCT group and BDCT group within herds, will reveal whether SDCT can be successful in Flanders, hence reducing the antibiotic use without harming the udder health.

Patterns of antimicrobial usage reduction in French rabbit farms - a trajectory analysis

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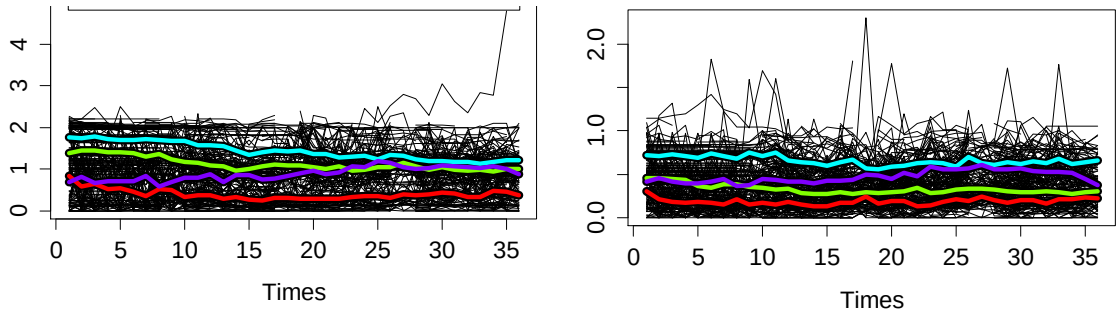
Since 2011, the French professional Rabbit Council (CLIPP) has established a plan for reducing use of antimicrobials in rabbit-farming sector. Within the framework of the plan, the Index of Frequency of Treatments with Antibiotics (IFTA), an indicator of usage based on counts of actual number of treatment days reported to the rearing period length in days [1], is collected at the batch level on rabbit farms to follow up the progress made in reducing the use of antimicrobials.
Whereas over the last six years collective reference points have demonstrated the reduction of usage at the sector level [2], professional rabbit-farming stakeholders have still reported contrasted experiences at the farm level, from individual success to marked difficulties. Our study therefore aimed to analyse on-farm data on a longitudinal perspective, to determine temporal trends in usages at the farm level.

Data on 167 farms, which recorded IFTA values over the period 2012-2015 in both mother and fattening rabbit successive batches, were compiled, represented and analysed. A joint-variable trajectory analysis was performed to identify particular patterns, considering jointly IFTA values recorded in fattening rabbits and in mother rabbits. The parallel evolution of the technical performances of the farms included in the analysis was complementarily addressed.

Regarding antimicrobial usage trajectories, four classes of farms differing by the initial level of usage and the trends in usage over the study period were identified (Figure 1). Whereas three classes exhibited a continuous decrease, more or less marked depending on the year, a fourth class representing ~20% of the farms considered, showed a slight increase of IFTA values during the last years, for both mothers and fattening rabbits. Additionally, the differential analysis of the technical performances recorded between the identified classes of farms raised hypothesis regarding circumstances which were likely to lead to a reduction in antimicrobial usage.

Figure 1: Farm trajectories (black lines) and the four patterns identified (colored lines) according to joint breeding (left) and fattening (right) batches IFTA values (167 rabbit farms, 2012-2015, France).



Conclusion
Individual on-farm records of antimicrobial usages are valuable insights to assess variability between farms at a given time but also regarding antimicrobial usage reduction as a temporal process. Different patterns were identified, including in particular a sub-group of farms which experienced difficulties in reducing persistently antimicrobial usage. Further investigations will be carried out within the framework of the National EcoAntibio plan to better understand these different patterns observed.

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Current antibiotic usage data capture methods for the UK dairy sector: how effective are they?

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Inappropriate antibiotic usage (ABU) in agriculture is a recognised concern due to the perceived association with antibiotic resistance (ABR) [1]. To address this issue, there is the need to strengthen knowledge and understanding of ABU through livestock surveillance [2,3].

The aim of this study is to review the current ABU data capture systems used within the UK dairy sector, and to assess their advantages and limitations.

Data capture methods in the UK Dairy Sector

There are two main ABU data capture methods available: veterinary sales data from marketing authorisation holders and the on-farm medicine book. Additionally, voluntary data capture for 2015 and 2016 has been provided through a software company (FarmVet Systems) [4]. They extract data from practice management systems and determine whether an antibiotic medicine has been delivered to cattle farms. The Veterinary Medicines Directorate (VMD) aggregate these data by active ingredient. Smaller voluntary subsets of ABU data are collected by consultants, retailers and milk processors. One example is the DataVet project – an online resource to capture clinical findings and ABU by vets and farmers [1] [5].

Information from both veterinary sales and FarmVet Systems provides an initial insight into ABU, and the start of an official benchmark for the sector. Collection and collation of these publically available data increases awareness of ABU to stimulate discussion and behaviour change. DataVet, through combining specific farm level data with medicine sales data, cattle tracing system cow identification and milk recording provides a more individual assessment of ABU [5].

However, a significant limitation of official data capture is the inability to determine ABU per species. Although FarmVet Systems and DataVet encompass this, within the DataVet benchmark model assumed treatment data is based solely on veterinary sales. Furthermore, within the dairy sector, treatment is predominantly at individual level leading to the question: do veterinary sales correlate with farm level ABU? The on-farm medicine book, is principally paper based, with a central collating system non-existent despite containing farm level data that is required [6].

Conclusions

The current data capture systems leave a knowledge gap on ABU and reasons for treatment. This makes it difficult to assess whether prudent ABU correlates with high health and welfare standards. Evaluating the impact of an industry-led pilot electronic medicine book (eMB) for cattle will provide information to guide ABU data capture in the sector, allowing a more in depth assessment of ABU at the farm level.

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Trends in antimicrobial use in veal calves (2014-2016) and associated risk factors

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The veal industry is known to be one of the highest users of antimicrobials among all livestock production systems, and in the period 2007-2009, the Belgian veal industry used 60 DDDvet/year. The objectives of the present study were to provide an overview of quantitative and qualitative use of antimicrobials in the largest veal veterinary practice in Belgium in the period 2014-2016, and (2) to identify risk factors associated with antimicrobial use (AMU) to help this sector to a further reduction. A retrospective cohort study was performed. AMU data were electronically collected from a single veterinary practice in Flanders, through their software program. Standard daily dose methodology was used to quantify AMU. Mixed linear and logistic regression was used to identify risk factors for AMU. The dataset consisted of 295 production cycles from 78 farms, involving 146.014 veal calves and 8 different integrations. The average AMU was 32,3 DDDvet/year ±SD=11,04, of which 76,2% was administered orally and 23.8% parentally. The total AMU over 2014-2016 did not significantly alter. A significant reduction in the use of critically important antibiotics, compared to the historical data (2007-2009) was noted. A reduction of 95,9% was achieved for fluoroquinolones (FQ) and third and fourth generation cephalosporins (CS) and 91,1% for colistin (C). Additionally a reduction in oxytetracycline (OTC), trimethoprim-sulphonamides (TMS), lincosamides (LS) and penicillin was seen. In contrast, there was an increased use of long-acting macrolides (MLA), doxycycline (DC), classic macrolides (CM) and aminosides (AS). Significant risk factors for total AMU were: year, breed, integration and month. Holstein Friesian calves and crossbreeds were treated significantly less than Belgian blue beef calves (26,4±10,6, 35,5±8,9 and 37,2±10,6, respectively). Production cycles started in May used less AMU than these started in September to December. A significant effect of integration on total AMU and on the use of different antimicrobials was found (FQ, OTC, C, TMS, LS, MLA, DC, CM and AS). Additionally, breed differences in the use of OTC, C and CM were present.

Conclusion
These data show that this veterinary practice used 46% less antimicrobials compared to data from 2007-2009 in Belgium. The shift away from critically important antimicrobials (FQ, CS, C), although partial replacement by the also critically important long-acting macrolides was done. This study showed the need for benchmarks adjusted for each breed, and identified the integrator as an influencer of AMU in veal farms and target for sensibilisation campaigns.

Monitoring of Antibiotic Use – Cross-Sectional and Longitudinal Data 2011 - 2015 in a German Livestock Sentinel

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Within the research project VetCAb (Veterinary Consumption of Antibiotics), antibiotic usage data in German livestock are collected and evaluated since 2011. The project started in 2008 to proof, if a monitoring system is feasible under the conditions of the German veterinary and farming system. In 2011, a pilot project was carried out as a cross-sectional study including nearly 3,000 animal holdings all over Germany. Since 2013, the VetCAb-Sentinel project is continued as a longitudinal study with ongoing participant recruitment and data collection. Data collection is based on official application and delivery forms, voluntarily provided by veterinarians and farmers. The VetCAb database stores information about the number of animals treated, treatment date and duration, name and amount of the medicinal product used, indication and application route. Up to now, more than 200,000 records for pigs, cattle and poultry of the years 2011, 2013, 2014 and 2015 were entered into the database, providing the basis for detailed evaluations.
Results show that the median of the treatment frequency (TF) in broiler (41.1→18.5), piglet (3.9→1.4), sow (1.3→0.6), weaner (12→2.4), fattening pigs (5.1→0.2), calves (0.4→0.3) and beef cattle (0.2→ 0) holdings decreased between 2011 and 2015, whereas the median of the TF in dairy cattle holdings remained almost constant. Furthermore, the percentage of animal holdings without antibiotic usage was calculated. In the second half year of 2015, 17.1% of the broiler, 24.9% of the piglet, 24.3% of the sow, 29.2% of the weaner, 31.4% of the fattening pigs, 24.7% of the calves, 11.5% of the dairy cattle and 53.2% of the beef cattle holdings did not use any antibiotics at all. We also evaluated the antibiotic usage per active compound and calculated the TF per active compound class as a percentage of the overall TF. In cattle and pig holdings, the highest proportion of the TF is allotted to the usage of beta-lactams, regardless the age and production group (2015). In broiler holdings, the highest proportion is allotted to the usage of aminoglycosides and lincosamides. Furthermore, the effect of different factors such as time, farm size, region and management on the TF was investigated, using multiple linear mixed models.
Results of the VetCAb study will be presented, with an emphasis on trends in antimicrobial usage in livestock during the years 2011-2015, the possible underlying reasons and consequences.

The restriction of the use of critically important antibiotics in veterinary medicine: acceptability and impact of a new policy on practices

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In March 2016, the French animal health authorities have enacted a decree restraining the use of critically important antibiotics (CIAs, last-generations cephalosporins and fluoroquinolones) in veterinary medicine. Before using these last resort antibiotics, an antibiogram is now requested to justify the treatment. The aim of this study was to evaluate the acceptability of this decree and its impact on veterinary medicine practices.

Semi-structured interviews with veterinarians were conducted in France. Thematic analysis was used to analyse transcripts. We surveyed 66 French veterinarians.

We identified reasons why CIAs had been used in veterinary medicine prior to the decree: respondents pointed out their numerous advantages in therapeutic, such as their galenic properties or their broad spectrum of action. The relationship between veterinarians and clients had also impacted their use: CIAs were deemed more effective by clients, who could pressure veterinarians for their prescription. Surprisingly, even though the new French decree implied a restriction on prescriptions, it has been well accepted by veterinarians, mainly because they considered it to be relevant and fair, putting an end to the misuse of CIAs in livestock farming and harmonising practices between veterinarians. Except in rare cases (veterinarians in an animal hospital practice), respondents testified that the decree has not increased the use of antibiograms but it has induced a change in prescriptions, strongly limiting CIAs use in animal health. Furthermore, we highlighted that the recourse to an antibiogram in veterinary medicine was multifactorial (46 factors gathered into 11 categories were identified) and varied between animal sectors: the recourse was quasi-systematic in poultry to guide antibiotics prescription, frequent in porcine but rare in both bovine and equine sectors.

In a context of a change in veterinary medicine, we discussed the reasons for the success of the implementation of this new decree. French veterinarians have embraced the new regulation regarding the prescription of CIAs in order to fight antimicrobial resistance and to reinforce or redefine their role. Respondents use the decree as a regulatory support to change their prescription habit, to limit client pressure on their prescriptions and to promote responsible and prudent use of antibiotics, fostering the use of alternatives. From a cultural and social point of view, the French decree introduced a paradigm shift reorienting veterinary practices towards a more global and preventive approach of animal health.

Antibiotic Monitoring and Benchmarking in UK Dairy Group

James B More BVM&S MRCVS
John Allen Kite Consulting

PERIOD OF ANALYSIS - APRIL 2016 TO MARCH 2017

Summary of Results

A total of 81 dairy farms participated in the project. Average size 259 range 130-1450. All produced milk for the dairy co-operative Arla and were additionally part of the retailer ASDA's Pathfinders/Business groups.

Data release forms were completed by the farmers to allow access to their medicine purchases for the analysis period, with a 100% return rate of data achieved from their veterinary practices.

Data was entered manually on to uniform template to allow processing.

Results presented to producer groups with benchmarking and best practice information.

Metrics

ANIMAL DAILY DOSE (ADD)

MG/KG(PCU)

Metrics further segmented by use and Highest Priority Critically Important Antibiotics (CIA), as defined by the World Health Organisation WHO CIA

Calculations based on EMA defined weight for dairy cows (425kg)For ADD, defined daily doses calculated at product level using doses/ duration factors from UK Summary of Product Characteristics. For injectable and oral products, if there is a dose range, the highest dose is chosen. For other products, 1 ADD = 1 or 2 tubes (lactating cow), 4 tubes (dry cow) and 1 unit (intra-uterine).

Results

On average cows had 3.94 ADD

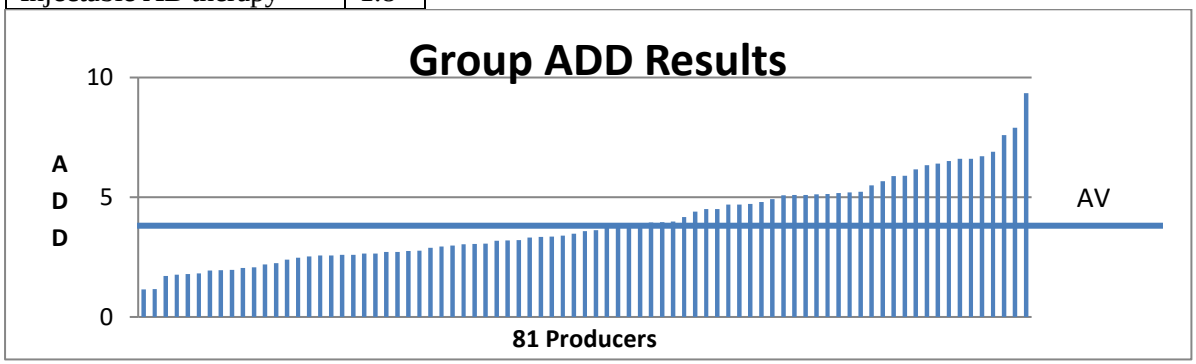
- Range of 1.15 – 9.35

On average cows had 1.6 attributed to CIA ADD • Range of 0.12 -5.09 (Fluoroquinolones 0.1, 3/4 generation Cephalosporins 0.94, Macrolides 0.56

Average mg/kg Population Corrected Units (PCU) 19.5 mg/kg

- Range of 3.3 - 72 mg/kg

	Average ADD
Dry cow AB therapy	0.53
Lactating cow AB therapy	1.42
Oral AB therapy	0.11
Uterine AB therapy	0.11
Injectable AB therapy	1.8



Conclusion

ADD proved to be an easily understood measure of antibiotic use on farm. Further segmentation allowed producers to focus on areas of highest usage and benchmark their performance against others. Milk processors gained insight into the levels and types of antibiotic used in their supply chain.

Antibiotic Monitoring/Benchmarking in Beef Sucklers Herds South West Scotland

James B More BVM&S MRCVS

Period of Analysis April 2015 March 2016 inclusive

Data release forms were completed by the farmers to allow access to their medicine purchases for the analysis period.

Data was entered manually on to uniform template to allow processing.

Data

Data was collected from 33 Beef/Suckler units based in South West Scotland

Included in this data set were one non-breeding finishing unit and 2 pedigree breeders.

Both extensively and intensively managed units were included. The smallest unit being 35 breeding adults and the largest 600 breeding adults.

There was a variety of management protocols from calves being sold direct from cow as stores to finished cattle going straight to slaughter.

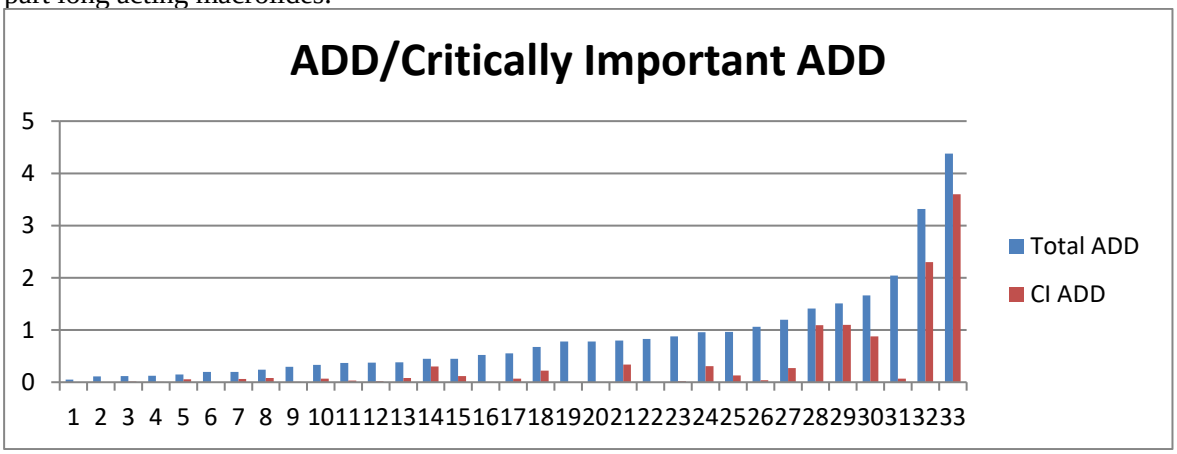
Metric

ADD, defined daily doses calculated at product level using doses/ duration factors from UK Summary of Product Characteristics. For injectable and oral products, if there is a dose range, the highest dose is chosen. For other products, 1 ADD = 1 or 2 tubes (lactating cow), 4 tubes (dry cow) and 1 unit (intra-uterine). Treatable weight calculated for all stock using standardised SDA recommendations when available, taking into account proportion of the 12-month period the animals were on premises. Metrics further segmented by Highest Priority Critically Important Antibiotics (CIA), as defined by the World Health Organisation.

Results

Average ADD 0.85 Range 0.05-3.60

Average ADD attributed to CIA 0.34 Range 0-3.6 The critically important products are for the most part long acting macrolides.



The two highest ADD figures are associated with units that had pneumonia outbreaks and used long acting macrolides. Additionally both these units had no vaccination protocols in place. Lower users tended to be smaller extensively managed farms or had vaccine protocols in place.

Conclusion

We were unable to use mg/kg(pcu) metric as a limited number of animals were slaughtered from the units. ADD as a metric proved to be well understood by producers and ha proved to be an excellent tool working with clients to refine herd health planning, clarifying vaccine and management protocols.

From ignorance to comprehensive surveillance of prescribed veterinary antimicrobials at farm level – data input and allocation of technical doses

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The Danish surveillance of prescribed veterinary medicine was launched in August 2000. Initially, the purpose was surveillance and research of antimicrobial use in animal production at farm level. Data collection was built on existing data providers: pharmacies and veterinarians, combined with reported sales from feed companies. Since then, VetStat has been applied for other purposes, e.g. control measures such as the "Yellow Card" initiative, a monitoring of antimicrobial usage at farm level in pigs.

Information from the pharmacies constitutes the core of VetStat, because all prescribed veterinary antimicrobials are sold through these to farmers, veterinarians and feed companies. The pharmacies report sales through the cash register to the Danish Medicine Agency, who forwards the information concerning veterinary use to VetStat.
For veterinarians a similar system exists, built on top of the practice administrative system: data on used or distributed medicines are recorded in relation to the invoice, and transferred together with other information on animal or herd level, through a system facilitated by the agricultural trade organization. Here the data on prescription medicines are aggregated to farm level and forwarded to VetStat.
Feed companies report sales of medicated feed, either directly through the interface of VetStat or by sending relevant information from their billing system by a suitable file format which is subsequently uploaded to VetStat.

Within VetStat, sales of antimicrobials have since 2002 been linked to technical dose values, which provides the opportunity to describe treatment patterns as Animal Daily Doses (ADD) within animal species and age group. Initially, dosages were allocated to each product based on the average approved dose for the main indication to each animal species. However, in 2014, these principles were changed. Nowadays, the ADD is allocated to the product, based on the principles described above, but antimicrobials with identical active compound, route of administration and strength, are given equivalent ADDs. Based on these basic standard doses, an ADD is allocated to the individual product to simplify the understanding for both the veterinarian and the farmer.

Reflections
Risk management relies on accurate, precise and comprehensive surveillance data. Consequently, the methods of collecting data have to ensure high data quality. Furthermore, the data collection must also be adjusted to fit the purpose for which data are to be used, e.g. research or policymaking. Therefore, the main question policymakers have to ask themselves is: 'how detailed data do we need'?

RefA²vi: Towards the formalization of a French professional reference network on the use of antibiotics at poultry farms level.

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[1]ITAVI; [2]CIPC-CIDEF-CICAR; [3]Anses

The French Agency for Food, Environmental and Occupational Health & Safety (Anses-ANMV) has been monitoring sales of antibiotics since 1999. However, this work does not make it possible to distinguish the different species of poultry, nor the different production sectors. Moreover, laboratories can sale some antibiotic specialties off-marketing authorization. Estimates allow estimating the breakdown between major categories of species (pigs, poultry, cattle…). Nevertheless, this allocation method does not always reflect the use at farm level. During the years 2000, Anses, and the French broiler and turkey's inter-professional organizations (CIPC-CIDEF) implemented surveys and monitoring tools. These works make it possible to have precise references on the antimicrobials uses, but they did not have been followed over time, except a monitoring tool for "Label Rouge" production sector, implemented by the French national union of the poultry labels (SYNALAF).

Currently poultry production organizations are committed to defining an indicator monitoring the reasoned use of antibiotics to measure progress made over time. This will also meet the expectations of citizens, retailers and public authorities on this topic. That is why, the French Poultry Institute (ITAVI), with the French poultry's inter-professional organizations (CIPC-CIDEF-CICAR) and Anses wish formalized a professional network to collect computerized data on use of antibiotics at farm level.

The RefA²vi project supported by "Ecoantbio2017" program aims to lead a reflection in this sense since 2013. In 2014 and 2015, two surveys allowed collecting data from poultry farms in all species and production types. This work aimed to discuss then to choose with the professional actors, the more pertinent indicators for all poultry productions. Finally, partners have envisaged a possible scheme of network organization. The computerized data on use of antibiotics recorded by poultry production organizations will be sent to CIPC-CIDEF-CICAR for anonymization and aggregation, in order to send them at ITAVI, which will calculate the exposure indicators following a proven method defined with Anses. ITAVI will ensure the network's animation (newsletter, organization of steering committee meetings).

Conclusion

Since the middle of this year, partners engaged a pilot phase for the RefA²vi network. The aims is to test, with some poultry production organizations, the technical feasibility of the imagined network's scheme (modalities for anonymization and data transfers, estimation of confidence index for indicators calculated with data provided from many sources …). In parallel, partners are establishing a membership charter to the RefA²vi network allowing to describe the roles, engagements of all network's stakeholders.

Antimicrobial usage evolution between 2010, 2013 and 2016 in a group of French pig farms

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Introduction

Monitoring antimicrobial usage in pig farms is a key element of a reduction plan. The objective of this study was to analyse the antimicrobial usage evolution in the same farms between 2010-2013-2016 and to identify the factors of variations.

Material & Methods

The study monitored antimicrobial usage by weight group in 2016 in 33 farrow-to-finish farms in the West of France. The antimicrobial usage had ever been registered twice for 23 of them in 2010 and 2013 and once for 10 of them in 2013. It was quantified by the number of Course Doses per produced pig per year (nCD/pig). Farmers were asked about the factors that could explain the evolution between 2013-2016.

Results

On average, antimicrobial usage significantly decreased over six years (-38%). However, a high variability of individual evolutions was observed: among the 23 farms with three annual data, 43% decreased their use between 2010-2013 (-3 nCD/pig on average) but had a stable use between 2013-2016 (-0,2 nCD/pig). 26% decreased their use between 2010-2013 (-4 nCD/pig on average) and also between 2013-2016 (-2 nCD/pig). 9% increased then decreased their use during the two periods (+4 then -7 nCD/pig). One farm had the opposite trajectory (-9 then +2 nCD/pig) and another always increased its use (+2 then +5 nCD/pig). Among the 33 farms with data in 2013-2016, 36% decreased their use (-2 nCD/pig on average), 39% had a stable use and 24% increased their use (+3 nCD/pig).

For sows, suckling piglets and fattening pigs, most of the farms had stable usage between 2013-2016 (Table 1). Only antimicrobial usage for weaned piglets was more frequently reduced.

Increases were explained by occurrence of sanitary problems (mainly urogenital, digestive and respiratory problems on sows, piglets and fatteners respectively). Decreases were explained by vaccination, stop of preventive treatments and improvement of herd management.

Discussion & Conclusion

This study highlights the variability of individual trajectories in antimicrobial usage, due to sanitary issues that may be different according to each weight group. It usefully complements the monitoring of average evolution at the country level.

Table 1: Repartition of the 33 farms according to their variation of nCD/pig between 2013 and 2016 for each weight group

Weight groups	**Number (and %) of farms concerned**		
	Decrease ≥ - 0,5 nCD / pig	**Stability]-0,5 ; +0,5[**	**Increase ≥ +0,5 nCD / pig**
Sows	8 (24 %)	16 (48 %)	9 (29 %)
Suckling piglets	5 (15 %)	15 (45 %)	13 (39 %)
Weaned piglets	18 (54 %)	7 (21 %)	8 (24 %)
Fattening pigs	4 (12 %)	27 (82 %)	2 (6 %)

Antimicrobial residues in colostrum of cows dried off with antimicrobials

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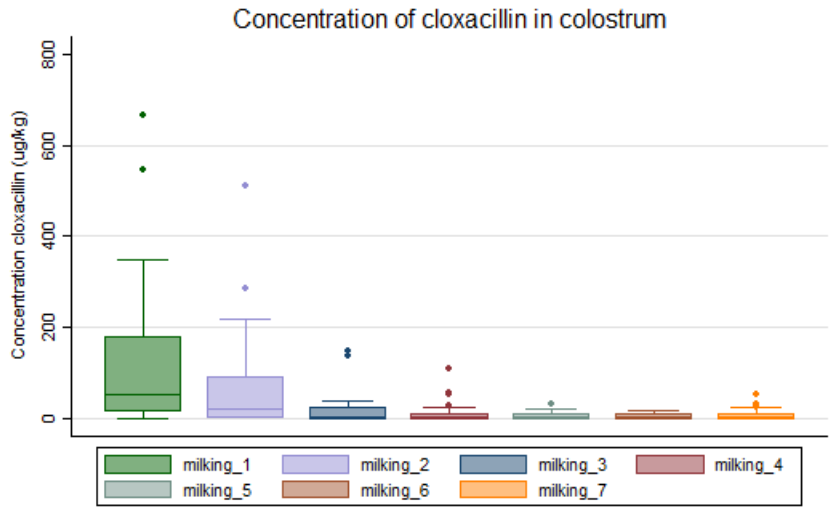
To determine the presence of antimicrobial residues in colostrum from cows who were dried off with dry cow antimicrobials, 129 cows (from 120 Dutch dairy herds) were sampled. All of these cows were dried off with antimicrobials and from each cow information was collected about, among other things, the length of the dry period, the administered dry cow antimicrobials and whether the cows were treated with other antimicrobials during the dry period. Directly after calving, colostrum samples were collected from all four quarters and analyzed as composite samples for the presence of antimicrobial residues, using microbial screening methods and confirmation with Liquid chromatography–mass spectrometry (LC-MS). Not all cows were sampled according to protocol and therefore results of only 118 cows (from 114 herds) were used in the data analysis. In the colostrum of 64% (95% confidence interval: 54-72%) of the cows residues of antimicrobials were found. None of the cows were treated with other antimicrobials during the dry period. The use of dry cow products containing two different antimicrobials (cloxacillin and ampicillin, neomycin and ampicillin or streptomycin and penicillin) was found to be significantly associated, resulting in higher odds of detecting antimicrobial residues in colostrum compared to the use of dry cow products containing only one antimicrobial (cloxacilline). To investigate the reduction of antimicrobial residues in colostrum in the three days after calving, a pilot study was conducted with 28 cows. From each cow ten samples were collected: three composite samples of all quarters directly after calving, a sample of the rest of the first milking and samples of the second to seventh milking after calving. By using the LC-MS method concentrations of residues were determined in samples screened positive. Figure 1 shows the reduction in concentration of cloxacillin residues in colostrum of the first seven milkings of 22 cows treated with cloxacillin at drying off. The total amount of antimicrobials in colostrum of all seven milkings and the total amount of antimicrobials consumed by calves during the first days after birth was low (<7 mg and <2 mg, respectively).

Conclusion
In the colostrum of 64% of cows, who were dried off with dry cow antimicrobials, residues of antimicrobials were detected. In the three days after calving the concentrations of these residues showed a steep decline and both the total amount of antimicrobials in the colostrum and the total amount of antimicrobials consumed by a calf was low.

Figure 1.



A comparison study of the antimicrobial prescription patterns in organic and conventional pig herds in Denmark

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Data from the national database VetStat covering sales of veterinary prescription medicine for all pig herds in Denmark were extracted for the year 2016. The aim was to look for differences and similarities in prescription patterns between organic and conventional pig herds. Information regarding herd type and number of animals at herd-level were extracted in the Danish Central Husbandry Register (CHR). The Danish Veterinary and Food Administration host both the VetStat and CHR database.
In 2016, there were 122 organic pig herds recorded in CHR. This corresponds to nearly 2 % of the total number of herds recorded in CHR. The herd size of the organic herds are in general smaller than the conventional, why the total number of organic pigs only corresponds to 0.8 % of the total number of pigs recorded in CHR. Out of the 122 organic pig farms, only 57 had antimicrobial prescription recorded in VetStat. The total number of antimicrobial prescription for organic herds in 2016 corresponded to 133 kg active compound, which is 0.2 % of the total amount of active compound sold for use in the Danish pig production that year. A larger proportion of the antimicrobials for organic farms is handed over directly from the vet (43% of the total amount of active compound) compared with the conventional farms (0.04 %). These differences can be explained by the Danish legislation saying weaner and finisher pigs in organic farms are only allowed to be treated once in their live span. In addition, the farmer can only get prescriptions for antimicrobials equivalent to treatment of animals in maximum five days. If any medicine is left after treatment it cannot be re-prescribed. Thus, the farmer has the obligation to return the rest of a package to the pharmacies for destruction. There are no official registration of the amount of returned medicine in Vetstat. In Vetstat, it is always whole packages that are registered why there may be a margin of error when reporting antimicrobial use in organic pig farms, where re-prescriptions are not possible.
Overall, the antimicrobial prescription in organic pig farms are much lower than in the conventional pig farms. For weaners the amount of antimicrobials prescribed is almost 14 times lower, when measured in ADD per produced animal per year. For finishers the amounts of antimicrobials prescribed is more than 4 times lower.
Similar to prescriptions for conventional pig farms, gastro-intestinal indications also represent the most often used indication in organic pig farms. Compared with the conventional production, a larger proportion is prescribed for respiratory indications in weaners and for arthropathic indications in finishers.

Antimicrobial treatments during the life cycle of 408 focal pigs

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In a longitudinal study between 2014 and 2016, 408 focal animals originating from 29 different breeding herds were followed through their whole life cycle until the end of their fattening. Of the 29 production systems, 19 were farrow-to-finish herds, another 9 sold the weaners to fattening farms, and one sold the piglets to a weaning farm which sold the weaners to a fattening farm. All antimicrobial treatments of the focal pigs were documented.
Of the 408 focal pigs, 266 from 19 different breeding herds were treated with an antimicrobial agent once (58% of the 266 pigs), twice (35%), three times (2%) or four times (5%) during their life. Of a total of 413 treatments (one treatment = one animal treated with one agent for any duration), 60% (249) were single-agent treatments and 40% (82*2 = 164) were two-agent treatments. Of the 413 treatments, 28% were applied to sucklers, 61% to weaners and 11% during the fattening period. Most treatments were administered via feed (55%), 14% via water, 30% per injection and 2% with a drencher. Gastrointestinal infections and respiratory diseases were the most frequent indications wi th 28% each. Streptococcal infections accounted for 20% of treatments. Other indications included a combination of gastrointestinal and respiratory diseases (6%), 3% meningitis, 2% after castration and 0.5% arthritis. Penicillins were most often applied (30% of treatments), followed by 19% tetracyclines, 19% colistin, 16% macrolides, 16% others (e.g. aminoglycosides, cephalosporines, quinolones). All agents were applied at therapeutical dosages according to age and weight of the pigs.

Table: Antimicrobial treatments (n = 413) to 266 focal pigs representing 29 German production chains

		Number of pigs		
Production stage (age; mean ± SD days)	**Administra-tion route**	**Indication**	**Administered Antimicrobial**	**Treatment duration** [mean ± SD days]
117 Sucklers (5 ± 4)	108 Injection	2 Arthritis	2 Penicillins	1.3 ± 0.5
		8 Castration	8 Penicillins	
		70 Streptococcus	42 Penicillins, 28 Other*	
		28 missing	14 Macrolides, 14 Other*	
	9 Drencher	9 Gastrointestinal	9 Colistin	
250 Weaners (33 ± 13)	194 Feed	71 Gastrointestinal	14 Penicillins, 29 Colistin, 28 Macrolides	7.3 ± 1.8
		14 Meningitis	14 Penicillins	
		71 Respiratory	14 Penicillins, 43 Tetracyclines, 14 Colistin	
		24 Gastrointestinal/ respiratory	24 Other*	
		14 missing	14 Colistin	
	56 Water	28 Dysentery	14 Colistin, 14 Macrolides	
		14 Pneumonia	14 Tetracyclines	
		14 Streptococcus	14 Penicillins	
46 Fatteners (102 ± 36)	31 Feed	10 Ileitis	10 Macrolides	5.6 ± 7.8
		15 Respiratory	15 Tetracyclines	
	15 Injection	14 Pneumonia	14 Macrolides	
		7 missing	6 Tetracycline, 1 Other*	

*Aminoglycosides, cephalosporines, quinolones, pleuromutilins, trimethoprims and sulfonamides

Conclusion
Most of the pigs were treated once in their life with penicillins when they were weaners or sucklers and had gastrointestinal or respiratory disorders. While the sucklers were treated individually by injection or drencher, weaners received the drug groupwise via feed or water and fatteners via feed or injection. However, 35% of the pigs from 10 herds never received antimicrobial treatment in their life.

INDICAVET antimicrobial tracking service

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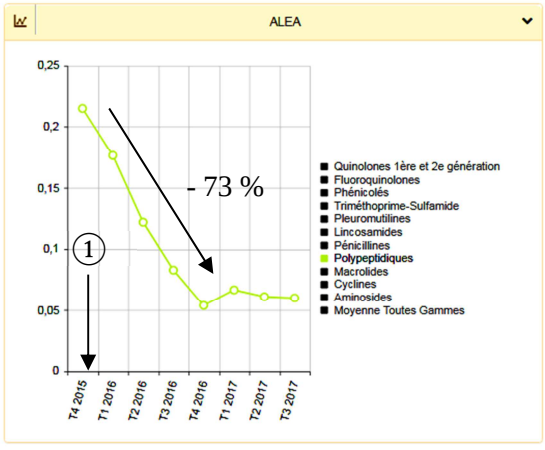
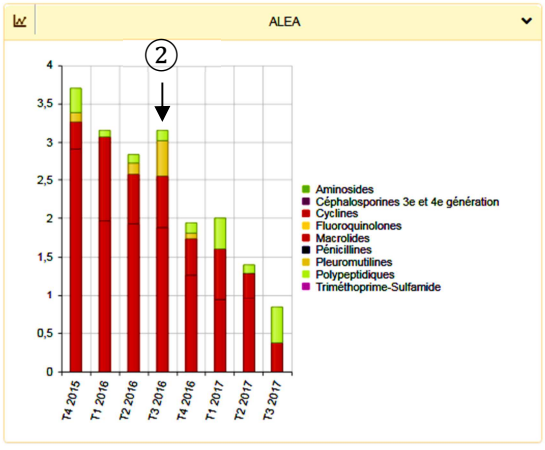
The phenomenon of antibiotic resistance has been a major concern in Human and Veterinary medicine for more than twenty years. There have been a number of initiatives to measure the consumption of veterinary antibiotics within Europe, such as annual monitoring of sales of veterinary antimicrobial products (ANSES), and information on the use of antibiotics derived from panels of farmers regularly published by French technical Institutes and joint trade organisations (CLIPP, INAPORC, IFIP, ITAVI). But these tools are not ideal, as underlined by ESVAC, such as errors that are derived from manual declaration of results from farmers, the absence of a user-friendly tool, harmonisation of the databases of prescribers and farmers and the time needed to process the results before publication of results.
INDICAVET has been developed to answer these challenges.

This software service is an innovative tool that measures the real consumption through the prescriptions of veterinarians, as recommended by ESVAC. It can be used by farmers and veterinarians. The software collects production data (kg of meat produced) on the one hand, and prescription data from veterinarians on the other. Then, antimicrobial consumption is evaluated through French and European official indicators (mg/kg, ALEA, DDDvet, DCDvet). In 2017, with three years of monitoring, more than 700 pig, broiler, laying hen and rabbit farms are included in the database. A demonstration version is available on the website https://indicavet.dbm-vi.eu. INDICAVET permits accurate monitoring, and enables quarterly results to be obtained by animal batch. The software can track the efforts of farmers and veterinarians and changes of use can be rapidly demonstrated as shown by the two following examples.

Example 1: evolution of usage of colistin in 165 pig farms after SPC change (①)



Example 2: evolution of antibiotic use in a rabbit farm after implementing biosecurity measures (②)



Conclusion

INDICAVET (www.indicavet.com) provides an answer to the challenges outlined by ESVAC and provides a management solution to all types of producers and prescribers. The software solution is intuitive and user friendly, allowing farmers and veterinarians to have a working dashboard of their antibiotic consumption, and to make appropriate decisions through a personalized follow-up with target figures and measure the efficiency of conducted actions. This software complements the general surveillance done by public authorities and the inter-professional surveillance initiatives, but also adds detail at individual farm and meat producer organization level.

"Ecology from farm to fork of microbial drug resistance and transmission" Interventions to reduce antibiotic use.

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"Ecology from farm to fork of microbial drug resistance and transmission" (EFFORT, **www.effort-against-amr.eu**) is an EU FP7 project that started on December 2013 and will last five years. The Effort project is based on field studies in 10 European countries that aim to link the antimicrobial usage (AMU), antimicrobial resistance (AMR) in different food-producing animal, the (farm) environment, and food of animal origin as well as companion animals and wildlife to quantify the exposure of humans to AMR through different exposure pathways. One part of the project is dedicated to the study of on-farm (Pig, Poultry) interventions tailored by veterinarians to assess their effect on AMU, animal welfare and performance. In Belgium, these farm specific interventions affect over 1.5 million broiler places. Each farm is analyzed individually; most actions are based on improved diagnostics, improved management, biosecurity and alternative additives.

In the final stage of the project we have identified some strategies that reduce the antibiotic usage in broiler farms in Belgium. Focus is on improving intestinal health with better diagnostics to control coccidiosis and bacterial enteritis, implementing vaccination for coccidiosis and using feed additives. For coccidiosis vaccination, the average days of treatment with antibiotics decreased from 8.8 days before vaccination to 4.5 days in the cycles after vaccination. When we focused on the treatment days for gut-health associated issues, we could see a decrease of 54%. Other interventions that have a positive effect to reduce antibiotic use are training of the farmers, improvement of water quality and use of alternative feed additives.

Keywords: antimicrobial resistance, eco-epidemiology, animal health, animal welfare, food safety

Evaluation of antimicrobial consumption in broiler farms using the EMA dose-based method

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Antimicrobial usage (AMU) in food producing animals may contribute to the development of antimicrobial resistance (AMR) in bacteria, against which the prudent use of veterinary antimicrobials is essential. Various monitoring tools have been proposed to quantify the antimicrobial use. In particular, the ESVAC (European Surveillance of Veterinary Antimicrobial Consumption) project developed by EMA aimed to harmonize the reporting of antimicrobial consumption data among European Member States, by means of the conversion of raw data (kilograms of active principles) to standardised units. The purpose of the present study was to describe and compare the usage of antimicrobial agents during 2015-2016 in a total of 139 production cycles of 15 broiler farms managed by two leading integrated Italian poultry industries (company A and company B). The farms (five belonging to company A and 10 to company B) were randomly selected in North-eastern Italy, from an area characterized by a high-density poultry production. Antimicrobial consumption data per cycle were analysed and converted using the ESVAC dose-based method, being reported as DDDvet/1000 slaughtered broilers and DCDvet/1000 slaughtered broilers. A linear mixed-effects model was applied to test the effect of year, Company, season and mortality on antimicrobial usage. The usage of "highest priority critically important antimicrobials (CIA)" was also considered.

Conclusion
Antimicrobial use in the selected poultry farms showed a significant overall reduction from 2015 to 2016. Company A performed a reduction of 37.3% DDDvet and 36.3% DCDvet, while company B of 33.4% DDDvet and 32.4% DCDvet. Moreover, a significant association between antimicrobial usage and the production company was found ($P<0.05$): AMU in farms from Company B (on average 9402 DDDvet/1000 slaughtered broilers per cycle) was significantly lower if compared to the usage in farms from Company A (on average 21508 DDDvet/1000 slaughtered broilers per cycle). AMU was higher in cycles occurring in winter and spring ($P<0.01$) and it was positively correlated with a higher mortality ($P<0.01$). The study evidenced the application of some highest priority CIA: polymyxins and quinolones for both companies and macrolides for company A. Taken together, these results may indicate a major "company effect" in drug usage, presumably due to different management approaches in prevention and treatment of poultry diseases. However, both companies were able to perform a 30% decrease of antimicrobial usage in the last year, indicating a common effort in response to the public AMR awareness.

Benchmarking antibiotic use on dairy farms in private veterinary practice in the UK and using the data to drive a reduction in antibiotic treatments.

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Various models are available for antibiotic surveillance. Actual antibiotic treatment data is hard to easily obtain over a large number of farms with different recording systems. Assumed treatment data based on veterinary sales to farms is currently used as the model to benchmark antibiotic usage in many veterinary practices. It has limitations but it has the ability to help vets and farmers to work towards reducing antibiotic use. Prior to the emergence of a European agreed model, a group of UK vets (XLVets) developed CCC (calculated cow courses) as a tool to benchmark and drive reductions in antibiotic use on UK dairy farms. CCC is based on UK data sheet dose rates and is very similar to DCDvet. The tool can differentiate adult and youngstock treatments and can benchmark against milk yield, herd size and production system (organic/conventional). In addition it identifies users of the highest priority critically important antibiotics.
Using benchmarked antibiotic data and implementing preventative veterinary advice our veterinary practice has reduced antibiotic use (measured by DCDvet per cow) by 25% and CIA antibiotic use by 70%. Using the mg/pcu metric the mean antibiotic usage in the 200 dairy farms studied is 21mg/pcu. Targeted advice based on an assessment of antibiotic data, can drive change and reduce antibiotic usage.

Conclusion
Veterinary antibiotic sales data can be used as a proxy for antibiotic treatments. Benchmarking antibiotic use can drive positive behavioural change in farmers and help reduce overall antibiotic use.

Antimicrobial use on Austrian dairy farms: a quantitative analysis at farm level by veterinary diagnosis

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As part of the three-year research project, Advancement of Dairying in Austria (ADDA), electronic treatment data on antimicrobial products both administered by veterinarians and dispensed to farmers were collated from the practice software systems of seventeen veterinary practices. A total of 253 farms, covering more than 14,000 bovine animals, were enrolled in the study. The study population was not randomised, but was a convenience sample of farmers contacted by their herd veterinarians. In accordance with Austrian law, veterinarians were required to assign a standardised diagnosis code to each use of antimicrobials. These diagnoses have been used in the present study to analyse antimicrobial use on each farm.

The analysis presented here quantified antimicrobial use in the form of the TD_{100} unit, which represents the number of treatment days per 100 production days and was calculated as follows:

$$\#\mathrm{TD}_{100} = \sum_{i=0}^{n} \frac{amount\ active\ substance\ (mg)}{DDD_{vet}\ (mg/\ kg)/\ d)\ x\ production\ days\ (d)\ x\ standardised\ weight\ (kg)} x100$$

where DDDvet referred to the Defined Daily Dose as defined by the European Medicines Agency and the standardised liveweight was set at 500 kg for a cow, 200 kg for youngstock and 80 kg for calves. NB. As this metric was based on DDDvet, drying off products were excluded, as the EMA has not defined DDDvet values for these products.

Using the diagnosis codes assigned by the treating veterinarian, antimicrobial use was analysed, and the results are shown in Figure 1 below.

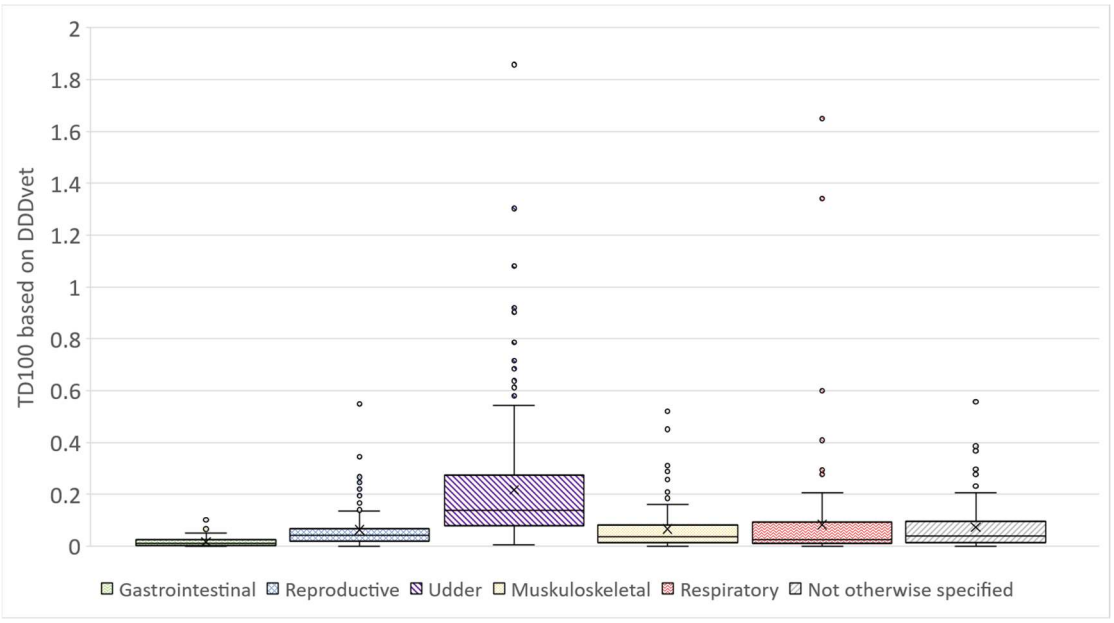

Figure 1: Number of antimicrobial treatment days per 100 production days (TD100) by diagnosis group and individual farm (N=248)

Conclusion

As would be expected for dairy farms, treatment for udder disease made up the majority of antimicrobial use in this study population, followed by treatments for respiratory disease. While AMU overall is relatively low compared to other livestock species, it is particularly important to note the outlying values, which demonstrate that a small number of dairy farms are routinely using a high level of antimicrobials. Future activities will focus on reducing AMU on these farms.

Evaluation of antimicrobial usages in broiler chickens from a veterinary prescription database

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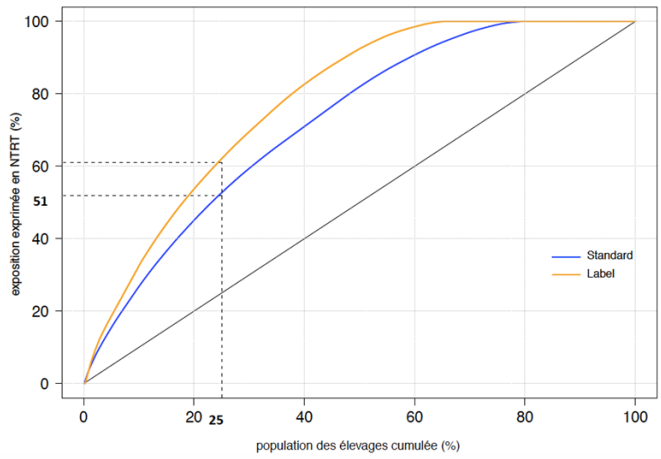
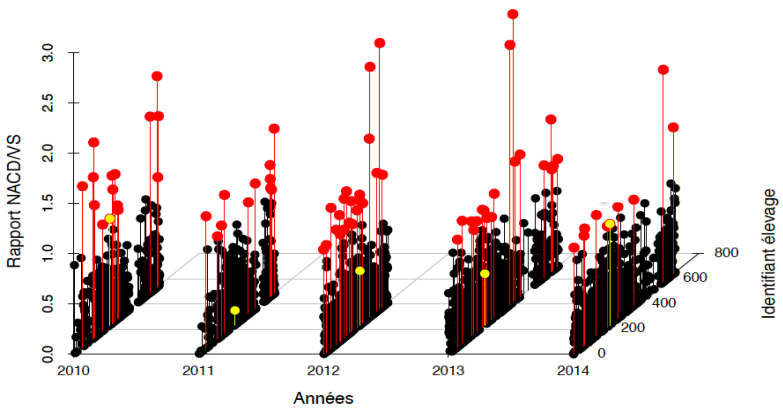
The aim of this study was to evaluate antimicrobials usage in broilers chickens, more specifically in conventional and outdoor quality production. For this purpose, a prescription database obtained from a network of veterinary practices in French region of Pays de La Loire, between 2010 and 2014, was analysed. A pharmaco-epidemiological approach was used to measure, in a qualitative and quantitative manner, antimicrobials usage.

Among the results, it was observed that the antimicrobial classes the most frequently prescribed for broiler chickens production are Beta-lactams and Fluoroquinolones. Average bird weight at treatment is estimated at 0.5 kg. Furthermore, several "at-risk" periods – including early-stage of farming- could be identified. Indicators of animal exposure to antimicrobials were calculated for conventional and outdoor broiler farms and a wide variation of pattern was observed between farms. From these indicators, we also provided an evaluation tool for the antimicrobials use in order to facilitate the monitoring by farmers and veterinarians.



Lorenz curve of antibiotics exposure in broiler chickens (standard and "Label rouge" production). Depending on the production, 25 % of farms are responsible for 50% to 60% of antimicrobials usage.



Classification of farms based on their antimicrobials exposure from 2010 to 2014. This graph can help to identify the high-usage farms.

Surveillance of antimicrobial consumption and resistance in Danish mink

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Only few antimicrobial compounds are registered to mink and today there are no general treatment guidelines. This might lead to suboptimal treatment of the animals and consequently, issues might arise regarding animal welfare, skin quality and the emergence of antimicrobial resistance.
Here we present data on ten years antimicrobial consumption alongside the resistance patterns in pathogenic bacteria in Danish mink.
The consumption of antimicrobials increased from 2007 to 2012, and has since fluctuated at relatively high levels. Further, the monthly drifts in amounts and compounds were analyzed. A characteristic pattern appears, e.g. high aminopenicillin consumption in May, as the kits are being weaned.
Overall, aminopenicillin is the most prescribed antimicrobial compound followed by tetracyclines and macrolides, to which pathogenic bacteria in general showed the highest resistant levels.
Antimicrobial resistance was recorded in many pathogens. *E. coli* showed high levels of resistance to ampicillin. About half of the *Staphylococcus* spp. was resistant to tetracyclines. The *Streptococcus* spp. showed high levels of resistance to tetracyclines and the macrolide, erythromycin.

Conclusion
The consumption of antimicrobials in the Danish mink production has been fluctuating at high levels the past years. Resistance to the most consumed antimicrobials was found in the bacterial pathogens isolated from mink. These findings underline the necessity for treatment guidelines and antimicrobial stewardship for fur animal production, to optimize and ensure future prudent use of antimicrobials.

Assigning defined daily doses for antimicrobials registered for usage in turkeys to enable a cross-country quantification and comparison of antimicrobial consumption in 60 French, German and Spanish turkey farms.

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Due to the rise of antimicrobial resistance (AMR), modern medicine risks falling back into a pre-antibiotic era. The most important catalyst of AMR is antimicrobial usage (AMU). For this reason the World Health Organization calls for a more responsible use of antimicrobials together with appropriate monitoring of AMU across all sectors involved, including veterinary medicine. Therefore we aimed to quantify AMU on conventional turkey farms in France, Germany and Spain, which represent 3 of the largest European turkey industries. Additionally, we aimed to determine turkey-specific Defined Daily Dose (DDDvet) and Defined Course Dose (DCDvet) values, as ESVAC values for broilers might not be applicable for turkeys.

Antimicrobial treatments were registered during 1 production round on 20 turkey farms in each country. DDDvet and DCDvet values were determined for turkeys as described by Postma et al. (2015) and compared with values for broilers, provided by ESVAC. Finally, antimicrobial consumption was quantified, using treatment incidence (TI) per 100 days as unit of measurement. Antimicrobial usage at farm level was obtained by summing up TI_{DDDvet} of all treatments ($TI_{DDDvetF}$).

For some active substances, $DDDvet_{Turkey}$ and $DCDvet_{Turkey}$ values differed considerably with ESVAC-values for broilers. For example, the $DDDvet_{Turkey}$ value for $ampicillin_{oral}$ is 5 times smaller than the $DDDvet_{broiler}$ value.
Over all farms, median $TI_{DDDvetF}$ was 10.0, meaning turkeys were treated with antimicrobials on average during 10.0% of their rearing period. Usage varied considerably between farms. 11.7 % of farms did not use any antimicrobials. $TI_{DDDvetF}$ of the remaining farms ranged from 0.2 to 66.6. Aminopenicillins, polymyxins, and fluoroquinolones were responsible for 73% of total AMU. The main indications for treatment were intestinal disorders (60.0%), followed by respiratory disorders (26.7%). Over 22 weeks of production, 91% of total AMU was administered in the first 11 weeks. On average, 10.0% of the farms was treating in week 1. This peaked on week 5 (18.8%) and 8 (18.6%) and fell under 10% after week 10.

Not all ESVAC DDDvet and DCDvet values for broilers can be applied to turkeys. However, AMU seems to be similar for the turkey and broiler industry concerning the amount and classes used. On the contrary, the timing of peaks in AMU did not match. The differences and similarities in AMU-characteristics between these different species, emphasizes the importance of studying AMU on species and farm level. Only then correct measures for a more responsible use in all food animal productions can be advised.

Reference

Postma, M., Sjölund, M., Collineau, L., Lösken, S., Stärk, K.D.C., Dewulf, J., 2015. Assigning defined daily doses animal: A European multi-country experience for antimicrobial products authorized for usage in pigs. J. Antimicrob. Chemother. 70, 294–302.

A Participatory Market Model Approach to AMU recording on-farm

Sinead Quealy[1], Dr Patrick Lynch[2],
[1]Co-Founder and Managing Director, VirtualVet; [2]Waterford Institute of Technology

Following over three years of research and development, in 2017 VirtualVet launched its multi-channel, proactive data collection service dedicated to the digitisation of on-farm animal treatments, including antibiotic and antimicrobial usage. The VirtualVet model demonstrates the value of consistent relationship building with farmers and vets to capture and digitise in near real-time all on-farm animal treatments. Our methodology is based on the concept of value creation from our collected data and has led us to explore, with Dr Patrick Lynch of Waterford Institute of Technology, the market model for animal health data[1].

The findings of our work to date are interesting. Our outline of the participatory approach is valid with the structure and actors identified taking shape according to the framework laid out. VirtualVet acts as a data farm aggregator (DFA) while in certain cases farmers and vets have co-created a data farm community (DFC). The DFC has a few benefits for its members; there is a reduction in duplication of animal health data records, both farmers and vets openly discuss and acknowledge the importance of recording the use of antibiotics to the animal ID and actively contribute and share outcome information with the DFA for use within the DFC, and farmers feel they are contributing evidence on which policy can be based in the fight against AMR.

In the wider data market, we see clear interest in antibiotic and antimicrobial usage information from food processors, retailers but most particularly from investors in the food industry. The participatory market model we present and are working to implement has shown encouraging signals. As we on-board more farmers and engage with the broader animal health and agri-food value chains, we see a universal awareness of issues surrounding antibiotic usage in food producing animals. At present in the food sector, much of the discussion is focused on how verification of usage could translate to market differentiated products – “whole of life free”, “free of human critical antibiotics” etc. In animal health and pharmaceutical sector, we see concern over policy changes and awareness of opportunities in vaccination programmes.

As identified in the participatory model, creating a revenue model is proving challenging as the complexity of transactions and the overlap in roles of buyers and sellers of data emerges.

Conclusion

VirtualVet can demonstrate the willingness of the value chain to engage in the near real-time surveillance of antibiotic usage on-farm. The participatory market model is gaining traction. Policy exists to promote near real-time on-farm surveillance. Farmers and vets will be both protected and liberated under the GDPR rollout from this May. The time is fast approaching when those working to understand and control AMU will be able to leverage the forces of a data driven market in animal health information in the pursuit of their societally crucial goals.

[1] https://www.frontiersin.org/articles/10.3389/fvets.2017.00145/full

The use of Electronic treatment and health registers and a joint database for the SuisSano/Safetyplus Program in Switzerland

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Introduction

In order to improve transparency concerning antibiotic consumption in Swiss pig production and to concurrently measure antibiotic use and health parameters the SuisSano/Safetyplus program was started in 2015. The most important evolution step in 2018 is a joint database connected with electronic treatment and health registers, which are obligatory for all participating farms. It is expected that more than 90% of all pig farms in Switzerland will participate at the program.

Material and method

Mandatory electronic data input are all antibiotic treatments including date of treatment, number of treated animals, age group (piglet, sow, weaning pig, finishing pig), average weight, indication, product and quantity. Health data include percentage of losses in each age group. For each participating farm, the number of produced animals per age group per year is stored in the database.
Antibiotic consumption is reported to the farmer by calculating an animal treatment index. Treatments with certain products, e.g. containing Highest Priority Critically Important Antibiotics, are multiplied by an additional factor.
For more profound analysis and international comparison, several calculation methods are carried out for internal use (e.g. therapeutic intensity, number of DCD_{VET}/animal/year).

Results

Using the electronic treatment register, antibiotic consumption of each participating farm can be demonstrated in relation to the overall program. Multiplication of treatments with certain products gives impulses to reduce such use. Based on additional analysis of joint data concerning antibiotic use and health, the management of the program is able to steer antibiotic consumption by adjusting benchmarks for treatment indices and multiplication factors for certain products.

Discussion and Conclusion

The electronic treatment register and the joint database are most useful tools in order to provide transparency and enable steering and reduction of antibiotic consumption in pig production within the SuisSano/Safetyplus program in Switzerland. Monitoring health data is essential to preserve animal welfare.

Analysis of antimicrobial use on British dairy farms; providing the tools for reduction

Hyde R, Remnant JG, Bradley AJ, Breen JE, Hudson CD, Davies PL, Clarke T, Critchell Y, Hylands M, Linton E, Wood E, Green MJ

Remarkably strong interactions between antimicrobial usage (AMU) and antimicrobial resistance (AMR) in livestock have been described (Chantziaras et al., 2014), and recently commissioned government reports have called for a reduction in antimicrobial use within the UK livestock industry (O'Neill, 2015). Newly published work (Hyde et al., 2017) has provided antimicrobial usage data for UK dairy farms, enabling an initial benchmark of British dairy AMU, as well as highlighting important factors associated with high usage.

AMU data were collected from a convenience sample of four veterinary practices across England, and a separate group of farms recording medicines usage electronically on farm, with the final dataset comprising of 81,640 cattle (around 5% of British dairy cows). AMU was calculated using ESVAC standard methodology, using both mass based (mg/PCU) and dose based (DDDvet, DCDvet) approaches. Median farm AMU was 16.0 mg/PCU, 4.0 DDDvet and 1.7 DCDvet respectively. The majority of farms exhibited relatively low AMU but a small portion of farms had extremely high levels of AMU, with the top 25% of farms using more than 50% of the total AMU. Multivariable statistical models revealed that the use of footbath and oral antibiotics resulted in significantly increased the odds of a farm being a "high user" (top 25% by mg/PCU). The cessation of antibiotic footbaths provides a great potential for rapid AMU reduction.

By benchmarking British dairy farms, it is possible to target "high" AMU farms and the authors have created freely available tools for UK veterinarians to calculate and automatically benchmark AMU on dairy farms within a veterinary practice. This will allow the preferential targeting of "high use" farms. By providing practitioners with the literature to identify key target areas, and the software tools to calculate and benchmark dairy cattle AMU, it is hoped that a rapid and significant reduction in AMU will occur on British dairy farms.

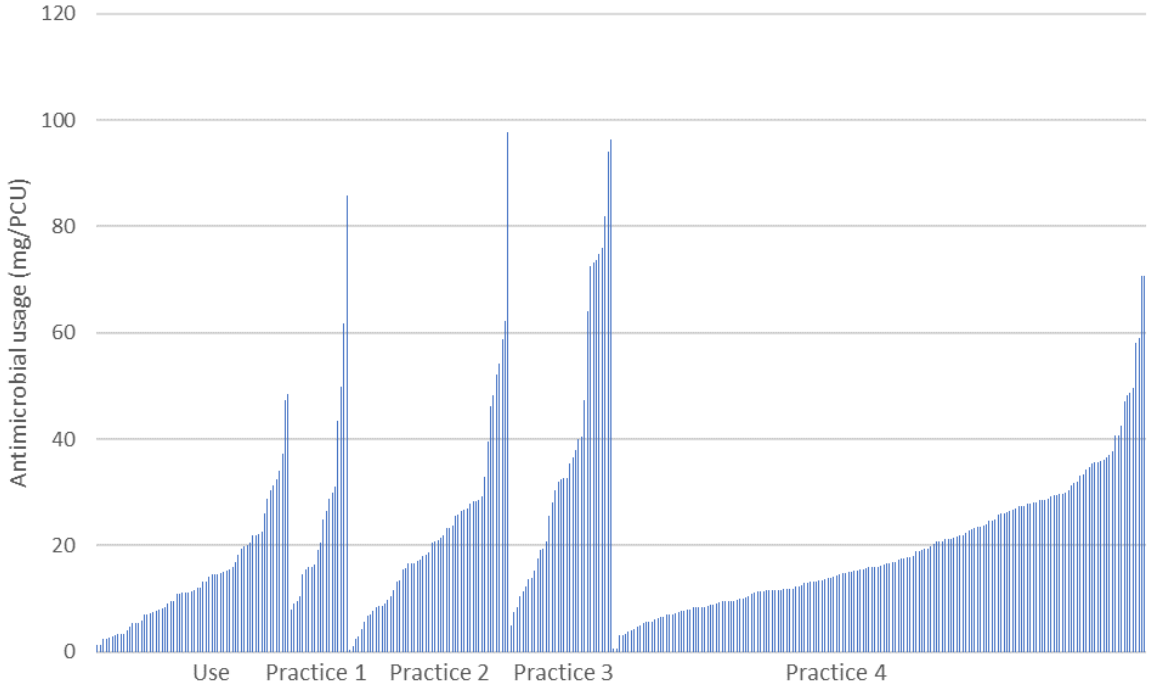

Figure 1: Antimicrobial usage (mg/PCU) from sales data to farms (n= 292) from four veterinary practices, and for usage data from farms (n=66) recording medicines usage electronically on farm.

The 3Rs of antimicrobial stewardship

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Antimicrobial resistance (AMR) is a challenge of global significance to human health, resulting in increasing mortality and growing pressures on health care systems across the world. Antimicrobial use in humans is considered to be the main driver of AMR, but the contribution of medicine use in food-producing animals is now widely acknowledged.

In response to increasing pressure from the media and consumer groups, some food companies have adopted 'antibiotic free' or 'raised without antibiotics' policies in their livestock supply chains. However, without systemic change in the agricultural system aimed at decreasing the underlying need for frequent or routine antibiotic therapy and prophylaxis, this approach risks compromising animal welfare, becomes wasteful and unsustainable, and ignores the fact that the transmission of resistant bacteria is not necessarily restricted by farm, retail supply chain, or geographical borders.

To achieve meaningful change in the way antimicrobials are used in agriculture and thereby reduce the risk of emergence of antimicrobial resistant pathogens in livestock, we propose that food companies address the antibiotics challenge in partnership, as a pre-competitive issue, and adopt the '3Rs' framework. This framework promotes practical and evidence-based solutions to **'**Replace, Reduce and Refine' the use of antimicrobials, and is sufficiently flexible to allow tailored stewardship programmes to be developed for individual species, production systems and farms across the world.

We propose three goals of antimicrobial stewardship in animal agriculture at farm, national or international level, embodied in the 3Rs:

Goal 1: REDUCE the annual usage of antimicrobial agents in animal agriculture, per unit of livestock produced (mg/PCU), whilst preserving animal health and welfare. Usage data should be monitored in terms of livestock species and antimicrobial classes, with a particular focus on the medicines considered highest priority critically important to human health.

Goal 2: REPLACE the use of antimicrobial agents in animal agriculture where possible, with sustainable solutions to prevent diseases such as vaccination and improved husbandry practices, to protect animal health and welfare.

Goal 3: REFINE the use of antimicrobial agents in animal agriculture, by ensuring the responsible and informed selection and administration of products to animals that have a clinical indication for treatment.

Conclusion

Multi-disciplinary, collaborative action is urgently required to preserve the efficacy of our vital portfolio of antimicrobial agents and address this One Health challenge of global importance. We propose that food companies unify behind a 3Rs approach to'replace, reduce and refine' the use of antimicrobials in livestock supply chains, and we present a number of examples of this framework being used in the UK agriculture industry.

AMCRA, the platform for the antibiotic policy in veterinary medicine in Belgium

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In Belgium, veterinary antimicrobial stewardship is characterized by initiatives taken by the sectors and the national competent authorities. In order to involve the different national stakeholders having a role in the use of antibiotics (AMU) in veterinary medicine, the Centre of Expertise on AntiMicrobial Consumption and Resistance in Animals (AMCRA), was created in 2012 as a platform aiming at safeguarding human and animal health and animal welfare by a substantial reduction of AMR in veterinary medicine. Since the foundation of AMCRA, editing and communicating advices and guidelines in a neutral and objective manner have been the focus of attention. This has resulted in a myriad of communication and sensitization tools. For instance, the AMCRA formularia are an online instrument providing an overview of preventive measures and, if AMU is necessary, recommendations of 1st, 2nd and 3rd choice antibiotic therapy for the most occurring bacterial diseases in food-producing and companion animals.

In 2014, AMCRA established its Vision 2020, with three main antibiotic reduction targets (50% less antibiotics by 2020, 75% less of the critically important antibiotics (CIAs) by 2020 and 50% less of feed medicated with antibiotics by the end of 2017) and seven action points to achieve these targets. In 2016, this plan was ratified by the Belgian Federal Ministries of Health and Agriculture and almost all relevant sector partners within the 'Covenant between the federal government and the sector partners concerning the reduction of the AMU in veterinary medicine', determining the commitments of the sector partners to ascertain that reduction targets will be achieved. The national competent authorities supported the targets with the publication in July 2016 of a Royal Decree regulating a restricted use of the CIAs and the establishment of a national data collection system on AMU, legally obliged for pigs, veal calves, broilers and laying hens since February 2017. In 2016 the achieved reduction in AMU was of -20% in total use, -56.1% in CIA use and -38.2% in use of feed medicated with antibiotics (taking 2011 as a reference year).
Veterinary antibiotic policy in Belgium has evolved from auto-regulation, with almost exclusively sector initiatives, to a co-regulation process where the government has taken additional actions to achieve a substantial reduction by 2020.

Analysing, benchmarking and reporting antimicrobial use for food-producing animals at the individual herd level in Belgium

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AMCRA is the Centre of Expertise on AntiMicrobial Consumption and Resistance in Animals in Belgium, assigned to establish and communicate advices and guidelines on a reduced and rational antimicrobial use (AMU) to all involved sectors in veterinary medicine. Besides the communication and sensitization tasks, since 2014 AMCRA is responsible for the analyses of AMU data collected within AB-Register, an online platform established by Belpork, the owner of the Belgian pig meat quality label Certus. Thereto, the 'scientific unit' of AMCRA has developed the methodology for the benchmarking of individual pig farms, based on the herd-level indicator BD_{100} (=treatment days per 100 days). The BD_{100} is an indicator representing the exposure of animals to antimicrobials and is used in the benchmarking of herds. To calculate the (kg) animals at risk of treatment, standard weights of the pig subcategories, proposed by EMA are used.
Thanks to the acquired expertise and experience in analysing and quantifying AMU in animals, since 2016 AMCRA is responsible for analysing the data collected within the national data collection system (DCS) (Sanitel-Med). In Belgium, the registration of AMU became compulsory in veal calves, broilers, laying hens and pigs with the Royal Decree of February, 27 2017. The dairy and beef sectors can use Sanitel-Med on a voluntary base.
Data registered in the private DCS flows into the national DCS, avoiding double input by herd veterinarians, which are responsible for the registration of what they prescribe, deliver at the herds or dispense to the animals. In addition to antimicrobials, zinc oxide usage, authorised for prevention of diarrhoea in weaners, needs to be registered in both private and national DCSs.
For pig farms using the AB Register platform, herd-level results are currently communicated to farmers twice/year through an individual report, with the results of all animal categories present at the herd. The benchmark population is composed by all herds providing AMU information within AB Register, harbouring the respective animal categories. The AMU as such is benchmarked, by comparing and categorising herds' results in three zones corresponding to two threshold values [median (P50) and 90th percentile (P90)] of the benchmarked population. In addition, also the type of antimicrobials used is benchmarked, referring to the AMCRA guidelines and the classification of the antimicrobials based on their priority in human and animal medicine. In the near future, benchmarking will be extended to the poultry and veal calf sector and to the veterinarians.

EMA, European Medicines Agency. 2013. Revised ESVAC reflection paper on collecting data on consumption of antimicrobial agents per animal species, on technical units of measurement and indicators for reporting consumption of antimicrobial agents in animals.
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/12/WC500136456.pdf

Quantitative trend analysis of AMR monitoring in commensal *E. coli* from Dutch livestock

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Since 1998, continuous monitoring of antimicrobial resistance (AMR) is performed in commensal *E. coli* from Dutch livestock. Objectives are: 1) monitoring trends in AMR in livestock, including effects of antimicrobial use (AMU) and 2) detecting emerging resistances in animals that may threat public health. This study aims to evaluate monitoring in commensal *E. coli*, by quantitative analyses of phenotypic data from Dutch livestock 1998-2016, testing whether effects of AMU interventions since 2009 could be detected.

Yearly, approximately 300 faecal samples per sector (broilers, pigs and calves) were collected randomly in slaughterhouses by the Dutch Food and Consumer Product Safety Authority (NVWA). Dairy cows were sampled by faecal floor samples from farms. From each sample, *E. coli* was isolated on MacConkey agar and one randomly selected colony was identified (MALDI-TOF). Susceptibility was tested for fixed panels of antimicrobials with broth micro-dilution. Susceptibility data (MICs) of >15.000 *E. coli* isolates were analysed to determine AMR-trends and aberrations in trends. Resistant proportions for antibiotic/species combinations were modelled in R using a log-linear model. The AIC and scaled deviance were used to assess the fit of the model.

Aberrations in AMR in livestock were identified from the data and quantified. Decrease per year in resistant proportions since 2009 was quantified for antibiotic/species combinations. Significant trends of increasing resistant proportions mostly preceded significant declines. Onset of trend changes in resistance levels varied for species/antibiotic combinations. A striking reduction of AMR was shown in broilers, especially for resistance to 3rd generation cephalosporins, caused by ESBLs.

Conclusion

This model was able to quantify trends in phenotypic AMR-monitoring. Significant decrease of AMR in *E. coli* from Dutch livestock was observed for all antibiotic classes since 2009, corresponding to both specific and general interventions leading to AMU reduction (64%) from 2009-2016. These findings demonstrate potential of AMR-monitoring programs to identify trends, related to interventions. As a result of this analytical evaluation, recommendations can be made for phenotypic AMR-data analysis: 1) using adjusted standard deviations for specific samples sizes in models - with time as a continuous variable - enables detecting trend changes over time, even with variable sample sizes and 2) using a Poisson or binomial distribution enables detailed interpretation of aberrations in proportions close to 0. However, relevance of aberrations in lower proportions should be weighted by the fit of the model for each outcome.

Key findings from a literature review on available indicators for quantification of antimicrobial usage in human and animals

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An increasing variety of indicators of antimicrobial usage has become available in human and veterinary medicine, with no consensus on the most appropriate indicators to be used. We conducted a literature review to provide guidance on the selection of indicators, intended for those aiming to quantify antimicrobial usage based on sales, deliveries or reimbursement data.

Antimicrobial usage is generally described as the number of technical units consumed normalised by the population at risk of being treated in a defined period. The technical units vary from number of packages to number of individuals treated daily by adding different levels of complexity such as daily dose or weight at treatment. These technical units are then related to a description of the population at risk, based either on biomass or number of individuals. Conventions and assumptions are needed for all of these calculation steps. However, there is a clear lack of standardisation, resulting in poor transparency and comparability.

Depending on the study objective, different requirements apply to antimicrobial usage quantification in terms of resolution, comprehensiveness, stability over time, ability to assess exposure and comparability. If the aim is to monitor antimicrobial usage trends, it is crucial to use a robust quantification system that allows stability over time in terms of required data and provided output; to compare usage between different species or countries, comparability must be ensured between the different populations. If data are used for benchmarking, the system comprehensiveness is particularly crucial, while data collected to study the association between usage and resistance should express the exposure level and duration as a measurement of the exerted selection pressure.

Major gaps hamper the identification of the most suitable indicator for a given study objective. One of them is the lack of a scientific basis to assess antimicrobial selection pressure. Future research should help to fill in these gaps and support a science-based selection of indicators of antimicrobial usage.

Monitoring antimicrobial usage with a business intelligence approach: the Classyfarm system for Italian pig farms

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Veterinary antimicrobials are extensively used in Italy and monitoring antimicrobial usage (AMU) in pig farms represents a priority for Italian Veterinary Services. Nonetheless, processing AMU data at farm level could be difficult not only due to issues on quality of data sources but also due to a potentially high data density. Indeed, information on usage of a single veterinary medicinal product (VMP) may encompasses data on: route of administration, active ingredients (AIs) present, species and/or age group exposed, farm characteristics, target of treatment, etc. Processing and depicting all this information require relevant resources and proper tools.
The Classyfarm system, formerly BioFaBenMa, started in 2014 analysing data on AMU in pig farms. Additionally, information on biosecurity and animal welfare is also collected. All collected data are processed using a business intelligence tool (iDashboards). Currently, a full digitalisation of antimicrobial prescriptions is not available in Italy; hence, monitoring AMU is feasible only on a limited number of farms. Data are collected on a convenience sample of 100-150 pig farms per year.
AMU is measured using a dose-based metric; namely, Defined Daily Dose Animal for Italy (DDDAit). DDDAit were established using, as primary data source, Italian summaries of product characteristics (SPCs). Scientific papers were also encompassed as additional sources of information. A specific DDDAit was assigned to each AI of every VMP which contains one or more antimicrobials.
AMU is collected separately per age groups (sows/boars, sucking piglets, weaners, finishers) and processed accordingly. Finally, AMU is expressed as days per animal per year which represents the potential days of exposure to antimicrobials of each age group present in a farm.
All the calculations are automatically performed by iDashboards and results are displayed via interactive dashboards. AMU, at farm-level, is showed per each reared age group and various stratifications of data are available, such as AIs, administration routes, and targets of treatment. Moreover, AMU can be aggregated at different geographical levels using a specific dashboard.

Conclusion
Business intelligence tools can provide a useful instrument for data analysis of AMU and cross-referencing information from different aspects of animal husbandry (e.g. population data, animal welfare, biosecurity status). Furthermore, a business intelligence approach can offer analyses on data from different sources, flexibility on calculations, and a widely customisable interface to illustrate results. Finally, the Classyfarm system could be a useful example of how AMU data can be processed and depicted even in larger dataset.

DANMAP - the scientific foundation for action on AMU and AMR in Denmark

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[2]National Veterinary Institute, Technical University of Denmark;
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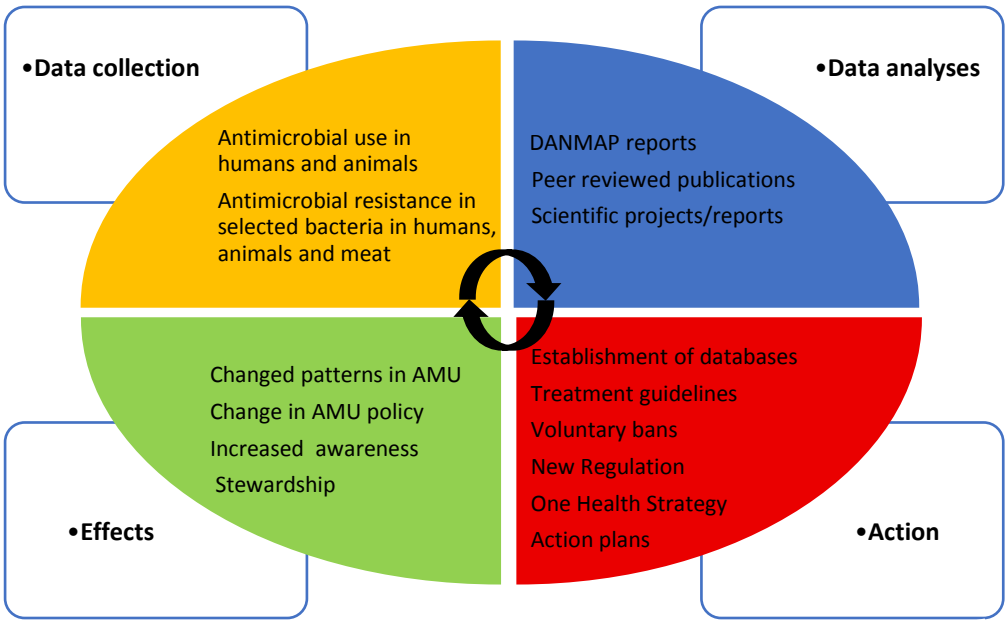
[4]Statens Serum Institut, Denmark.

Background. For more than two decades, the Danish Integrated Antimicrobial Resistance Monitoring and Research programme (DANMAP) has documented the use of antimicrobial agents in humans and animals alongside the occurrence of antimicrobial resistance in selected bacteria in humans, animals and meat. The information is used for research, risk assessment and risk management, and forms the knowledge foundation for continuous optimisation of data collection and analyses, treatment guidelines, and interventions for antimicrobial usage.

Results. DANMAP has developed since its beginning and some major scientific achievements are: Establishment of new or improved databases for registering antimicrobial use and occurrence of antimicrobial resistance (VetStat, MedStat, MiBa) and development of methods for quantifying antimicrobial use in humans and different animal species to enable interspecies comparisons.
DANMAP has also provided the scientific foundation for treatment guidelines for humans and several animal species and supports official regulations i.e. the "Yellow Card initiative" to regulate antimicrobial usage in pigs and cattle at herd level. Most recently, an official "One Health Strategy against AMR" was published as a joint collaboration between public and veterinary health based on the evidence from DANMAP. Furthermore, two national action plans were implemented setting benchmarks for the antimicrobial use in humans and for antimicrobial use in animals and antimicrobial resistance in animals and food.

Conclusion. The DANMAP programme has monitored trends in antimicrobial use and resistance in humans, animals and meat for over two decades, and thereby provided the "data for action" in the area of antimicrobial usage and resistance in Denmark. The One Health approach, with a close multidisciplinary collaboration across sectors, involving human and veterinary medicine, the public health and veterinary authorities and the food industry is paramount.

Figure 1. Overview of the inputs to and outcomes of DANMAP, actions taken and effects hereof.



Comparison of national defined standard values DDD_{ch}/DCD_{ch} and the european standard values DDD_{vet}/DCD_{vet}

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Introduction:
Based on the proposal by the ESVAC project (EMA), we developed Defined Daily Doses (DDD_{ch}) and Defined Course Doses (DCD_{ch}) for Switzerland as technical units to collect data on antimicrobial consumption. DDD_{ch} and DCD_{ch} were compared to the DDD_{vet} and DCD_{vet} recently published by the EMA.

Material & Methods:
DDD_{ch} and DCD_{ch} were defined for all drugs containing antimicrobial ingredients and approved for pigs in Switzerland. DDD_{ch} were defined by using the highest authorized daily dosage according to the national Summaries of Product Characteristics (SPC). DCD_{ch} were calculated by multiplying the corresponding DDD_{ch} unit with the maximum treatment duration as presented by the SPCs.
DDD_{ch}/ DDD_{vet} as well as DCD_{ch}/ DCD_{vet} were compared by calculating the ratios of corresponding values for each product. The influence of dosage form or number of active components in a single product on these ratios was analyzed.

Results:
92 approved products containing antibiotics were included in the study and 118 ratios were calculated. Although the mean ratio was 1.05 for the DDD_{ch}/ DDD_{vet} ratios and 0.93 for the DCD_{ch}/ DCD_{vet} ratios, 35 corresponding values for the DDD_{ch}/ DDD_{vet} ratios and 44 values for the DCD_{ch}/ DCD_{vet} ratios showed a deviation of more than 20%.
Injectables showed a significant higher DDD_{ch}/ DDD_{vet} ratio (1.16) than premixes (0.81) ($p=0.02$). Daily dosages in Switzerland are lower than EMA values when ingredients are combined in one product whereas higher dosages were found for single ingredient products in Switzerland ($p<0.01$). None of these effects could be observed concerning DCD_{ch}/ DCD_{vet}.

Conclusion:
The newly defined values DDD_{ch} and DCD_{ch} partly show considerable differences to the published DDD_{vet} and DCD_{vet}. The great benefit of DDD_{vet} and DCD_{vet} for international comparison is undisputed, but we propose the use of nationally defined units for more accurate national monitoring of antimicrobial usage.

Calculation of antimicrobial treatment frequencies and their impact on sales volumes of antimicrobial active substances in Germany

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According to national law, the surveillance of sales volumes of antimicrobial active substances for veterinary use (SVs) and the calculation of antimicrobial treatment frequencies (ATFs) were established in Germany in 2011 and 2014, respectively. For the biannual determination of individual ATFs, farms of certain categories and sizes have to report the numbers of treated animals and of treatments days for every antimicrobial product administered. For each farm and for all antimicrobial active substances contained, the data is added together and set in proportion to the average number of animals kept. With respect to the different categories, nationwide median and third quartile values of ATFs are calculated. Farms with an individual ATF exceeding the median have to evaluate their antimicrobial usage in cooperation with a veterinarian. Those exceeding the third quartile are additionally obliged to submit a written action plan for assessment by the competent authority.

From 2011 to 2016, a reduction in SVs of 964 t (56.5 %) was determined. This is in line with the decreasing values of medians and third quartiles of ATFs since 2014. The greatest reduction in SVs (433 t, 35.0 %) occurred from 2014 to 2015. This correlates with the first execution of measures resulting from median and third quartile ATF exceedance

Conclusion
The established system based on ATFs provides an effective tool to monitor antimicrobial consumption. Additionally, it facilitates the reduction of antimicrobial usage by promoting the professional exchange between veterinarians and farmers. This results in an appropriate evaluation of antimicrobial usage on a herd level and subsequently in taking adequate measures. To what extent the ATFs are useful for benchmarking and if further performance indicators should be added remains to be discussed. Therefore, the evaluation of the ATF system, which is also implemented into national law, is due five years after its establishment.

At national level, the establishment of the ATF system demonstrated an impact on SVs leading to a further and more pronounced reduction. SVs provide the amounts of antimicrobial substances sold but unfortunately do not allow for statements concerning their actual usage. As a result of the implementation of both surveillance systems in Germany, sales volumes could be reduced and, referring to the ESVAC report 2015, meanwhile stabilized in the midfield compared to other European countries.

The use of an antimicrobial practice sales report to benchmark farm purchases and as an active tool in herd health management

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Objectives:
Concerns regarding the development of antimicrobial resistance has increased the awareness of the requirement for increased AntiMicrobial Stewardship (AMS) based on sound principles of the appropriate medicine at the appropriate time. The aim was to develop a tool for reporting and benchmarking of antimicrobial use to be used to identify trends in prescribing patterns on farms, between farms and at a national level. AMS can then be applied on individual units and at a business level to ensure the medicines at our disposal are being used responsibly.

Materials and Methods:
It is well reported that medicine use recording is variable in on-farm records, with under reporting frequently identified with some using non-electronic methods. This makes reporting using farm records both technically difficult and unreliable. As such, practice sales data and prescription records can be used as a proxy for antimicrobial use. A tool was developed by Origin Animal Health using data automatically uploaded from the Client Management Software (CMS), manual entry of medicine prescription records and basic farm information. This data is then accessible at two levels: an individual farm report, or macro-analysis.

The individual farm report visually displays total antimicrobial sales over the past 12 months in three different metrics as defined by the European Surveillance of Veterinary Consumption Group (ESVAC); This is then represented against the previous 12 months' sales for the farm, as well as the mean over all farms for these metrics and, where relevant, UK sector-specific targets. The antimicrobial use is then further broken down to provide management data for the farmer and veterinary advisor including an indicator of the uptake of selcetive dry cow therapy.
There is also a distribution chart of all farms' data for use as a benchmarking tool.

Collation of this data allows macro-level analysis including trends in sales of different antimicrobial classes. This allows comparisons between different farming systems and categorisations. This may include but is not limited to milking frequency, production level, and somatic cell count level.

The reports stimulate discussions around the AMS on farm – benchmarking total usage; indicating the socio-political aspects surrounding the use of HP-CIAs; discussing disease reduction and appropriate therapeutics considering non-antibiotic approaches; discussing the implications of selective dry cow therapy.

Conclusions:
A bespoke reporting tool using farm records allows the integration of AMS reports into active herd health planning as well as macro-reporting to monitor ongoing trends together with reporting to external stakeholders.