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REDUCING ANTIMICROBIAL CONSUMPTION IN RABBIT FARMING IS FEASABLE: THE STATE OF PLAY IN ITALY

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ABSTRACT

Rabbit industrial breading is the food production system with the highest consumption of antimicrobials (AMU). A cross-over study on AMU in industrial rabbit breeding was performed in 2018-2019 in 17 out of 32 herds previously investigated in 2010-2015. Raw data on AMU were standardized according to rabbit production (kg rabbit biomass sold for slaughter) and animal daily dose per kg body weight (ADD). Herd-level antimicrobial resistance (AMR) against eight antimicrobials was assessed in commensal *Escherichia coli* isolated from fresh faeces (five isolates per herd).The herd level AMR indicator was the mean antimicrobial resistance index (ARI) towards: aminosidine, cefotaxime, colistin, enrofloxacin, chloramphenicol, tetracycline, sulfadiazine. MICs were interpreted according to EUCAST epidemiologic cut offs. Over the study period there was no reduction of production of rabbits at slaughter age. Results showed a statistically significant ($P < 0.001$) decrease from 77.6, in 2010, to 27.0, in 2019, of the overall ADD consumption (-65%). The average consumption of antimicrobials was statistically significantly ($P < 0.001$) declining over the time period, involving all antimicrobial classes: aminoglycosides, bacitracines, betalactams, macrolides, pleuromutilines, polymyxins, quinolones, sulfonamides and tetracyclines. Compared to all herds surveyed in 2010-2015, there was a strong and statistically significant ($P < 0.001$) correlation between low AMU and being among the group of 17 herds still in business and investigated in 2018. There was a slight reduction of the mean *E. coli* herd ARI in the 2018-2019 study, with a change of the frequency distribution towards lower ARI values. This study provides evidence that AMU can be reduced in industrial meat rabbit breading without apparent impact on the overall production. A lowering of AMR at herd level seems occurring after 10 years AMU reduction.

Key words: antimicrobial consumption, antimicrobial resistance, meat rabbit production.

INTRODUCTION

Rabbit breading is the food production system with the highest consumption of antimicrobials (AMU). Attemps to reduce AMU have been reported in Italy with a longitudinal study following 32 rabbit meat industrial holdings from 2010 to 2015. This study showed a decrease of the overall consumption of antimicrobial animal daily doses (ADD) per kg of biomass (live rabbits sent to slaughter), yet the reduction was mainly attributable to limited colistin usage, as the study highlighted a significant shift to fluoroquinolones consumption (Agnoletti *et al*., 2018). In 2019 the WHO AGISAR (WHO, 2019) classified fluoroquinolones, as well as colistin, among the antimicrobials with highest priority to preserve (HP-CIA) among the group of critically import antimicrobials for human therapy. The possibility of switching to usage of quinolones as a shortcut to colistin consume restrictions introduced in Italy in 2016 to comply with EMA risk assessment (EMA, 2016) requires strict surveillance. Adminstration of antimicrobials in industrial herding of meat rabbit occurs mostly by oral route for group treatment. Since the 2010-2015 above reported study several initiatives to increase awarness on antimicrobial resistance (AMR) in rabbit breeding took place. Further important regulations entered into force (2019/6/EU, 2019/4/EU) to ban the preventive use of antimicrobials in

animal groups and to require laboratory evidence for methaphylaxis and therapeutic usage in flocks. This is a follow-up study aimed to verify whether the regulation framework and stakeholder awareness acted on the AMU of meat rabbit holdings that partecipated the first study and agreed to provide data on AMU and samples for evaluating herd level indicators of AMR.

MATERIALS AND METHODS

Study design and data collection

A cross-over study on the AMU in industrial rabbit breeding was performed pairing in 2018-2019 17 herds surveyed in 2010-2015 (Agnoletti *et al.*, 2018). Shortly: a subset of 17 out of 32 herds available for data and sample collection were followed up in 2018 (two semesters) and 2019 (first semester). Data on AMU were collected from the veterinary prescriptions, feed delivery documents and farm drug register. Data on the total weight of live rabbit sold to slaughter were collected from the commercial files and the pre-slaughter veterinary certifications. AMR was assessed at herd level using commensal *E. coli* isolated from fresh faeces. Five isolates were selected to represent the AMR indicators at herd level. Farmers adhesion was voluntary after information on the study aim.

Collection of indicator *E. coli* and antimicrobial susceptibility testing

Sampling of feaces, *E. coli* isolation, identification and antimicrobial susceptibility testing were performed as previously described (Agnoletti *et al*., 2018).

Statistical Analysis

At the time of analysing the first study data, there was no agreed definition for the defined daily dose (DDDvet) for antimicrobials used for meat rabbits, therefore the ADD (animal daily dose per kg body weight) for meat rabbits was set as the active ingredient amount (in mg) required to treat 1 kg of rabbit body weight per day as provided by the pharmaceutical company and in accordance with EMA principle. Given that a DDDvet for antimicrobials authorised for meat rabbit is still lacking, the same ADDs were used for the 2018-2019 study. Data were collected with Excel spread sheets, then managed and analysed in R (R Core Team, 2019). Logistic or linear regression models were used. The significance level of 95% was used for hypothesis testing. Antimicrobial resistance index (ARI) was calculated as previously described (Agnoletti *et al.*, 2018). Normality was tested with Shapiro-Wilk before using paired samples t-test to compare the means of herd level indicators of AMR (ARI).

RESULTS AND DISCUSSION

During the 2015–2019 period the sample of 17 rabbit herds consumed between 0.32 and 157ADD to produce one kg of rabbit biomass (slaughter age), the median value was 52.3. Over the period there was 65% decrease of overall ADD consumption. AMU reduction was statistically significant ($P < 0.001$) (Figure 1). No differences in production (kg rabbit biomass at slaughter) with the same overall number of does were observed among the 17 rabbit herds. A stable production from 2010 to 2019 may be attributed to many factors, such as better overall breeding conditions: biosecurity, welfare, type of cages, disease prevention plans, genetic improvement. These data were not collected for this study, yet it is of relevance these herds were able to keep their production targets despite significant reduction of AMU.

There is a strong and statistically significant ($P <0.001$) correlation between a low AMU and being among the group of 17 herds investigated in the second study. Herds with higher frequency of semesters with high AMU were more likely to be closed after 2015. High frequency semesters with high AMU may be a proxy to incapability to manage bacterial disease or to the use of AM as surrogate of poor breading practices, low food quality, insufficient biosecurity measures, poor animal health plans and poor welfare. As much as in our knowledge, among the 15 holdings not participating the 2018-2019 study eight were closed after 2015, while the others did not provide their availability to collect data. This means that the 17 herds followed up in 2018-2019 may represent the best herds, and thus bias estimates, however this study did not intend to estimate current AMU situation in the meat

rabbit system in north-east Italy yet it was a cross-over study to detect whether differences in AMU occurred over the period. In the previous 2010-2015 study involving 32 herds we observed AMU decreasing, mostly colistin, yet an increased fluoroquinolones use was evident and statistically significant over the period. In the sample of 17 holdings followed up in this study the average consumption of all AM classes was statistically significantly ($P < 0.001$) declining over the time period 2010-2019 for all antimicrobial classes (Figure 2).

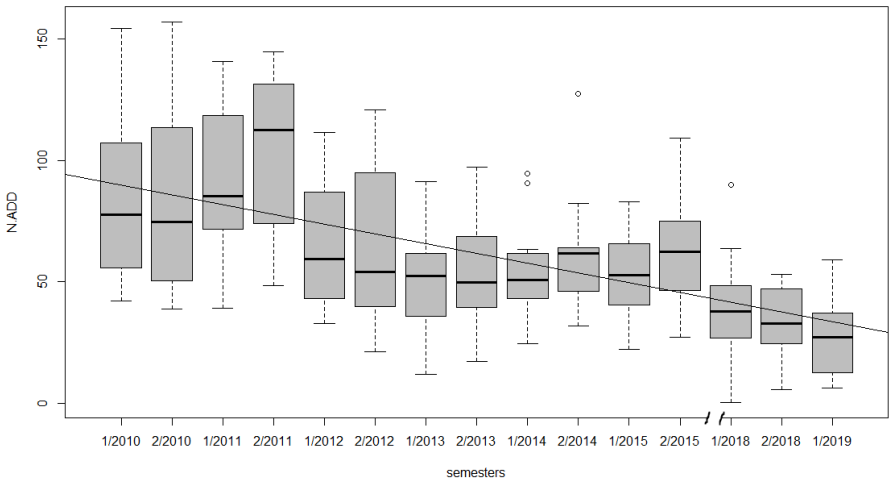

Figure 1: Seventeen rabbit meat industrial holdings were followed up in 2018-2019, after a 2010-2015 previous longitudinal study. Boxplots describe the variability of the amount of ADD used to produce 1 kg of biomass (live rabbit) at slaughter age, per semester, per holding. The line describes the simple linear regression model ($P < 0.001$) of the number of ADD (all antimicrobials) over 15 semesters.

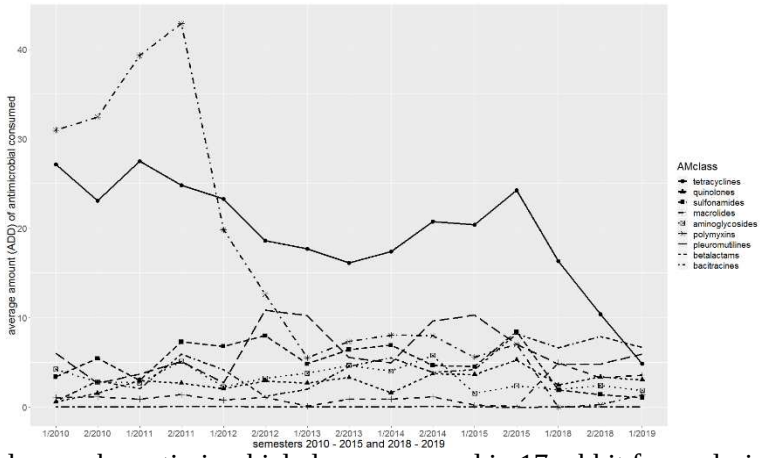

Figure 2: Antimicrobial usage by antimicrobial class consumed in 17 rabbit farms during 2010-2019.

At the time of writing this manuscript data on AMR in *E. coli* indicators at herd level were available for 15 herds. The mean herd *E. coli* ARI of 15 holdings tested in 2014-2015 is described in Figure 3. There was a slight reduction of the mean *E. coli* ARI in the second study, there was also a change of the frequency distribution towards the lower ARI values, yet this change was not statistically significant.

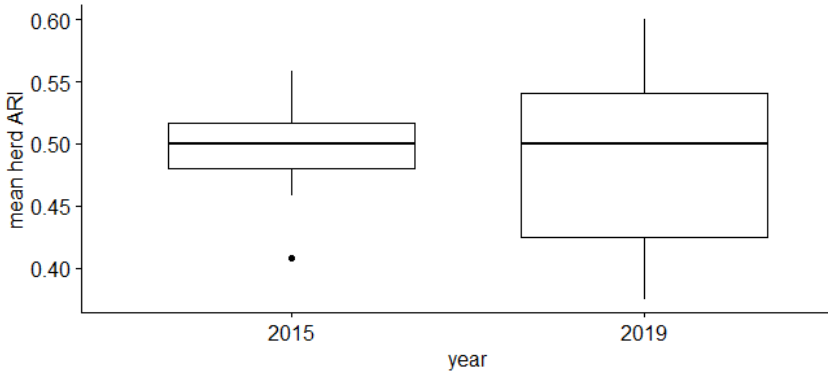

Figure 3: Boxplots show the frequency distribution of the average heard *E. coli* ARI recorded for the first study in 2014-2015 (left boxplot) and the second study in 2018-2019 (right boxplot). The difference of mean ARI of 15 paired herds is not statistically significant**.**

CONCLUSIONS

The availability of rabbit holdings for a follow-up study in 2018-2019 is strongly associated with low usage of antimicrobials. Herds with higher frequency of semesters with high AMU were more likely not be involved in this study: one out of two (8/15) of them that did not participate have gone out of business after 2015. High frequency semesters with high AMU seems a proxy of incapability to manage bacterial diseases and/or of low farm management quality. The group of 17 followed up rabbit holdings decreased AMU and did not switch their consumption to critically important antimicrobials, including those of highest priority such as fluoroquinolones. Despite differences are not statistically significant, the herd level indicator ARI for *E. coli* records a slight change of the frequency distribution towards lower values, thus encouraging keep going with prudent use of antimicrobials in this animal breeding sector.

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REFERENCES

Agnoletti F., Brunetta R., Bano L., Drigo I., Mazzolini E. (2018). Longitudinal study on antimicrobial consumption and resistance in rabbit farming. *Int J Antimicrob Agents 51 (2018)*, 197-205.

Clinical and Laboratory Standards Institute (CLSI). Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; approved standard. 4th ed.Wayne, PA: CLSI; 2013. Document VET01-A4.European Medicine Agency (EMA, 2016). Overview of comments received on 'Updated advice o the use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health' (EMA/CVMP/CHMP/231573/2016)

European Committee on Antimicrobial Susceptibility Testing (EUCAST). MIC distributions and ECOFFs. EUCAST. Available from: http://www.eucast.org. [Accessed December 2019].

R Core Team (2019). R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria. URL https://www.R-project.org/.

Regulation (EU) 2019/6 of the European Parliament and of the Council of 11 December 2018 on veterinary medicinal products and repealing *Directive 2001/82/EC* *https://eur-lex.europa.eu/eli/reg/2019/6/oj*

Regulation (EU) 2019/4 of the European Parliament and of the Council of 11 December 2018 on the manufacture, placing on the market and use of medicated feed, amending Regulation (EC) No 183/2005 of the European Parliament and of the Council and repealing Council Directive 90/167/EEC https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=uriserv:OJ.L_.2019.004.01.0001.01.ENG&toc=OJ:L:2019:004:FULLWHO. (2019) Critically important antimicrobials for human medicine, 6th revision https://www.who.int/foodsafety/publications/antimicrobials-sixth/en/