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Trends and correlates of antimicrobial use in broiler and turkey farms: a poultry company registry-based study in Italy

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Background: Antimicrobial usage (AMU) in livestock plays a key role in the emergence and spread of antimicrobial resistance. Analysis of AMU data in livestock is therefore relevant for both animal and public health.

Objectives: To assess AMU in 470 broiler and 252 turkey farms of one of Italy's largest poultry companies, accounting for around 30% of national poultry production, to identify trends and risk factors for AMU.

Methods: Antimicrobial treatments administered to 5827 broiler and 1264 turkey grow-out cycles in 2015–17 were expressed as DDDs for animals per population correction unit (DDD_{vet}/PCU). A retrospective analysis was conducted to examine the effect of geographical area, season and prescribing veterinarian on AMU. Management and structural interventions implemented by the company were also assessed.

Results: AMU showed a 71% reduction in broilers (from 14 to 4 DDD_{vet}/PCU) and a 56% reduction in turkeys (from 41 to 18 DDD_{vet}/PCU) during the study period. Quinolones, macrolides and polymyxins decreased from 33% to 6% of total AMU in broilers, and from 56% to 32% in turkeys. Broiler cycles during spring and winter showed significantly higher AMU, as well as those in densely populated poultry areas. Different antimicrobial prescribing behaviour was identified among veterinarians.

Conclusions: This study evidenced a decreasing trend in AMU and identified several correlates of AMU in broilers and turkeys. These factors will inform the design of interventions to further reduce AMU and therefore counteract antimicrobial resistance in these poultry sectors.

Introduction

Antimicrobial usage (AMU) in food-producing animals contributes to selection of resistant bacteria, which may cause antimicrobial therapy failure in animals, as well as lower productivity and increased veterinary costs.[1] Moreover, resistant bacteria can be transferred to humans, contributing to increased mortality/morbidity and healthcare costs.[2] Serious concerns have been raised regarding the use of Critically Important Antimicrobials (CIAs) and Highest Priority CIAs.[3] In recent years, poultry has showed alarming antimicrobial resistance levels in indicator bacteria such as *Escherichia coli*,[4] which may be partly explained by widespread antimicrobial mass medication.[5]

Antimicrobial sales data for livestock showed that AMU in Italy was considerably higher than in other EU countries, ranking third in 2016 with an average of 294.8 mg of antimicrobials per population correction unit (PCU).[6] Yet, an AMU reduction was observed during 2010–16 (30% mg/PCU drop), albeit without differentiating amongst drug spectra. Italy is one of the main poultry producers in Europe, with more than 1 million tonnes of broiler meat and almost 310000 tonnes of turkey meat produced in 2017.[7] As AMU levels and associated risk factors in these sectors are unknown, we performed a 3 year retrospective analysis of AMU and its correlates in broiler and turkey farms in Italy using both mass- and dose-based AMU quantification methods.

Materials and methods

Study design and population

Data were retrieved for the years 2015–17 from a digital registry of purchased antimicrobials of one of Italy's main poultry companies.

Antimicrobials purchased were always administered in full. Production accounted for ~25% and 33% of Italy's total broiler and turkey production, respectively.[7] The Italian poultry industry is vertically integrated; thus, the company controls all production stages. Data collected for each production cycle included: body weight (kg) produced, prescribing veterinarian and amount of active substances administered. Overall, 5827 broiler and 1264 turkey grow-out cycles were investigated from 470 and 252 farms, respectively. Cycles lasted 110 and 140 days, on average, for female and male turkeys, and 35–50 and 46–54 days for female and male broilers, respectively. The number of broilers and turkeys slaughtered yearly was also retrieved.

AMU was assessed by applying the European surveillance of veterinary antimicrobial consumption (ESVAC) guidelines.[8] Indicators were mg/PCU and DDD for animals (DDD_{vet})/PCU. DDD_{vet} is the average dose per kg of animal per species per day. PCU was calculated as the number of slaughtered animals multiplied by the standard weight at treatment (1 and 6.5 kg for broilers and turkeys, respectively). Farm-level AMU was assessed for each production cycle using the Italian standardized doses (DDD_{ita}) to generate the dose-based indicator (N DDD_{ita}/kg) using Agnoletti's method.[9] DDD_{ita} defines the amount of each active substance required to treat 1 kg of body weight per day following EMA principles.[10] DDD_{ita} was defined for each active substance following the summary of product characteristics (SPC). When a dosage range was provided, the maximal dosage was used. This guaranteed a higher level of precision as compared with DDD_{vet}, as it was specific for Italian medicines.

Geographical location (longitude/latitude) of each farm was extracted from the National Data Registry[11] (Figure S1 and S2, available as Supplementary data at *JAC* Online) and elevation above sea level (a.s.l.) was obtained from the layer 'European Digital Elevation Model' v.1.1. The processed raster file (25 m resolution) was imported in QGIS v.2.18 and digital terrain mapping (DTM) cell values related to farm location were extracted using the point sampling tool plugin. Each farm was classified according to elevation (plain: <300 m; or hill/mountain: ≥300 m a.s.l.) and region (Northern, Central or Southern Italy) (Figure S3). Densely populated poultry areas are more susceptible to infectious diseases[12] and consequently to AMU. A Thiessen polygon map layer was generated in ArcGIS v.10.5.1 from the location of each farm to represent estimated population density distribution. Poultry density classes were defined as low–medium (minimum–median), high (median–third quartile) or very high (third quartile–maximum). Astronomical seasons and sex of reared animals were also considered.

The company described the actions[13] taken to reduce AMU as: (i) relocation of parent farms to low-density areas to reduce *Mycoplasma* prevalence (2010); (ii) training farmers regarding health management and animal welfare; and (iii) improvements in ventilation and biosecurity in fattening farms (2013). In 2014, tetracyclines were banned in broilers and used in turkeys only for *Mycoplasma*. Since 2015, AMU data have been certified by Certificazione Qualità Agroalimentare (CSQA), a third-party institution, and interventions on drinking water quality have been undertaken. Moreover, turkey eggs have been disinfected in the hatchery with nebulized peroxides. Since 2016, infrastructural and managerial interventions have also been implemented at the hatcheries (e.g. strict egg quality checks, ban of formalin, all-in/all-out incubators). In 2017, colistin was banned in broilers and fluoroquinolones have been used only in exceptional cases. Renewal of broiler farms started in 2013, reached 65% completeness in 2015 and was finished in 2017. Renewal of turkey farms started in 2013 and reached 40% in 2017.

Statistical analysis

Potential risk factors for AMU were assessed using linear mixed models, stratified by species. Tested predictors included: year, geographical area, elevation, poultry density class and season; for turkeys, sex was also included. The farms and production cycles therein were considered as random and repeated effects, respectively. Given the skewness of DDD_{ita}/kg data for broilers, the square root transformation was applied. The effect of the veterinarian on AMU was separately assessed using linear mixed models stratified by geographical area. Analyses were performed using SAS v.9.4.

Results

AMU showed a decreasing trend during 2015–17 in both broilers and turkeys. For broilers, this ranged from 204 mg/PCU (2015) to 88 mg/PCU (2017), and from 14 to 4 DDD_{vet}/PCU; for turkeys, from 490 to 265 mg/PCU, and from 41 to 18 DDD_{vet}/PCU. The different antimicrobial classes are given in Table 1. In broilers, Highest Priority CIA use decreased from 20% of the total mass of administered antimicrobials in 2015 to 8% in 2017 and from 33% to 6% as

Table 1. DDD_{vet}/PCU administered in 2015–17 in 5827 broiler and 1264 turkey grow-out cycles from 470 and 252 Italian farms, respectively

	Broilers			Meat turkeys		
	2015	2016	2017	2015	2016	2017
Highest priority CIAs[a]	4.62	1.12	0.24	22.93	11.76	5.80
quinolones	0.38	0.32	0.17	2.41	1.20	1.13
macrolides and ketolides	0.19	0.07	0.06	0.99	0.60	0.35
polymyxins	4.04	0.73	0.00	19.52	9.96	4.32
High priority CIAs	7.47	3.48	2.64	12.27	6.69	4.84
aminoglycosides	0.00	0.00	0.00	0.10	0.03	0.01
penicillins (natural, aminopenicillins and antipseudomonal)	7.47	3.48	2.64	12.17	6.66	4.83
Highly important antimicrobials	2.00	1.21	1.15	6.00	7.31	7.40
amphenicols	0.14	0.06	0.45	0.02	0.00	0.01
lincosamides	0.001	0	0	0	0	0
sulphonamides, dihydrofolate reductase inhibitors and combinations	1.86	1.15	0.70	3.49	5.86	5.29
tetracyclines	0	0	0	2.49	1.45	2.10
Important antimicrobials	0.001	0.0001	0	0	0.0001	0
aminocyclitols	0.001	0.0001	0	0	0.0001	0
Total DDD_{vet}/PCU	14.10	5.81	4.03	41.19	25.76	18.05

[a]All antimicrobials have been grouped and classified according to WHO.[3]

Table 2. Associations between mean DDD_{ita}/kg ± SEM and different variables in 2015–17 in 5827 broiler and 1264 turkey grow-out cycles from 470 and 252 Italian farms, respectively, using linear mixed models

	Broilers			Meat turkeys		
	n	Mean DDD_{ita}/kg ± SEM	*P*	*n*	Mean DDD_{ita}/kg ± SEM	*P*
Year						
2015	1890	5.49 ± 0.13	<0.001	446	17.66 ± 0.43	<0.001
2016	1968	2.45 ± 0.08		423	12.56 ± 0.32	
2017	1969	1.34 ± 0.05		395	9.64 ± 0.32	
Geographical area						
Northern Italy[a]	2819	2.12 ± 0.08	<0.001	728	14.62 ± 0.30	0.019
Central Italy[b]	1502	3.51 ± 0.11		536	11.86 ± 0.35	
Southern Italy[c]	1506	4.37 ± 0.12		0	—	
Elevation						
plain (<300 m a.s.l)	3926	2.63 ± 0.07	0.040	1043	13.96 ± 0.26	0.037
hill/mountain	1901	3.96 ± 0.11		221	11.04 ± 0.47	
Poultry density[d]						
low/medium	920	2.54 ± 0.12	<0.001	424	11.23 ± 0.35	<0.001
high	1823	3.09 ± 0.10		604	14.16 ± 0.32	
very high	3084	3.20 ± 0.08		236	15.61 ± 0.61	
Astronomical season						
autumn	1473	2.12 ± 0.09	<0.001	NA	NA	NA
winter	1351	3.54 ± 0.14				
spring	1481	3.83 ± 0.13				
summer	1522	2.80 ± 0.10				
Gender						
female	NA	NA	NA	431	12.56 ± 0.41	0.063
male/mixed sex				833	13.91 ± 0.27	

NA, not applicable.
[a]Regions: Lombardia, Friuli Venezia Giulia, Trentino Alto Adige, Veneto, Piemonte (broilers only).
[b]Regions: Emilia Romagna, Lazio, Marche, Umbria, Toscana (turkeys only).
[c]Regions: Campania, Molise, Puglia, Abruzzo (broilers only; for turkeys the few farms in Abruzzo were grouped with Central Italy).
[d]Classes were calculated according to the quartiles of the distribution.

doses, while in turkeys, Highest Priority CIAs decreased from 38% of the total mass of administered antimicrobials in 2015 to 22% in 2017, and from 56% to 32% as doses.

DDD_{ita}/kg statistics for broilers and turkeys are reported in Table 2. For broilers, geographical location, season and elevation were significantly associated with AMU, with higher AMU in Southern Italy, in winter/spring and in hilly/mountainous areas. Moreover, the more densely the area was populated with poultry, the more antimicrobials were consumed. No differences were observed in AMU among veterinarians according to geographical area, with a decreasing trend over years (Table S1). In turkeys, increased AMU was found in Northern Italy and plain areas (Table 2). Similar to broilers, AMU was associated with increased poultry density, whereas no significant association was found with sex. Different prescribing behaviour was identified amongst veterinarians in Central Italy; all veterinarians showed reduced antimicrobial prescribing during the 3 year period (Table S1).

Discussion

This study provided an overview of AMU in Italy's poultry sector and identified significant effects of time and location. Results also showed the positive outcomes of an AMU-reduction plan, with improvements at both infrastructural and managerial levels in a vertically integrated poultry company. Similar results concerning improvements in biosecurity, management and farm microclimate have been reported for pigs.[14]

Turkeys required 4-fold higher AMU than broilers, which is explainable by turkeys' higher predisposition to disease[15] and a longer production cycle in the same environment, where litter/microclimate quality may worsen. A tendency towards higher AMU in male/mixed sex turkeys was observed, which is a possible reflection of the longer commercial lifespan and different physiology in male turkeys, as they exhibit lower resilience to environmental stressors.[16,17] However, lack of statistical significance might be due to antimicrobials being mostly administered during the first period of the production cycle.

Seasonal and geographical variables played a major role. Yet, seasonal effects on AMU were not assessable in turkeys, as their production cycles last almost 5 months. In broilers, the highest AMU was observed in spring. Although broilers are raised in sheds with climate control systems, increased AMU during spring might be due to marked temperature shifts between day and night and, consequently, to lack of early intervention to adjust microclimatic parameters to avoid heat/cold stress. Moreover, spring cycles have chicks housed in winter (i.e. the most sensitive phase during the least favourable period). Hilly/mountainous areas in Italy are expected to present more favourable conditions for poultry farming due to lower poultry density, better air circulation and generally colder climate. However, high AMU in broilers was found in these areas. This might be due to these areas being mostly in Central/Southern Italy, characterized by a delayed level of farm renewal. Conversely, when stratifying by geographical area, most veterinarians showed similar antimicrobial prescribing behaviours, suggesting a primary influence of climate. Veterinarians play a central role in antimicrobial stewardship,[18] and training farmers about responsible AMU may have contributed to raising awareness. AMU data is useful to benchmark poultry holdings to improve farmers' perception of AMU and penalize those requiring higher AMU, similar to the 'yellow card policy' in Denmark.[19]

In conclusion, this study showed a significant AMU reduction in recent years in a substantial part of Italy's poultry sector and identified several correlates of AMU entailing significant effects of season, location and production type.

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Transparency declarations

None to declare.

Supplementary data

Figures S1–S3 and Table S1 are available as Supplementary data at *JAC* Online.

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