

# Survey of quantitative antimicrobial consumption per production stage in farrow-to-finish pig farms in Spain

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## ABSTRACT

**Objectives:** To characterise antimicrobial use (AMU) per production stage in terms of drugs, routes of application, indications, duration and exposed animals in farrow-to-finish pig farms in Spain.

**Design:** Survey using a questionnaire on AMU during the six months prior to the interview, administered in face-to-face interviews completed from April to October 2010.

**Participants:** 108 potentially eligible farms covering all the country were selected using a multistage sampling methodology; of these, 33 were excluded because they did not fulfil the participation criteria and 49 were surveyed.

**Results:** The rank of the most used antimicrobials per farm and production stage and administration route started with polymyxins (colistin) by feed during the growing and the preweaning phases, followed by  $\beta$ -lactams by feed during the growing and the preweaning phases and by injection during the preweaning phase.

**Conclusions:** The study demonstrates that the growing stage (from weaning to the start of finishing) has the highest AMU according to different quantitative indicators (number of records, number of antimicrobials used, percentage of farms reporting use, relative number of exposed animals per farm and duration of exposure); feed is the administration route that produces the highest antimicrobial exposure based on the higher number of exposed animals and the longer duration of treatment; and there are large differences in AMU among individual pig farms.

in animals (eg, Jensen and others 2004, Grave and others 2006). According to Bondt and others (2013), from a theoretical point of view, the best way to quantify the exposure to AMs in a population is to closely monitor the applied treatments of individual animals, or at least of individual farms, and relate this to the total population at risk.

At the European level, the ESVAC project (European Medicines Agency 2012) is the most valuable attempt to produce harmonised AMU data in animals, but the project has two main constraints on the data collected: the figures come from sales and not from consumption of AMs and they are not disaggregated by animal species. However, the next step in the ESVAC project is to develop harmonised systems to collect data per species and to develop harmonised units of measurement. Other criticisms have also been presented (Bondt and others 2013). Nowadays, there is a broad consensus that AMU data per animal species are needed for proper understanding and analysis of AM exposure in animals (eg, Callens and others 2012, Moreno 2012, Bondt and others 2013). In the words of Callens and others (2012), in this context the collection of more detailed and accurate animal species level data implies the collection of data directly at the end-user level.

Intensive pig farming is one of the livestock activities having putative higher AMU. Nevertheless, the lifespan of commercial fattening pigs is about six to seven months and covers different production stages (from birth until weaning; postweaning and growing phase; and finishing period) having diverse needs of AMs (Jensen and others 2011). These dissimilar stages need additional effort to properly characterise AMU in the pig production.

In Spain, fattening pig production can take place in different farm types. Among these, 14 per cent were farrow-to-finish farms (performing breeding, preweaning, growing

## INTRODUCTION

One of the main forces for the selection of antimicrobial (AM)-resistant bacteria in people and animals is their exposure to AMs (eg, Smith and others 2002). The purposes of monitoring usage of AMs in animals are manifold and have been reviewed elsewhere (eg, Jensen and others 2004, Grave and others 2006, Chauvin and others 2008).

Since the beginning of the twenty-first century, increased effort has been made to accurately measure antimicrobial use (AMU)



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and finishing at the same site) in the year of the study (2010) and were chosen to take part in a survey with the following objective: to characterise AMU per production stage in terms of drugs, routes of application, indications, duration and exposed animals. A comparative analysis of some of the data belonging to the finishing stage has been previously published (Moreno 2012).

## MATERIAL AND METHODS

### Questionnaire design, sampling and eligibility criteria

Detailed information about the questionnaire, the sampling and the eligibility criteria has been previously published (Moreno 2012). Briefly, a 14-page questionnaire consisting mainly of open questions was used in face-to-face interviews completed from April to October 2010. Questions were referred to AMU during the six months prior to the interview. Records of AM treatments included administration route (in-feed, in-water and per injection), growing phase (preweaning, growing and finishing), name of commercial product (including pre-mixes in feed medications), manufacturer, dose, length of treatment, indication (therapeutic, prophylactic and both (metaphylactic)), intended disease (respiratory, digestive and others) and number of treated animals during the last six month (Moreno 2012).

The sampling frame was obtained from the official Spanish data records (currently Ministerio de Agricultura, Alimentación y Medio Ambiente) updated at January 2010. A multistage sampling methodology was applied with peninsular, autonomic communities as the primary sampling units and farms as the secondary sampling units. The size of the sampling frame was 15 Autonomic Communities and 2,968 FtF farms (January 2010). Therefore, inclusion criteria were peninsular farrow-to-finish farms officially registered. Sample size calculations (WinEpiscope 2.0) were based in the worst-case scenario (eg, 50% expected relative frequency of farms reporting AMU of any specific antimicrobial), with 95% confidence level, an expected error of 10% and an infinite population). These assumptions led to a sample size calculation of 97 farms. An expected participation percentage of 90% was then used, to obtain a final sample size of 108 farms.

## RESULTS

### Study participation

As reported previously (Moreno 2012), of the 108 potentially eligible farms, 33 (30.6 per cent) were excluded because they did not fulfil the participation criteria (a farrow-to-finish farm in full operation during at least six months before the interview), resulting in 75 eligible farms, of which 49 (65 per cent) were surveyed.

### Main descriptive questionnaire-based data of surveyed farms

The mean number of sows (n=49) was 389 (IQR, 131–523); the mean number of finishers (n=49) was 1783

(IQR, 490–1982); the mean length in days of the production cycle (n=47) was 191 (IQR, 170–195), distributed as preweaning (mean=26; IQR=24–28), growing (mean=49; IQR=32–52) and finishing (mean=118; IQR=104–124); 92 per cent of the farms produced standard white pigs, 6 per cent produced Iberian pigs and 2 per cent both types of pigs.

### Descriptive analysis of records of AMU

We collected 564 records reporting use of AMs and/or zinc oxide and identified the use of 26 different AMs belonging to 10 classes (AMCs):  $\beta$ -lactams (amoxicillin, ampicillin, penicillin, ceftiofur and cefquinome), polymyxins (colistin), tetracyclines (doxycycline, tetracycline, chlortetracycline and oxytetracycline), fluoroquinolones (enrofloxacin, marbofloxacin and danofloxacin), lincosamides (lincomycin), aminoglycosides/aminocyclitols (streptomycin, gentamicin, neomycin, apramycin, framycetin and spectinomycin), macrolides (tylosin, tilmicosin, tulathromycin, erythromycin and spiramycin), pleuromutilins (tiamulin), potentiated sulphonamides (sulphonamides and trimethoprim), and phenicols (florphenicol).

Per production stage, the highest number of records came from the growing phase (263, 47 per cent), followed by the finishing (190, 34 per cent) and the preweaning phases (111, 20 per cent). The highest figures per administration route arose from injection (274, 49 per cent), followed by feed (175, 31 per cent) and water medications (115, 20 per cent). Water medications were not reported during the preweaning stage.

Combinations of two or more AMs (excluding zinc oxide) were very frequent among feed medications (62 per cent), and scarce among water (9 per cent) and injection medications (20 per cent). These data also showed an elevated number of feed medicated records containing zinc oxide that were mainly used in the preweaning (63 per cent) and growing phases (65 per cent).

Of the 564 records, 515 (91.3 per cent) had information regarding the indication of the AM (104 from preweaning, 238 from growing and 173 from finishing). A prophylactic indication was in 34.2 per cent of the records (176), whereas 65.8 per cent showed a therapeutic or metaphylactic use. According to these data, prophylactic use decreased from the preweaning (49.0 per cent) and the growing (41.6 per cent) phases to the fattening phase (15.0 per cent).

Records of therapeutic/metaphylactic indications were mainly associated with the parenteral route (65.5 per cent), followed by water administration (28.3 per cent). The most used AMs for these indications by the parenteral route during all the production stages were  $\beta$ -lactams (mainly amoxicillin and penicillin) and fluoroquinolones (enrofloxacin).

By water, the most used AMs were amoxicillin, colistin and doxycycline in the growing stage, and doxycycline, lincomycin and colistin during the finishing period. By

contrast, records for prophylactic use were most frequent for medicated feed (70.5 per cent), colistin, amoxicillin and zinc oxide being the most used.

Of the 564 records, 497 (88.1 per cent) had information about the number of treated animals (88 from preweaning, 244 from growing and 165 from finishing). Considering group treatment as the administration of an AM to all the pigs of the same production group (Callens and others 2012) we recorded 199 of 497 group treatments (40 per cent); most of them were administered via feed (145, 72.9 per cent) and fewer by injection (34, 17.1 per cent) or water administration (20, 10 per cent), and fewer during the finishing phase (35/165, 21.2 per cent) than during the preweaning (56/88, 62.5 per cent) or growing (108/244, 44.3 per cent) phases.

The mean number of treated animals per 1000 animals at risk was calculated only when figures of use in three or more farms were available, and ranged as follows: for feed administration, from 982 per 1000 (polymyxins) to 976 per 1000 ( $\beta$ -lactams) in the preweaning stage, from 1000 per 1000 (lincosamides, tetracyclines, aminoglycosides, pleuromutilins, sulphonamides-trimethoprim and macrolides) to 982 per 1000 ( $\beta$ -lactams) in the growing stage, and from 1000 per 1000 ( $\beta$ -lactams) to 680 per 1000 (pleuromutilins) in the finishing stage; for water administration, from 464 per 1000 ( $\beta$ -lactams) to 170 per 1000 (lincosamides) in the growing stage and from 670 per 1000 ( $\beta$ -lactams) to 238 per 1000 (polymyxins) in the finishing stage; for injection, from 606 per 1000 ( $\beta$ -lactams) to 87 per 1000 (lincosamides) in the preweaning stage, from 353 per 1000 (polymyxins) to 22 per 1000 (phenicols) in the growing stage and from 298 per 1000 (polymyxins) to 29 per 1000 (phenicols) in the finishing stage.

Finally, 507 of the 564 records (89.9 per cent) also had information regarding the duration of the

treatment (104 from preweaning, 232 from growing and 171 from finishing). These data were only analysed under the farm-level approach presented below.

### Analysis of AMU based on farm data

All the farms used at least one AM during the study period. Table 1 summarises the AMCs detected per production stage. The most used AMCs were  $\beta$ -lactams (mainly amoxicillin) and polymyxins (colistin). The median number of different AMCs used by farm and production stage were as follows: 2 in the preweaning stage (range 0–5), 4 in the growing phase (range 0–8), 3 in the finishing stage (range 1–8) and 5 in the full cycle (range 2–9).

Analysis of the AMCs used during the three production stages by farm reveals that 33 farms (67 per cent) used at least one AM during the full production cycle (from preweaning to finishing); of these, 14 (29 per cent) used two different AMCs and 4 (8 per cent) used three different AMCs (all included  $\beta$ -lactams and three polymyxins plus fluoroquinolones). When the analysis was restricted to oral use (feed or water medication), 11 (22 per cent) farms used the same AM during the full production cycle; of these, 5 (10 per cent) used two different AMs (all but one included polymyxins). The most used AMs during the full production cycle were  $\beta$ -lactams (25 farms, 51 per cent), polymyxins (9 farms, 18 per cent) and fluoroquinolones (9 farms, 18 per cent).

### Analysis of indications

All the farms recognised at least one therapeutic treatment and all but two at least one preventive treatment. Table 2 summarises the indications detected per farm and production stage. As obtained from the records, farm AMU during the preweaning stage was more for preventive (57 per cent of farms) than therapeutic (39 per cent) use; therapeutic (94 per cent) and preventive

**TABLE 1:** Farm-level figures of use of antimicrobials and zinc oxide in 49 Spanish farrow-to-finish pig farms per production stage expressed as percentages of farms exposed (number of farms)

Antimicrobial classes	Preweaning stage (1–26 days)	Growing stage (27–75 days)	Finishing stage (76–193 days)	Full cycle (1–193 days)
Any	94 (46)	98 (48)	100 (49)	100 (49)
$\beta$ -lactams	80 (39)	90 (44)	57 (28)	96 (47)
Polymyxins	65 (32)	80 (39)	37 (18)	90 (44)
Fluoroquinolones	29 (14)	53 (26)	41 (20)	63 (31)
Aminoglycosides	35 (17)	45 (22)	37 (18)	63 (31)
Tetracyclines	4 (2)	41 (20)	47 (23)	59 (29)
Lincosamides	10 (5)	33 (16)	39 (19)	53 (26)
Macrolides	4 (2)	18 (9)	22 (11)	33 (16)
Pleuromutilins	4 (2)	24 (12)	24 (12)	33 (16)
Sulphonamides-trimethoprim	2 (1)	18 (9)	8 (4)	27 (13)
Phenicols	2 (1)	6 (3)	14 (7)	16 (8)
Zinc oxide	57 (28)	73 (36)	16 (8)	84 (41)

$\beta$ -lactams: amoxicillin, ampicillin, penicillin, ceftiofur and cefquinome; polymyxins: colistin; tetracyclines: doxycycline, tetracycline, chlortetracycline and oxytetracycline; fluoroquinolones: enrofloxacin, marbofloxacin and danofloxacin; lincosamides: lincomycin; aminoglycosides/aminocyclitols: streptomycin, gentamicin, neomycin, apramycin, framycetin and spectinomycin; macrolides: tylosin, tilmicosin, tulathromycin, erythromycin and spiramycin; pleuromutilins: tiamulin; phenicols: florphenicol

**TABLE 2:** Farm-level figures of indications for antimicrobial use in 49 Spanish farrow-to-finish pig farms per production stage expressed as percentage of farms exposed (number of farms)

Indication	Prewaning stage (1–26 days)	Growing stage (27–75 days)	Finishing stage (76–193 days)	Full cycle (1–193 days)
Therapeutic	39 (19)	94 (46)	92 (45)	100 (49)
Digestive disorders	27 (13)	65 (32)	55 (27)	76 (37)
Respiratory disorders	12 (6)	65 (32)	78 (38)	80 (39)
Other disorders	10 (5)	39 (19)	18 (9)	49 (24)
Unspecified disorders	2 (1)	8 (4)	4 (2)	10 (5)
Preventive	57 (28)	86 (42)	43 (21)	96 (47)
Digestive disorders	43 (21)	73 (36)	35 (17)	86 (42)
Respiratory disorders	18 (9)	41 (20)	20 (10)	59 (29)
Other disorders	12 (6)	20 (10)	4 (2)	31 (15)
Unspecified disorders	6 (3)	12 (6)	10 (5)	18 (9)

**TABLE 3:** Farm-level figures of use of antimicrobials and zinc oxide in 49 Spanish farrow-to-finish pig farms per production stage expressed as number of treated animals per 1000 animals at risk and percentages of farms exposed

Antimicrobial classes	Administration route	Prewaning stage (1–26 days)		Growing stage (27–75 days)		Finishing stage (76–193 days)	
		Mean* (na)	%† (n)	mean (na)	% (n)	mean (na)	% (n)
Any	Any	749 (46)	94 (46)	921 (48)	98 (48)	503 (48)	100 (49)
β-lactams	Feed	418 (21)	43 (21)	552 (27)	57 (28)	82 (4)	8 (4)
	Water			106 (11)	24 (12)	71 (5)	14 (7)
	Injection	379 (30)	63 (31)	103 (36)	84 (41)	56 (21)	43 (21)
Polymyxins	Feed	561 (28)	57 (28)	740 (36)	76 (37)	177 (9)	22 (11)
	Water			85 (12)	27 (13)	58 (12)	24 (12)
	Injection	21 (6)	14 (7)	29 (4)	8 (4)	24 (4)	8 (4)
Fluoroquinolones	Injection	23 (12)	29 (14)	136 (24)	53 (26)	60 (17)	41 (20)
Tetracyclines	Feed	41 (2)	4 (2)	184 (9)	18 (9)	124 (8)	16 (8)
	Water			88 (13)	27 (13)	132 (21)	43 (21)
	Injection	5 (1)	2 (1)	2 (1)	2 (1)	7 (3)	6 (3)
Aminoglycosides	Feed	20 (1)	2 (1)	204 (10)	20 (10)	76 (4)	8 (4)
	Water			30 (6)	14 (7)	35 (6)	12 (6)
	Injection	115 (16)	33 (16)	19 (13)	29 (14)	14 (8)	24 (12)
Lincosamides	Feed	41 (2)	4 (2)	265 (13)	27 (13)	56 (3)	8 (4)
	Water			14 (4)	8 (4)	82 (13)	27 (13)
	Injection	5 (3)	6 (3)	7 (3)	6 (3)	17 (7)	18 (9)
Macrolides	Feed			83 (4)	10 (5)	49 (3)	10 (5)
	Water			20 (1)	2 (1)	20 (1)	2 (1)
	Injection	22 (2)	4 (2)	23 (4)	8 (4)	26 (6)	12 (6)
Pleuromutilins	Feed	20 (1)	2 (1)	146 (7)	16 (8)	83 (6)	12 (6)
	Water			2 (1)	2 (1)	2 (1)	2 (1)
	Injection	10 (1)	2 (1)	30 (5)	12 (6)	27 (6)	14 (7)
Sulphonamides-trimethoprim	Feed			104 (5)	12 (6)		
	Water			18 (2)	4 (2)		
	Injection	60 (1)	2 (1)		4 (2)	3 (3)	8 (4)
Phenicol	Injection	2 (1)	2 (1)	1 (3)	6 (3)	4 (7)	14 (7)
Zinc oxide	Feed	571 (28)	57 (28)	735 (36)	73 (36)	163 (8)	16 (8)

\*Number of treated animals per 1000 animals at risk

†Percentage of farms exposed

na: number of farms having data of treated animals; n: number of farms reporting use; β-lactams: amoxicillin, ampicillin, penicillin, ceftiofur and cefquinome; polymyxins: colistin; tetracyclines: doxycycline, tetracycline, chlortetracycline and oxytetracycline; fluoroquinolones: enrofloxacin, marbofloxacin and danofloxacin; lincosamides: lincomycin; aminoglycosides/aminocyclitols: streptomycin, gentamicin, neomycin, apramycin, framycetin and spectinomycin; macrolides: tylosin, tilmosin, tulathromycin, erythromycin and spiramycin; pleuromutilins: tiamulin; phenicol: florphenicol

(86 per cent) use increased during the growing phase and the pattern shifted to therapeutic (92 per cent) versus preventive (43 per cent) indications at the finishing stage. The percentages of farms reporting AMU for treatment of respiratory and digestive disorders during finishing (78 and 55 per cent, respectively) and growing (65 per cent) phases were high, and lower during the preweaning stage (12 and 27 per cent, respectively). The growing stage also produced the highest figures of farms using AMs for prevention of digestive (73 per cent) and respiratory (41 per cent) diseases. The use of zinc oxide was mostly related to the prevention of digestive disorders.

### Analysis of AM exposure by farm

The figures for number of treated animals per record were used to calculate farm-level figures of animals treated per 1000 animals at risk (Table 3). In farms having several records of the same AM in a production stage, only the record having the highest number of treated animals was used. In addition, for computing the summarised measure of AMU, only the higher AM treatment was considered. The mean values of this farm-level measure were high in the three production stages, especially during the growing (921 treated animals per 1000 animals at risk per farm) and the preweaning stages (749 per 1000).

The rank of the most used AMs per farm and production stage and administration route started with polymyxins (colistin) by feed in the growing (740 per 1000) and the preweaning phases (561 per 1000), followed by  $\beta$ -lactams by feed during the growing (552 per 1000) and the preweaning phases (418 per 1000); next in the ranking were the most used AMs by injection, which were  $\beta$ -lactams in the preweaning phase, whereas the most used AM by water were tetracyclines (mainly doxycycline) during the finishing stage, ranked as twelfth.

These figures highlight the importance of the oral route, especially feed administration, as contributing the most to AM exposure: the highest figures of treated animals per production stage were for feed administration (among the 17 farm-level figures, there were more than 100 treated animals per 1000, 11 were by feed administration, 2 by water administration and 4 by injection).

### Analysis of duration of AMU by farm

The data regarding the duration of AM treatments (89.2 per cent of the records) were used for calculating farm-level figures of duration of AM use (Table 4). Because there was no information regarding the timing of the treatments belonging to the same production stage, only the record of each AM having the longest duration was used. The longest AM treatment on each farm, irrespective of the AM and the administration route, was chosen to compute an overall measure of AM exposure length per farm.

The longest durations corresponded to feed administration, especially in the growing stage (lincosamides, 26 days; polymyxins, 24;  $\beta$ -lactams, 22). Nevertheless, we

only detected significant differences (95 per cent) between production stages for polymyxins and lincosamides administered by feed, and  $\beta$ -lactams, lincosamides and macrolides when administered by injection.

In addition to summarised data per production stage, Table 4 also contains cumulative data of the total days of exposition to AMCs. The ranking of the highest mean values was as follows: pleuromutilins (39 days), polymyxins (34), aminoglycosides (34),  $\beta$ -lactams (27) and lincosamides (26), all of them by feed.

## DISCUSSION

An increasing number of studies analysing AMU in commercial pig production have been published since the beginning of the twenty-first century, but their objectives and methodologies differ, and consequently comparative analysis of the results was hampered.

Some authors have previously collected records of AMU in pigs at the farm level (Rajic and others 2006, Timmerman and others 2006, Casal and others 2007, Rosengren and others 2007, 2008, Van der Fels-Klerx and others 2011, Callens and others 2012), from practitioners (Chauvin and others 2002, Jordan and others 2009) or using both sources (Merle and others 2012). In the present study, farm-level records have been collected and used for producing information about AMU using two approaches: record based and farm based. Since the number of records per farm varied in our study from 3 to 30 (0–15 in the preweaning stage, 0–10 in the growing stage and 1–13 in the finishing stage), farm-based analysis allowed circumventing repetitive information belonging to some farms that could overestimate various record-based figures of AMU; in addition, the farm is the epidemiological unit of concern for AM exposure and several authors (Timmerman and others 2006, Jordan and others 2009, Van der Fels-Klerx and others 2011) have also detected large differences in AMU among individual farms.

Some putative weaknesses (lower sample size than designed and lower response percentage than expected) of this study have been previously showed and discussed (Moreno and others, 2012); nevertheless the medium and larger farms were well represented and, consequently the potential bias of the AMU estimation is believed to be low since these farms produced the majority of the commercial pigs coming from Spanish farrow-to-finish farms. In addition, the methodologies employed for collection, check, debug and analysis of the data were the same for all the farms and production stage, minimizing the bias in the comparative analysis of these factors. The first objective of this study was the analysis of AMU by production stage and our results showed that the growing stage (from 26 to 75 days of life approx.) has the highest AMU. These results agree with previous observations when finishers were compared with younger animals in other European pig-producing countries like Denmark (Jensen and others 2011),

**TABLE 4:** Farm-level figures of duration of use of antimicrobials and zinc oxide in 49 Spanish farrow-to-finish pig farms per production stage expressed as days (mean, minimum and maximum)

Duration	Administration route	Prewaning stage (1–26 days)		Growing stage (27–75 days)		Finishing stage (76–193 days)		Full cycle* (1–193 days)	
		Mean (na)	Min–max	Mean (na)	Min–max	Mean (na)	Min–max	Mean (na)	Min–max
Any	Any	9 (46)	1–30	24 (47)	2–60	12 (48)	1–75	44 (49)	6–102
β-lactams	Feed	14 (16)	6–30	22 (25)	7–60	13 (4)	6–30	27 (30)	6–87
	Water	–		6 (12)	4–9	5 (5)	4–7	8 (13)	4–14
	Injection	1.8 (31)	1–4	2.5 (35)	1–6	2.4 (23)	1–4	5 (40)	1–11
Polymyxins	Feed	14 (26)	6–30	24 (35)	7–55	22 (10)	6–75	34 (42)	6–89
	Water	–		7 (13)	3–15	7 (12)	3–15	8 (21)	3–30
	Injection	2.0 (7)	1–3	2.8 (4)	2–3	2.3 (4)	1–3	3.8 (9)	1–7
Fluoroquinolones	Injection	2.5 (12)	1–3	2.6 (21)	1–5	2.8 (16)	1–4	4.6 (28)	1–9
Tetracyclines	Feed	10 (1)		22 (6)	7–49	12 (7)	7–15	18 (12)	7–64
	Water	–		7 (12)	4–30	6 (22)	4–36	9 (24)	4–36
	Injection	3 (1)		–		2.5 (2)	2–3	2.5 (2)	2–3
Aminoglycosides	Feed	15 (1)		27 (8)	7–60	41 (4)	15–75	34 (11)	7–75
	Water	–		6 (7)	4–15	5 (7)	4–7	8 (10)	5–15
	Injection	1.9 (15)	1–4	2.5 (11)	1–4	2.4 (9)	1–3	3.4 (21)	1–10
Lincosamides	Feed	8 (3)	3–15	26 (12)	7–60	10 (4)	3–15	26 (14)	3–78
	Water	–		5 (5)	4–6	6 (12)	4–7	7 (14)	4–12
	Injection	2 (2)		1 (2)		2.8 (9)	1–4	2.8 (11)	1–4
Macrolides	Feed	–		21 (4)	9–33	32 (3)	15–50	28 (6)	14–50
	Water	–		7 (1)		7 (1)		14 (1)	
	Injection	1.5 (2)	1–2	1 (4)		3.1 (7)	1–5	2.6 (11)	1–5
Pleuromutilins	Feed	15 (1)		36 (6)	20–55	22 (7)	6–60	39 (10)	6–70
	Water	–		2 (1)		2 (1)		4 (1)	
	Injection	2 (1)		2 (5)		2.5 (6)	2–4	3.9 (7)	2–6
Sulphonamides/ trimethoprim	Feed	2 (1)		27 (5)	15–40	–		23 (6)	2–40
	Water	–		4 (2)		–		4 (2)	
	Injection	–		–		3 (4)		3 (4)	
Phenicols	Injection	3 (1)		2 (1)		2.3 (7)	1–4	3	1–7
Zinc oxide	Feed	15 (26)	6–30	23 (35)	5–60	10 (8)	7–15	33 (39)	7–69

\*Sum of the longest treatment per production stage

na: number of farms having data of duration; β-lactams: amoxicillin, ampicillin, penicillin, ceftiofur and cefquinome; polymyxins: colistin; tetracyclines: doxycycline, tetracycline, chlortetracycline and oxytetracycline; fluoroquinolones: enrofloxacin, marbofloxacin and danofloxacin; lincosamides: lincomycin; aminoglycosides/aminocyclitols: streptomycin, gentamicin, neomycin, apramycin, framycetin and spectinomycin; macrolides: tylosin, tilmicosin, tulathromycin, erythromycin and spiramycin; pleuromutilins: tiamulin; phenicols: florphenicol

Belgium (Callens and others 2012) or Germany (Merle and others 2012), and also Canada (Rajic and others 2006, Rosengren and others 2007, Rosengren and others 2008). It is interesting to note that these similar results were obtained in spite of the different measures of AMU employed for each study: animal daily doses (ADDs) (Jensen and others 2011); treatment incidence (TI) (Callens and others 2012); daily dose per animal year (Merle and others 2012); percentages of farms using AMs (Rajic and others 2006); or probabilities of exposure (Rosengren and others 2007, Rosengren and others 2008). The higher use of AMs after the weaning of piglets has been related to their most vulnerable status to infectious diseases (Rajic and others 2006).

For drugs not used for the treatment of chronic diseases, like AMs, usage should ideally be given in terms of treatment rates per age group (Grave and others 2006). The number of exposed animals was thought to

best express AM selection pressure (Chauvin and others 2008) but cannot be calculated without the appropriate data; for instance, it cannot be calculated from the Danish Vetstat database because the number of treated pigs was not recorded (Hybschmann and others 2011). A proxy for this measure (Jensen and others 2011) is the defined ADD (introduced in the veterinary field by Jensen and others 2004) and related measures, which have been calculated in different pig studies (Bondt and others 2013, Hybschmann and others 2011, Jensen and others 2011, Van der Fels-Klerx and others 2011, Merle and others 2012). ADD has also been used to calculate TI in pigs (Timmerman and others 2006, Callens and others 2012); nevertheless, these measures need prior agreements on recommended dosages and average animal weights before producing comparable results; for instance, Merle and others (2012) used 12.5 kg for piglets, 25 kg for weaners and 70.2 for fatteners; Jensen

and others (2011) used 15 kg for weaners and 50 kg for slaughter pigs; Bondt and others (2013) used 10 kg for piglets and 50 kg for fattening pigs; and Callens and others (2012) used a standard growth table from birth to 10 weeks and the average daily weight for fatteners.

The number of treated animals, although this does not include AM dosage, is a straightforward and useful parameter for AMU estimation, and its major practicability of calculation at the farm level makes this measure very useful, especially for the analysis of group treatments since its information bias is very low. We are more confident on the questionnaire-collected data when the answer was 'all' the animals were treated in comparison with records showing a figure, since these quantitative data are more prone to recall bias, and the effect produced (over or underestimation of the true exposure) cannot be properly addressed.

Some minor differences among producing stages were also detected in our study regarding the most frequently used AMCs. When analysing the percentages of farms using AMs and the number of animals treated (Table 3) showed that  $\beta$ -lactams and polymyxins were the most frequently employed during the preweaning and the growing phases, although the route of administration was almost exclusively the feed for polymyxins, whereas  $\beta$ -lactams were administered by feed and injection. Besides the lower figures, the finishing stage showed that the most employed AMs were polymyxins (by feed) and tetracyclines (by water). Colistin and amoxicillin were also the most used AMs for group treatments by the oral route during the lifespan of commercial fattening pigs in Belgium (Callens and others 2012); nevertheless, the Belgian data for injectable medications showed higher use of tulathromycin and lower use of enrofloxacin compared with the Spanish data.

Differences in the most used AMs per production stage have also been detected in Canadian pig production (Rajic and others 2006), the most commonly reported AMs being the following: in feed, the combination tetracyclines/sulphonamides/penicillins in weaners, tylosin and the combination tetracyclines/sulphonamides/penicillins in growers, and tylosin and lincomycin in finishers; by injection, penicillin, trimethoprim/sulphonamides and oxytetracycline in weaners, and penicillin and oxytetracycline in growers and finishers. Equally, data for in-feed AMs in pigs in the USA (Apley and others 2012) showed a different pattern of use, with tetracyclines (chlortetracycline and oxytetracycline) and macrolides (tilmicosin and tylosin) the most frequently employed AMCs.

Callens and others (2012) reported that 93 per cent of all the group treatments in Belgium were for prophylactic purposes and only 7 per cent for metaphylactic treatments; in addition, preventive treatments were applied in 98 per cent of the farms. In the present Spanish survey, 96 per cent of the pig farms also employed preventive treatments; 188 of the 564 records

met the criterion of group treatment and included information about indication; of these, 161 (85.6 per cent) reported a preventive use. The distribution of these 188 group treatments per production stage in our study showed that they were more frequently used during the growing (54 per cent) and preweaning (28 per cent) stages, and less during finishing (18 per cent), whereas Callens and others (2012) reported 90 per cent of use from birth to 10 weeks of age, and 10 per cent during the fattening period.

Among these 188 group treatments, feed was the most frequently employed administration route for preventive indications, mainly containing combinations of colistin and amoxicillin plus zinc oxide in the preweaning and growing stages and different AMC combinations in the finishing stage. The use of the parenteral route for prevention was only relatively frequent during the preweaning stage, being used mainly for administration of  $\beta$ -lactams (amoxicillin, penicillin and ceftiofur); we detected a low use of cephalosporins, which were the most frequently parenterally administered AMs in the Belgian study (Callens and others 2012).

Trends on the therapeutic use of AMs in pigs in Denmark based on the data retrieved from the VetStat database (Jensen and others 2011) showed differences among age groups in the most frequently employed AMs. In the sows/piglets group they were penicillins, pleuromutilins, trimethoprim-sulphonamides and tetracyclines; in weaners, they were tetracyclines, macrolides, pleuromutilins and lincosamides; and in finishers they were tetracyclines, pleuromutilins and macrolides. Although there are differences in the AM groups between studies (for instance, Jensen and others 2011 differentiated penicillins, aminopenicillins, penicillin combinations and cephalosporins whereas we combined all of these) some differences are clearly noted, especially the higher used of polymyxins (colistin) and fluoroquinolones in our study and the higher use of macrolides and pleuromutilins in the Danish study.

According to Casal and others (2007) the percentages of farms in Spain using AMs for therapy in finishers (2001–2003) were 94 per cent for respiratory diseases and 90 per cent for digestive diseases, whereas the corresponding figures in our 2010 study (78 per cent and 55 per cent) are lower; equally, preventive treatments were detected in 58 per cent of the studied farms (2001–2003) versus 43 per cent in the present study (2010). Although the spatial coverage of both studies is not fully equivalent, these figures could indicate a reduction of AMU in finishers in Spain.

Although methodological differences preclude an in-depth comparative analysis of the AMs most used for treating gastrointestinal and respiratory bacterial infections, we detect some differences with other authors (Jensen and others, 2011). Different studies have indicated that AMs in pigs are mainly administered by the oral route, although quantification fluctuates due to the different measures employed. For instance, Timmerman

and others (2006) reported 69 kg of AMs administered orally versus 1 kg injected; Stevens and others (2007) and Rajic and others (2006) reported that the most common method of administering AMs was in the feed (between 20 and 75 per cent, and between 80–100 per cent of farms, respectively, depending on the production system and/or the animal age); Merle and others (2012) indicated that 92 per cent (based on applications) or 97 per cent (based on weight in kg) of all the AMs were administered orally to pigs, whereas in our study this percentage was lower (51.4 per cent of records); Rosengren and others (2008) calculated probabilities of exposure ranging between 0.17 and 0.78 for feed, between 0 and 0.06 for water, and between 0.0003 and 0.04 for parenteral administration.

Although the length of AM treatment is another critical point for full understanding of AM exposure, we have only found references to this topic in two studies (Chauvin and others 2002, Stevens and others 2007). French data (Chauvin and others 2002) on group treatments were reported without repartition per administration route and production stage, whereas US data (Stevens and others 2007) are separated according to indication (growth promotion, prevention and therapy), hindering comparative analysis with our results. Nevertheless, noteworthy is the long duration of in-feed treatments (ranging from 3 to 60 days), especially during the growing stage (from 7 to 60 days); even considering the same production stage and administration route, most of the AMs showed wide ranges in duration of oral treatments (in feed, 12–24 days during preweaning, 24–53 during growing and 8–69 during finishing; in water, 2–26 during growing and 3–32 during finishing), probably indicating a discretionary use. The cumulative exposure data presented in Table 4 indicate that the mean number of days of exposure during the lifespan of a commercial pig is 44 days (23 per cent of the lifespan), with a maximum value of 102 days (53 per cent of the lifespan); these figures are conservative since all the treatments for the same production phase on a farm were assumed to be simultaneous, and consequently we did not sum duration of treatments. These long-term AM exposures were mostly due to feed medications and highlight the role of feed medications as the most involved in AM exposure in animals.

Callens and others (2012) discussed the contribution of AM sales by veterinarians on their prescription behaviour (Maes and others 2010 showed that, in Belgium, 43 per cent of the income of pig veterinarians results from the selling of medicines); nevertheless, the Spanish legislation in Veterinary Medicines does not permit veterinarians to carry out this commercial activity (Anon 2010).

To minimise the deleterious effects on public health from AMU in animals, without unnecessary restrictions of their therapeutic use for combating bacterial diseases compromising the animal health and welfare, we need to test tentative microbiological withdrawal times for AMs, having in mind the role of suspension of AM

exposure on the fitness and removal of AM-resistant bacteria in animals, especially from the intestinal microbiota. Food animal species like pigs which have a relatively long lifespan and the lowest AMU during the end of their lifespan would be good candidates for testing this approach.

In conclusion, we previously showed that AMU in the pig finishing period varies according to the production system, being higher in finisher farms than in farrow-to-finish-farms (Moreno 2012). Now, a national survey based on data from questionnaires but from a limited number of farms has studied AMU in farrow-to-finish farms and demonstrated the following: the growing stage (from weaning to the start of finishing) has the highest AMU according to different quantitative indicators (number of records, number of AMs used, percentage of farms reporting use, relative number of exposed animals per farm and duration of exposure); feed is the administration route that produces the highest AM exposure based on the higher number of exposed animals and the longer duration of treatment; and there are large differences in AMU among individual pig farms.

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