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A register-based study of the antimicrobial usage in Danish veal calves and young bulls

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ABSTRACT

High antimicrobial usage and multidrug resistance have been reported in veal calves in Europe. This may be attributed to a high risk of disease as veal calves are often purchased from numerous dairy herds, exposed to stress related to the transport and commingling of new animals, and fed a new ration. In this study, we used national register data to characterize the use of antimicrobials registered for large Danish veal calf and young bull producing herds in 2014.

A total of 325 herds with veal calf and potentially young bull production were identified from the Danish Cattle database. According to the national Danish database on drugs for veterinary use (VetStat), a total of 537,399 Animal Daily Doses (ADD_{200}) were registered for these 325 herds during 2014. The amount of antimicrobials registered in 2014 varied throughout the year, with the highest amounts registered in autumn and winter. Antimicrobials were registered for respiratory disorders (79%), joints/limbs/CNS disorders (17%), gastrointestinal disorders (3.7%) and other disorders (0.3%). Of the registered antimicrobials, 15% were for oral and 85% for parenteral administration. Long-acting formulations with a therapeutic effect of more than 48 h covered 58% of the drugs for parenteral use. Standardized at the herd-level, as ADD_{200}/100 calves/day, antimicrobial use distributed as median [$CI_{95\%}$] for starter herds (n = 22): 2.14 [0.19;7.58], finisher herds (n = 24): 0.48 [0.00;1.48], full-line herds (n = 183): 0.78 [0.05;2.20] and herds with an inconsistent pattern of movements (n = 96): 0.62 [0.00;2.24]. Full-line herds are herds, which purchase calves directly from a dairy herd and raise them to slaughter.

Furthermore, we performed a risk factor analysis on the 183 herds with a full-line production. Here, we investigated, whether the number of suppliers, the number of calves purchased, the frequency of purchase, the average age at introduction, the average time in the herd and vaccination influenced the amount of antimicrobials used in the herds. The final multivariable regression analysis revealed that the number of calves introduced was positively associated with the antimicrobial use in the herd.

1. Introduction

High antimicrobial usage and multidrug resistance have been found in Belgian and Dutch veal calves (Catry et al., 2007; Pardon et al., 2012a; Bos et al., 2012). In the same countries antimicrobial usage in veal calves has been found to exceed that of pig, poultry, dairy and beef cattle production (Pardon et al., 2012a; Bondt et al., 2013). An explanation may be that producers of pigs and poultry receive animals from a limited number of suppliers, while veal calf producers typically purchase calves from numerous dairy herds. A large number of suppliers, new feed and stress related to the transport and commingling of new animals exposes veal calves to a high risk of disease and may explain the higher use of antimicrobials (Pardon et al., 2012a).

Veal calf production can generally be divided into two types; white and rosé veal calf production. White veal calves are primarily fed on calf milk replacer and are slaughtered at around 6–8 months of age, while rosé veal calves are weaned in the beginning of the fattening period and subsequently fed on roughage and concentrate, until they are slaughtered at around 8–12 months of age (Bos et al., 2012). Additionally, rosé veal calf production can be divided into rosé starter and rosé finisher herds with large differences in antimicrobial usage (Bos et al., 2013).

Denmark only produce rosé veal calves. The vast majority of Danish rosé veal calves, are bull calves purchased from domestic dairy herds. Some of the calves are slaughtered as veal (8–12 months of age) (EU Regulation EC, 2007), while some are slaughtered as young bulls (>12 months of age) (Danish Agriculture and

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Food Council, 2016). In 2014, around 200,000 veal and young bulls were slaughtered in Denmark (Danish Agriculture and Food Council, 2015). Heifers only make up around 1% of the total number of produced calves (SEGES, 2016). After arrival in a specialized veal calf herd, the calves receive calf milk replacer until around 8 weeks of age, after which they are typically fed on a ration of grain and concentrate or on a total mixed ration based on corn silage. The calves are predominantly Danish Holsteins, though a small percentage of them are Holstein crossbreds. Specialized Danish rosé veal calf producers generally keep the calves in compartments of multiple straw-bedded pens or cubicles, where each unit may hold 6–50 calves of the same age, depending on the producer. Typically, an all-in-all-out production is implemented at pen level, but not at compartment level. Depending on the facilities, this may result in calves of different ages being housed under the same roof, thus facilitating the transmission of airborne pathogens (Mars et al., 1999; Niskanen and Lindberg, 2003).

In herds with a Veterinary Advisory Service Contract, Danish veterinarians can prescribe drugs for use within 63 days (Anon., 2016). This means that most Danish veal and young bull producers have a veterinary visit at least every second month. All prescription-only drugs for veterinary use are registered in the national database VetStat, which holds detailed information on each purchase of drug such as the date, prescribing veterinarian, receiving herd ID, species, age group and clinical indication (Stege et al., 2003). In addition, the Danish cattle database holds detailed information on all Danish cattle and their movements, including the date of birth, date of movement and herd ID of the sender and recipient.

There is limited research into the overall disease occurrence in Danish veal calf production. A study from 1984 found pneumonia and enteritis to be the predominant diseases (Madsen, 1984). In Swiss and Belgian white veal calves, respiratory disease was found to be the main indication for antimicrobial treatment (Pardon et al., 2012a; Lava et al., 2016b), with a peak incidence in the third week after arrival (Pardon et al., 2012b). The second most common indication for treatment of Belgian white veal calves was diarrhea (12%), while arrival prophylaxis made up 13% of the treatments (Pardon et al., 2012a). Group treatments were widely applied in the production in both countries (>84%) (Pardon et al., 2012a; Lava et al., 2016b).

Recent risk factor studies on white veal calves in Switzerland have demonstrated purchase of calves and herd size to be significantly associated with the use of metaphylactic treatments (Lava et al., 2016a), while the lack of quarantine and clinical examination upon arrival, as well as shared airspace for several groups of calves were associated with an increased antimicrobial usage (Lava et al., 2016b). To the best knowledge of the authors, no risk factor study on rosé veal calf production has so far been carried out. Therefore, based on register data, our aim was to characterize antimicrobial usage in Danish veal calves specified in the following two objectives:

a Describe the total amount of antimicrobials registered for all large Danish herds with a veal calf and potentially young bull production in 2014.
b Identify risk factors influencing the amount of antimicrobials registered at herd level in large Danish herds which purchased calves and raised them to slaughter (full-line production).

2. Materials and methods

2.1. Study population

Based on the Danish Cattle database, herds included in the study population had to fulfill the following three criteria:

1. No delivery of milk to a dairy in 2014
2. Slaughter more than 100 bull calves in 2014
3. Less than 80% of the cattle in the herd should be of dairy or mixed breeds

Bovines which had stayed in one of the study herds in the period 01 January, 2014–31 December, 2014 were included. For these animals, all movements were extracted from the Danish Cattle database until 31 December 2014. Based on the definition of veal by the European Council (EU Regulation EC, 2007), calves were defined as being less than 366 days of age at the time of slaughter. Only bovines which were calves (<366 days of age) at the time of introduction in one of the study herds were retained in the final dataset.

For each calf, we consecutively numerated each herd through which the calf had passed, aside from the originating dairy herd, markets and delivering traders. Based on this, we defined four different types of herds: Starter and full-line herds, where ≥95% of the calves entering the herd came directly from the herd where they were born (possibly through a market or delivery trader); and finisher herds, where ≥95% of the entering calves came from a starter herd. Herds with a low average age of exit (<250 days) or a high variance in the age at exit (>10 days) were checked manually, to differentiate starter and full-line herds. Herds, which did not fulfill the definitions of starter, finisher or full-line herds, were defined as herds with inconsistencies in movements.

The number of registered calves on the first day of each month was extracted from the Danish Cattle database. We calculated a weighted herd size for 2014 based on this information and taking into account the number of days in each month. Additionally, calf mortality from day 0–180 was calculated for each herd as a modified Kaplan-Meier estimate. The Kaplan-Meier estimate follows a specific cohort of calves during the first 180 days of their lives, for which a mortality risk is calculated as the number of fallen and euthanized calves divided by the number of calves at risk (Nielsen et al., 2010). Due to availability of data, the calf mortality was stated for the period between 01 October, 2014 and 30 September, 2015, covering calves born between 01 April, 2014 and 31 March, 2015. For each herd, we summarized the number of calves purchased, the average age at introduction, the average time in the herd, frequency of purchase, purchase from markets and delivering traders, and the number of suppliers (excluding delivering traders and markets). Furthermore, we calculated the proportion of calves slaughtered <366 days of age out of the total number of slaughtered bovine.

2.2. Antimicrobial prescriptions

In VetStat, all prescription-only drugs for production animals are registered in detail at the time of purchase by farmers (from either pharmacies or veterinarians) (Stege et al., 2003). We retrieved records on antimicrobials for calves registered by both pharmacies and veterinarians in 2014 from VetStat on 01 June, 2015. Antimicrobials registered by veterinarians were manually checked and systematic errors were corrected. Furthermore, registrations with an invalid code of indication (e.g. disease in other species) were deleted.

For each herd in the study, the amount of antimicrobials registered in VetStat for calves was used as a measure for the amount of antimicrobials used. Antimicrobials were quantified as the number of Animal Daily Doses (ADD_{200}) (Jensen et al., 2004). Based on the official Danish quantification of antimicrobials, we used a standard weight of 200 kg for calves (personal communication Erik Jacobsen, Danish Veterinary and Food Administration). The standard dose, ADD_{200} corresponds to the treatment of one 200 kg calf for one day. For comparison between herds, the amount of antimicrobials was standardized in agreement with the official

unit as the number of Animal Daily Doses per 100 calves per day (ADD_{200}/100 calves/day). This unit approximates the percentage of calves treated daily at the herd assuming that all calves weigh 200 kg (Anon., 2014). Based on the Anatomical Therapeutic Chemical classification system, antimicrobial products were grouped according to active substance as amphenicols, combination products (all except sulphonamide/trimethoprim and lincospectin), macrolides, sulphonamide/trimethoprim, tetracyclines, simple or extended-spectrum penicillin products, lincospectin, lincosamides, cephalosporin, aminoglycosides and colistin. The products were further characterized as intended for parenteral or oral use, based on the definitions in VetStat. Clinical indication according to diagnostic grouping in VetStat (Stege et al., 2003) was categorized as gastrointestinal, respiratory, joint/limbs/Central Nervous System (CNS) or other disorders (covering the three VetStat diagnostic groups reproduction, udder and metabolism as well as missing disorders). In addition, information about registered vaccines against respiratory disorders was extracted.

2.3. Statistical analyses

For all large Danish herds producing veal calves and young bulls, a descriptive analysis was performed, including the total amount of antimicrobials registered, quantified as ADD_{200}, according to months of registration, route of administration, antimicrobial active substance and clinical indication, as stated in VetStat.

For full-line herds, we performed a multivariable regression analysis with ADD_{200}/100 calves/day as the response variable. Potential risk factors included: Herd size, number of suppliers, number of calves purchased, frequency of purchase, average age at introduction, average time in the herd and vaccination.

The number of calves introduced was 10 log-transformed to improve linearity with the outcome. Additional continuous risk factors with a non-linear relationship with the outcome were each categorized into three categories according to their distribution. Prior to categorization, the correlation between all continuous explanatory variables were investigated two at a time, and if Spearman's coefficient >0.6 only one of the parameters was included in the final model.

Initially, each possible risk factor was tested with the outcome in a univariable analysis. If found to be significant ($p < 0.05$), pairwise post-test comparisons were performed using the contrast procedure in the Least-Squares Means package in R (Lenth and Herv, 2015). For the multivariable analysis, all factors sufficiently associated with the outcome ($p < 0.20$ in univariable analysis) were included. All biologically plausible interactions were assessed individually to see, if they significantly improved the model including all risk factors. Following this, the model with all risk factors was reduced by stepwise backward elimination. To improve the residuals of the model, the outcome was Box-Cox transformed. Due to null-values, we added half the minimum value to the outcome prior to the Box-Cox transformation.

Data management was carried out using the software SAS® (SAS Institute Inc., 2014), while statistical analyses were performed in R (R Core Team, 2014).

3. Results

3.1. Descriptive analyses of the study population

A total of 333 herds fulfilled the initial inclusion criteria. Subsequently, 8 herds were excluded due to cessation (1), systematic incorrect registrations (1), partly beef production (2) and combined starter-/full-line production (4).

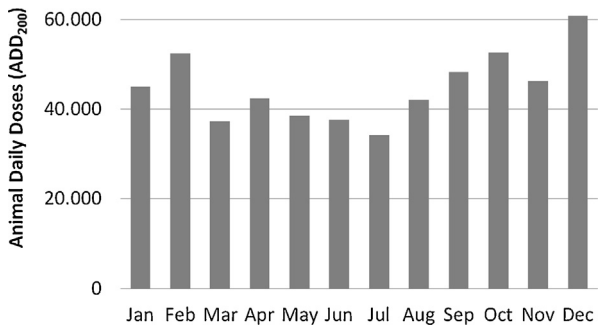

Fig. 1. Variation in the amount of registered antimicrobials in 2014 for 325 Danish herds producing veal calves and young bulls. Antimicrobials are quantified as Animal Daily Doses for calves (ADD_{200}), illustrated according to the month of prescription.

Of the cattle present in the remaining 325 herds, 242,474 (98.7%) of them had entered one/more study herds as calves <366 days of age and 3224 (1.3%) as bovine ≥366 days of age. The latter category of cattle was excluded from further analysis. Of the 242,474 calves entering, 176,897 (73.0%) were slaughtered as veal (<366 days) with a median slaughter age at 300 days, $CI_{95\%}$ [271;354], while 43,780 (18.1%) were slaughtered as young bulls (≥366 days), with a median slaughter age of 403 days, $CI_{95\%}$ [369;814] at the time of slaughter. The remaining 21,797 (9.0%) calves were not slaughtered prior to 01 January, 2015.

Based on the movement of calves, we defined 22 starter herds, 24 finisher herds, 183 full-line herds and 96 herds with inconsistent movements of calves. Herds with inconsistencies in movements received calves by the second to seventh movement of the calf after it left the dairy herd (average 2.3 movements).

The majority of starter-, finisher and full-line herds slaughtered more than 90% of their calves as veal <366 days of age, while herds with inconsistent movements slaughtered a larger proportion of young bulls ≥366 days (Table 1).

In total, twelve herds purchased calves from delivering traders and 19 herds purchased from markets. From these sources, the herds received a median number of six calves (ranging from 1 to 398) and nine calves (ranging from 1 to 269), respectively.

3.2. Descriptive analyses of antimicrobials registered for all large Danish herds producing veal calves and young bulls

In 2014, a total of 1,062,376 ADD_{200} were registered for calves in VetStat. Of these, 537,399 ADD_{200} (51%) were registered for the selected 325 large veal calf and young bull producing herds, with 532,438 ADD_{200} (99%) originating from pharmacies and 4961 ADD_{200} (1%) from veterinarians.

The amount of antimicrobials varied between seasons, with the largest amounts of antimicrobials registered in autumn and winter (September–February) (Fig. 1).

Of the registered antimicrobials, 85.4% were for parenteral use and 14.6% for oral use. Long-acting formulations with a therapeutic effect of more than 48 h covered 58% of all antimicrobials for parenteral use. Amphenicols, macrolides and extended penicillins were the primary active substances of long-acting formulations. For oral use, the majority of antimicrobials were soluble tetracyclines (Fig. 2). Lincospectin, lincosamide, cephalosporin, aminoglycoside and colistin only covered a total of 1603 (0.3%) ADD_{200} and are therefore not illustrated in Fig. 2.

Respiratory disorders were the primary indication for antimicrobial use, accounting for 78.9% of all ADD_{200} in 2014. Joints/limbs/CNS disorders accounted for 17.1%, gastrointestinal disorders for 3.7% and other conditions for 0.3% of the total amount of ADD_{200} (Fig. 2).

Table 1
Characteristics of 325 Danish herds producing veal calves and young bulls in 2014. Herds are characterized according to their type of production as either starter, finisher, full-line or herds with inconsistent movements. Values are presented as the median and 95% confidence interval.

	Starter	Finisher	Full-line	Inconsistent
Number of herds	22	24	183	96
Number of introduced calves[a]	1597 [445;3764]	512 [186;2074]	474 [203;2533]	524 [226;2349]
Proportion of veal calves produced[b]	0.97 [0.32;0.99]	0.97 [0.12;1.00]	0.94 [0.18;1.00]	0.60 [0.21;0.99]
Number of purchases (in 2014)[c]	71 [25;169]	21 [7;35]	53 [18;115]	63 [19;135]
Number of suppliers[d]	27 [6;65]	1 [1;7]	8 [1;70]	14 [2;75]
Average age at introduction (days)	32 [27;44]	151 [100;266]	32 [19;98]	NA
Average length of time in herd (days)	172 [97;210]	166 [112;276]	263 [220;374]	257 [94;483]
Number of herds using vaccines	3	0	17	5
Mortality day 0–180 (%)[e]	4.2 [0.00;10.0]	0.0 [0.0;10.3]	3.7 [0.2;11.8]	4.0 [0.0;19.0]

[a] Total number of introduced calves during 2014.
[b] Of the number of calves passing through the herd, the proportion of veal calves has been calculated as the number of calves slaughtered as veal (<366 days of age) divided by the number of cattle slaughtered (≥366 days of age) (which entered the herd as calves).
[c] Frequency of purchase is defined as the number of days during 2014, where the herd received calves.
[d] Seven full-line herds had more than one supplier.
[e] Information on mortality was not available for 52 herds, covering three starter, eight finisher, 16 full-line and 24 herds with inconsistent movements.

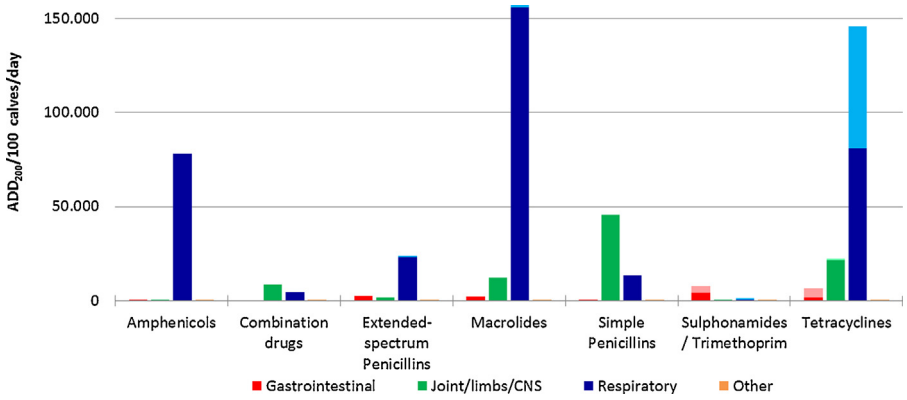

Fig. 2. Antimicrobials according to active substance and clinical indication registered for use in 325 Danish herds producing veal calves and young bulls in 2014. The total amount of the seven most registered antimicrobial active substances. Antimicrobials are quantified as Animal Daily Doses for a calf (ADD_{200}). Dark colors indicate parenteral and light colors oral administration. Combination drugs all include Penicillin-combination drugs.

Antimicrobials registered for respiratory disorders primarily included macrolides (37%) and tetracyclines (34%), while simple penicillins (50%) were most often registered for joints/limbs/CNS disorders, and sulphonamides/trimethoprim (39%) and tetracyclines (33%) for gastrointestinal disorders.

Standardized at the herd-level, antimicrobial use, measured as ADD_{200}/100 calves/day, distributed as follows (median [$CI_{95\%}$]) for starter herds (n = 22): 2.14 [0.19;7.58], for finisher herds (n = 24): 0.48 [0.00;1.48], for full-line herds (n = 183): 0.78 [0.05;2.20] and for herds with an inconsistent pattern of movements (n = 96): 0.62 [0.00;2.24]. Starter herds used significantly more antimicrobials than all other herd types ($p < 0.001$), while no difference was demonstrated in antimicrobial usage between any of the other production types (Fig. 3).

3.3. *Risk factors for use of antimicrobials in large Danish full-line herds producing veal calves and young bulls*

Of the previously described 325 herds, 183 had a full-line production and were included in the risk-factor analysis. Of these herds, 6 (3%) had not purchased antimicrobials in 2014.

Several of the investigated risk factors were correlated, and therefore not all factors could be included in the model. The number of suppliers was positively correlated with the herd size (Spearman's coeff = 0.67) and the number of inserted calves (Spearman's coeff = 0.69), like herd size was correlated with the number of inserted calves (Spearman's coeff = 0.98). We kept the number of inserted calves in the model, since we found this to be the most valid parameter of the investigated parameters.

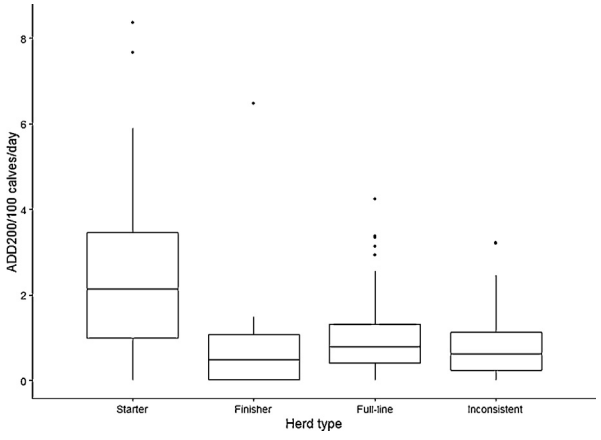

Fig. 3. Antimicrobials registered in relation to herd type in 325 Danish herds producing veal calves and young bulls. Antimicrobials are quantified as Animal Daily Doses (ADD_{200}) per 100 calves per day.

In the univariable analyses, antimicrobial usage was significantly higher in herds with a short average length in the herd (<291 days), large number of purchases per year (>61) or a large number of introduced calves. Herds which introduced calves at a low (12–28 days) or high (35–240 days) age had a significantly lower use of antimicrobials than herds where calves were introduced at a medium (39–34 days) age. Herds introducing young calves kept the calves significantly longer time in the herd, compared to herds which introduced calves older than 29 days of age

Table 2
Univariable comparisons of risk factors for the amount of registered antimicrobials in 183 Danish herds producing veal calves and young bulls in 2014. Antimicrobials are standardized at the herd level as Animal Daily Doses (ADD_{200}) per 100 calves per day.

Potential categorical risk factors	Number of herds (%)	ADD_{200}/100 calves/day median [$CI_{95\%}$]	p-value[a]
Average age at introduction (days)			<0.001
12–28	62 (34)	0.73 [0.15;1.73][a]	
29–34	48 (26)	1.27 [0.32;2.30]	
35–240	73 (40)	0.60 [0.00;2.09][a]	
Average length of time in herd (days)			<0.001
131–255	56 (31)	1.10 [0.00;3.19][a]	
256–290	61 (33)	0.86 [0.21;2.14][a]	
291–641	66 (36)	0.47 [0.06;1.31]	
Number of purchases (in 2014)			0.004
7–45	65 (36)	0.59 [0.00;2.01][a]	
46–60	52 (28)	0.60 [0.19;2.14][a]	
61–233	66 (36)	0.96 [0.18;2.49]	
Purchase of calves from markets or delivering traders			0.980
–	174 (95)	0.78 [0.05;2.24]	
+	9 (5)	0.83 [0.29;1.67]	
Vaccination			0.927
–	166 (91)	0.77 [0.05;2.26]	
+	17 (9)	0.83 [0.28;1.97]	
Potential continuous risk factors	Estimate	SE	
Log_{10} (Calves introduced)	1.52	0.13	<0.001

[a] For categorical variables, a *t*-test or ANOVA was performed on the Box-Cox transformed outcome ($(ADD_{200}/100\ calves/day + 0.00275)^{0.424}$). Superscripts of lower case letters indicate non-significance in the antimicrobial usage between strata of the given variable. For the continuous variable, the result from the univariable linear regression on a non-transformed outcome is presented.

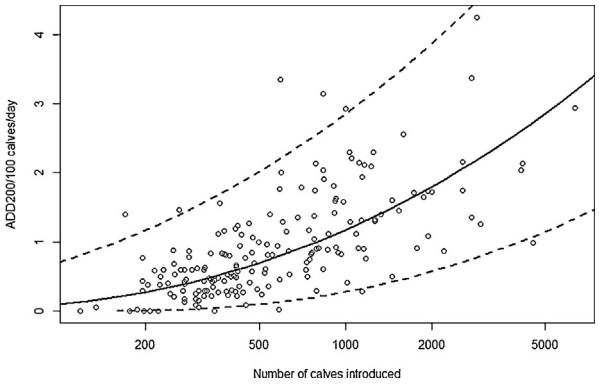

Fig. 4. Prediction lines for the antimicrobial usage based on the number of introduced calves in 183 Danish full-line herds producing veal and young bulls. Prediction lines are estimated based on a linear regression analysis with the number of introduced calves as only significant risk factor for antimicrobial usage in Danish veal calf herds. The x-axis is on the log-scale.

(p = 0.037). No effect was demonstrated from purchase from markets/delivering traders or vaccination (Table 2). Only one vaccine was used against respiratory disorders. This was a combination vaccine holding inactivated bovine respiratory syncytial virus (BRSV), parainfluenza-3-virus (PI-3) and *Mannheimia haemolytica* serotype A1.

The initial regression analysis included average age at introduction, average length of time in the herd, frequency of purchase, vaccination, breeding of own calves and number of calves introduced. The final model had $(ADD_{200}/100\ calves/day + 0.00275)^{0.424}$ as outcome and log10(number of introduced calves) as only significant risk factor (p < 0.001) with an intercept of −1.04 (SE = 0.16) and an estimate of 0.70 (SE = 0.06). The predicted antimicrobial use (back-transformed) as a function of the number of introduced calves is presented in Fig. 4.

4. Discussion

Antimicrobials registered for the selected 325 large veal calf and young bull producing herds, covered 51% of the total amount of antimicrobials registered for calves in Denmark. The majority of antimicrobials (78.9%) were registered for respiratory disease. This is in line with previous studies showing bovine respiratory disease to be the clinical indication of 56.1% (Pardon et al., 2012b) to 73% (Lava et al., 2016b) of the antimicrobial treatments. Penicillin is the recommended first drug of choice for respiratory diseases (SEGES Dairy and Beef Research Centre et al., 2013), yet, in our study, this accounted for only 9% of the antimicrobials registered for respiratory disorders (Fig. 2). Incongruence between recommendations and use may be due to tradition, unawareness or a lack of clinical effect.

The second largest amount of antimicrobials was registered for joints/limbs/CNS disorders (17.1%). This VetStat category includes a number of various disorders which clinically are not related, e.g. omphalitis, arthritis, otitis media and interdigital phlegmon. Based on VetStat registrations, it is not possible to specify which clinical conditions registered drugs are supposed to target. Arthritis is more prevalent in young calves, while interdigital phlegmon typically is seen in older calves >240 days of age. Hence, a large amount of antimicrobials may be used for the latter, but only cover a relatively small number of treatments due to the treatment of heavier cattle (Ortman and Svensson, 2004). Pardon et al. (2013) found otitis and arthritis to represent 1.5% and 1.6% of the initial causes of antimicrobial treatment, which can be explained by a high prevalence of *Mycoplasma bovis*. *M. bovis* is highly prevalent among veal calves in Europe (Arcangioli et al., 2008; Radaelli et al., 2008; Pardon et al., 2013) and North America (Soehnlen et al., 2012). Recently, *M. bovis* has also been found in Danish veal calf herds (Nielsen, 2016) and may be responsible for a proportion of the treatments of joints/limbs/CNS and respiratory disorders in young calves. Mycoplasmas are innate resistant to penicillin (Taylor-Robinson and Bébéar, 1997), which may explain the relatively low use of penicillin (Fig. 2).

Although injection of antimicrobials requires a higher workload, more on-farm awareness and well-educated staff (Pardon et al., 2012a) compared to peroral administration, the vast majority of antimicrobials used in Danish veal calves and young bulls were administered parenterally (85.4%). Only 14.6% were administered orally, in contrast to white veal calf production in Switzerland (84.6%) (Lava et al., 2016b) and Belgium (95.8%) (Pardon et al., 2012a). An explanation of this difference in administration routes may be found in the feeding. Shortage on roughage for white veal calves reduces ruminal development to a well-functioning fermentative process, enabling oral administration of antimicrobials. The official Danish guidelines on antimicrobial treatment of cattle merely recommend oral administration of antimicrobials for gastrointestinal disorders of calves, such as *Escherichia coli* infections in preweaned calves. Caution against oral administration is based on limited absorption, as well as side effects for the intestinal flora (SEGES Dairy and Beef Research Centre et al., 2013). Additionally, oral administration of antimicrobials has been found associated with the development of antimicrobial resistance (Bos et al., 2012; Burow et al., 2014). Despite the allocation of oral antimicrobial treatments for gastrointestinal disorders, the majority of oral treatments were registered for respiratory disorders (Fig. 2).

Large variation was seen in antimicrobial usage between herd types (Fig. 3). As the majority of treatments is targeted respiratory disorders in the beginning of the fattening period (Pardon et al., 2012b), starter and full-line herds are expected to house the majority of diseased calves. In full-line herds, treatment of disease in the beginning of the production period is evened out by a longer time in the herd, which may explain the significantly lower use of antimicrobials compared to starter herds. Compared to Danish pig herds, Danish veal calf and young bull producing herds seem to use less antimicrobials. As shown in Fig. 3, the median standardized usage of antimicrobials (ADD_{200}/100 animals/day) was 2.14 in starter herds, 0.48 in finisher herds, 0.78 in full-line herds and 0.62 in herds with inconsistent movements. The median use of antimicrobials in Danish pig herds in 2012–2013 was around 8.0 for weaners, 0.8 for finishers and 1.8 for sows (Fertner et al., 2015). This higher usage in weaner pigs may be explained three main factors, Firstly, the indication of treatment differed, with gastrointestinal disorders being the primarily indication for treatment in pigs (Jensen et al., 2014), while respiratory disorders dominated in large veal calf and young bull producing herds. Secondly, pigs are categorized into more age-groups, which imply the standard weights for pigs being closer to the actual weight at treatment (15 kg (weaners), 50 kg (finishers) and 200 kg (sows/piglets)) compared to veal calves and young bulls (200 kg), where the applied standard weight is higher than the expected weight at treatment. Thirdly, the higher turn-over of pigs, where finishers are slaughtered at the average age of 5–6 months (Danish Agriculture and Food Council, 2014) may explain a higher usage.

One ADD_{200} may represent the treatment of one 200 kg calf or three 67 kg calves in one day. This means that when we use ADD_{200} for all veal calf and young bull producing herds, the estimated number of treatments in starter herds is likely to be underestimated, compared to the estimated number of treatments in finisher herds. We assumed that all registered drugs for a given age group on a given herd were actually consumed by that group of animals at the point in time where the drugs were purchased. This is most likely not the case. However, due to the long study period (one year) we expect irregularities in purchase patterns to be evened out to reflect an averagely actual usage.

The number of introduced calves and the number of suppliers were strongly correlated, which hindered the inclusion of both factors in the final risk factor analysis. Both factors are proxies for the risk of introducing pathogens and may impact the antimicrobial usage. Woolums et al. (2013) found the detection of respiratory disease in nursing beef calves to be positively associated with herd size. In addition, Taylor et al. (2010) and Cusack et al. (2003) reported commingling of cattle from various sources to increase the risk of respiratory disease, like Lava et al. (2016a) reported the purchase of veal calves to increase mortality, unwanted early slaughter and the application of metaphylaxis. Taylor et al. (2010) further reported purchase of calves from markets as a risk factor of respiratory disease. As demonstrated in our results, relatively few calves were sold on markets or through delivering traders in Denmark, which may explain, why we did not see an effect of these factors on the amounts of antimicrobial used. Due to the setup of the study as purely based on data from registers, it was not possible to study the effect of influencing factors in the management such as housing and shared air space.

Registration of purchased vaccines against BRSV, PI-3 and *Mannheimia haemolytica* serotype A1 was not found to influence the amount of antimicrobials. Due to the limited amount of herds using vaccines, we chose to dichotomize the variable in the risk factor analysis, as usage or not. A part of the insignificance may be explained by the limitations in our data. We only evaluated the effect on vaccination in the veal calf and young bull producing herd and not in the supplying dairy herd. Neither did we evaluate the administration procedure. An optimal vaccination program would require the supplying dairy herd manager to administer the vaccine 2–3 weeks prior to delivery in order to ensure sufficient immunoresponse at the time of arrival in the veal calf herd (Cusack et al., 2003). Another explanation of the insignificance may be found in the variety of pathogens. In Denmark, the most prevalent pathogens isolated from severe outbreaks of calf pneumonia in mono- or multi-culture include BRSV, *Pasteurella multocida*, *Histophilus somnus*, *Mannheimia haemolytica*, *Trueperella pyogenes* (Tegtmeier et al., 1999), Bovine coronavirus (Liu et al., 2006) and recently *M. bovis* (Nielsen, 2016), while PI-3 seems to play a minor role (Tegtmeier et al., 1999). Hence, a range of other pathogens may be involved in respiratory disorders than those three included in the vaccine. Cusack et al. (2003) did also not find any effect of vaccination on the prevalence of respiratory disorders and attribute the non-significance to the possibility of multiple pathogens being involved in the infection, making it infeasible to vaccinate against all.

Studies on antimicrobial treatment incidences in white veal calves in European countries have previously been carried out (Pardon et al., 2012a; Lava et al., 2016b). Treatment incidences in these two studies were not comparable to our results due to two issues: The lack of standardized standard dosages and the lack of standardized standard weights. Approved dosages of products with identical active substance and administration route have been found to differ almost four-fold between countries and up to ten-fold within the same country (Postma et al., 2015). Likewise, a consensus on approved standard weight is lacking. Previous publications have suggested or applied standard weights of 164 kg (Pardon et al., 2012a; Lava et al., 2016a,b), 140 kg (European Medicines Agency, 2015) and 172 kg (MARAN, 2016). Considering the large differences between white and rosé veal calves, it might be worthwhile to differentiate standard weights as done in the Netherlands (white (160 kg), rosé starter (77.5 kg) and rosé finisher (232.5 kg)) (Bos et al., 2013).

In VetStat, calves are defined as all bovines that have not calved. Hence, it is not possible to distinguish between heifers, young bulls and veal calves. We therefore excluded herds which seemed to produce heifers for dairy herds. Despite of the selection of large veal calf producers only, we still found quite some variation in production, e.g. herds producing both veal and young cattle. This may indicate a more heterogeneous Danish veal calf production compared to countries with a larger production of veal calves (Bos et al., 2012).

5. Conclusion

Based on register-data, we characterized the amount of used antimicrobials for large Danish herds producing veal calves and young bulls in 2014. Respiratory disorders followed by joints/limbs/CNS disorders were the diagnostic groups for which most antimicrobials were registered. The majority of antimicrobials were administered parenterally (85.6%), mainly with long-acting formulations.

For full-line herds we found the number of introduced calves to be positively associated with the amount of registered antimicrobials.

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