Vetstat - Monitoring usage of antimicrobials in animals

N. Dupont and H. Stege

University of Copenhagen, Grønnegårdsvej 2, 1870 Frederiksberg C, Denmark

Abstract

Following increasing focus on antimicrobial (AM) usage and risk of bacterial resistance, an on-going, national monitoring system of all veterinary drug use was implemented in Denmark in 2000. Information is reported by veterinarians and pharmacies and stored in a central database, Vetstat. Information includes prescribing veterinarian, receiving herd, product name, amount of product, animal species, age group and diagnostic group. Based on this information, various estimates of the Danish AM usage for production animals are regularly presented. The estimates may include conversion from amount of active compound to "Animal Daily Doses" (ADD) and different means of adjusting for number of animals available for treatment. Consequently these conversions introduce risks of inconsistency, misclassification and disagreement when reporting AM consumption.

The aim of this paper is: 1) to describe the structure and content of Vetstat, 2) to discuss possible pitfalls when designing a system as Vetstat and 3) briefly present the overall AM usage in Danish cattle herds from 2007 to 2011, including a discussion of the main sources of errors.

Results: In 2011 an estimated 13.7 tons AM were prescribed for cattle equivalent to 8.7 grams AM per live cattle in 2011. The total amount of AM resembles approximately 18.7 million ADD, which would imply that 3.4% cattle>2 years of age and 5.2% of cattle <1 year of age were treated daily. The most used AM for systemic treatment in 2011 were narrow spectrum penicillins. Diseases related to the mammary glands were the predominant indication for AM treatment (29% of treatments).

Keywords: antimicrobial consumption, surveillance system, pharmaco-epidemiology, Vetstat

Introduction

The association between resistant bacteria strains and use of antimicrobials (AM), especially growth promoters for production animals is well established (Agersø and Aarestrup, 2013; Lathers, 2001; Martel *et al.*, 2001; Aarestrup *et al.*, 2001). The possibility of such resistant bacteria entering the human food chain caused growing concern in Europe during the 1990s. Consequently, an EU conference ("The Microbial Threat") was held in Denmark in 1998. One of the recommendations issued was to monitor the veterinary use of AM more closely. In order to comply with these recommendations, Denmark instigated an on-going surveillance program in 2000 of the medical consumption for (production) animals, collecting all data in a national database, Vetstat (Stege *et al.*, 2003).

The aims of this on-going Danish program are:

1. monitor veterinary usage of drugs in animal production;
2. help practitioners in their work as farm advisors;
3. provide transparency as a basis for ensuring compliance with 2 rules and legislation and
4. provide data for pharmaco-epidemiological research." (Stege *et al.*, 2003).

The purpose of this paper is to:

1. describe the structure and content of Vetstat;
2. discuss possible pitfalls when designing a system as Vetstat and
3. briefly present the overall AM usage in Danish cattle herds from 2007 to 2011, including a discussion of the main sources of errors when reporting AM consumption.

Vetstat - structure and content

Vetstat is a relational database on an Oracle platform and is owned and managed by the Ministry of Food, Agriculture and Fisheries. During the nineties many legislative regulations were passed by the Danish government to curb AM sale. The regulations included limits on veterinary profits from sale of AM and a ban on use of growth promoters in production animals (Aarestrup *et al.*, 2010). All AM and the largest majority of all other veterinary therapeutic drugs are prescription-only in Denmark. Virtually all sale of veterinary medicine are made through pharmacies, veterinary practitioners or feed mills. Data on medicine consumption are therefore submitted to Vetstat by these three entities (Figure 1). Pharmacies and feed mills purchase drugs directly from the drug manufacturers. Veterinary practitioners purchase drugs for use in practice from pharmacies. All pharmacies, veterinary practitioners, veterinary practices and feed mills have a unique ID. Content of entries to Vetstat are shown in figure 2.

Vetstat's definitions of animal species, age group and diagnostic group are shown in table 1.
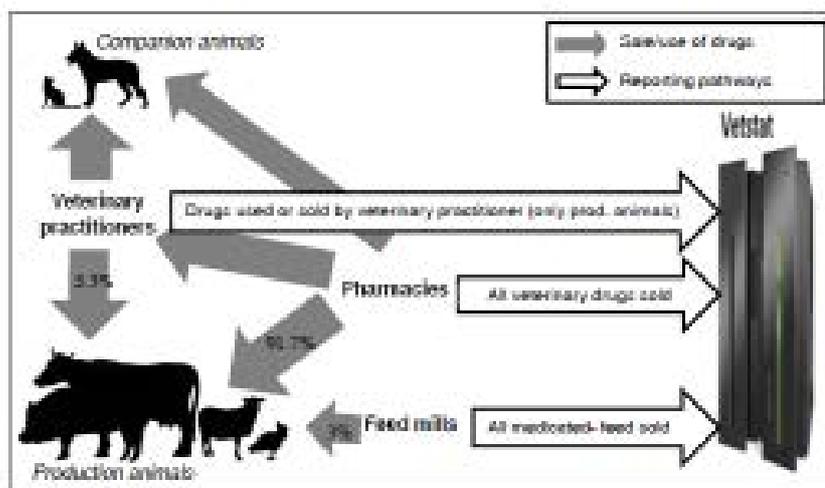

Figure 1. Reporting pathways- Vetstat and percentage of total kg AM active compound reported for production animals in 2011.
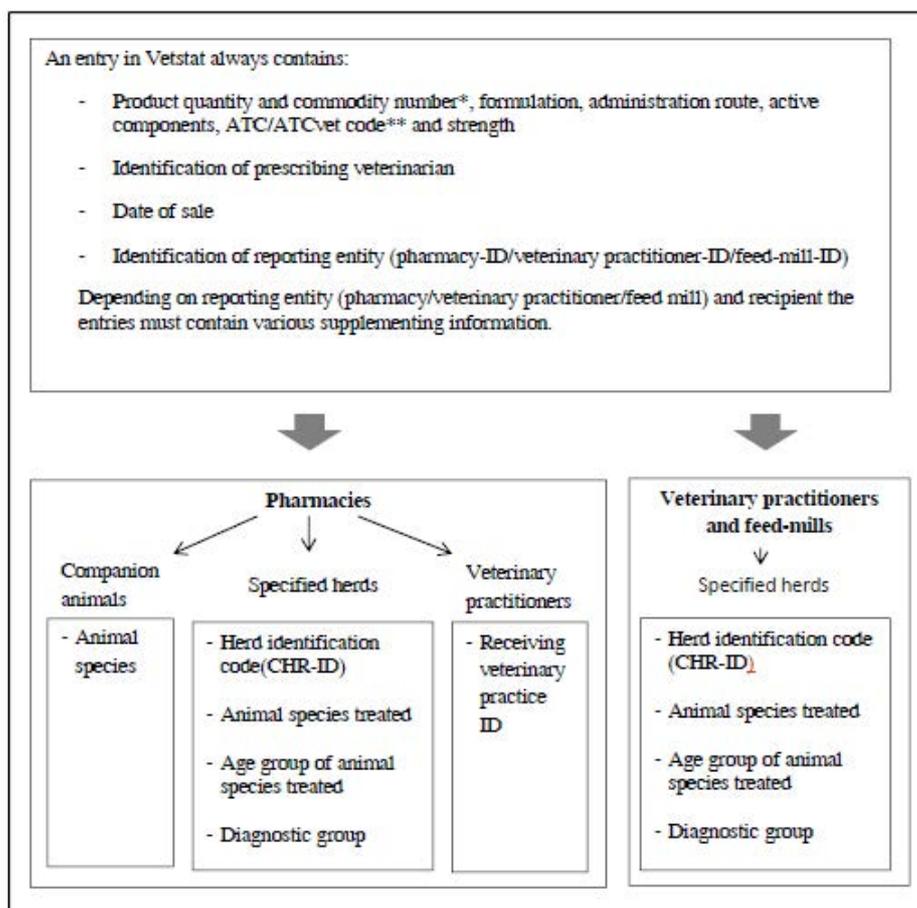
An entry in Vetstat always contains:

- Product quantity and commodity number*, formulation, administration route, active components, ATC/ATCvet code** and strength

- Identification of prescribing veterinarian

- Date of sale

- Identification of reporting entity (pharmacy-ID/veterinary practitioner-ID/feed-mill-ID)

Depending on reporting entity (pharmacy/veterinary practitioner/feed mill) and recipient the entries must contain various supplementing information.

Pharmacies

Companion animals	Specified herds	Veterinary practitioners
- Animal species	- Herd identification code(CHR-ID) - Animal species treated - Age group of animal species treated - Diagnostic group	- Receiving veterinary practice ID

Veterinary practitioners and feed-mills

Specified herds

- Herd identification code (CHR-ID)

- Animal species treated

- Age group of animal species treated

- Diagnostic group

Figure 2. Content of entries according to reporting entity and recipient of drug.

*The Nordic commodity number identifies name of medicinal product, strength, form and size of packaging.

**The Anatomical Therapeutic Chemical classification system identifies all human drugs in a five-digit hierarchical system. Products with the same active substance in the same pharmaceutical formulation are given the same ATCcode. The ATCvet system is the veterinary counterpart (Dahlin et al., 2001).

All Danish pharmacies have electronic and standardized billing systems. These are linked to Vetstat, which ensures automatic transfer of data on all veterinary drug purchases. This improves the validity of data on quantity and commodity number of drugs sold.

Electronic journal systems are used by most Danish veterinary practices[1]. These softwaresystems automatically transfer data on all treatments regarding production animals to Vetstat in connection with billing. The software-systems are developed and distributed by private companies and there are no official guidelines or

Submission of data to Vetstat

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[1]TANG-dyrlægeløsning(TANG data) and Vetvision(Novasoft).

Table 1. Vetstat definitions of animal species, age group (including according standard weight) and diagnostic group.

Animal species	Age group (standard weight -kg)	Diagnostic group
Pigs	Breeding animals, gilts, suckling pigs (200) Weaners (15) Finishers (50)	Reproduction, urogenital system Udder Gastro-intestinal system Respiratory system Joints, limbs, hooves, CNS, skin Metabolism, digestion, circulation
Cattle	Bulls, cows (600) Calves <12 months (100) Heifers, steers (300)	
Sheep, goats	>12 months (50) <12 months (20)	
Mink	Not recorded (1)	Other (mink only)
Aquaculture	Not recorded (1)	Red mouth disease Furuncolosis Brood syndrome Other
Poultry	Broilers (0,2) Layers (1) Rearing flocks (1)	Abdominal organs Coccidiosis Enteritis Hepatitis Salpingitis Other Respiratory system/organs
Other production animals*	Not recorded (1)	
Horses	Not recorded (500)	Not recorded
Pets	Not recorded (not given)	

*Llamas, rabbits, deer, ostriches

legislation on the setup. A few veterinarians choose to report data directly into Vetstat, either manually on the Vetstat webpage or by discs sent to the Ministry of Food, Agriculture and Fisheries. According to Danish legislation veterinarians must report drugs used for production animals at least once per month.

Only few substances are approved for pre-mixed medicated feed for production animals. The purchases are reported directly to Vetstat by the feed-mills.

Herd identification code- system

Since 1993 all Danish herds have been legally required to register in the Central Husbandry Register (CHR-register). The CHR-register is, as Vetstat, owned and managed by the Ministry of Food, Agriculture and Fisheries. All herds are given a unique identity code (CHRID) relating to the geographical coordinates of the herd in question (Madec *et al.*, 2001). In addition to information on geographical location the register also contains data on production type and number of animals present in the herd (animal species, age group) and contact information on the herd owner

(Mousing *et al.*, 1997). By law all changes in number of animals must be reported to the CHR-register no later than 7 days after the event for cattle and once per year for pigs[2].

All Danish drugs, both human and veterinary, must be approved either by the Danish Health and Medicines Authority or the European Medicines Agency. Newly approved veterinary drugs are registered into Vetstat every second week manually by a ministry employee. Information must include:

- Commodity number
- Active component(s)
- Strength
- Package size
- Formulation
- Administration route
- ATC/ATCvet code
- Average daily maintenance dose per kg live animal for the main indication according to relevant animal species (DMDkg)

Standard values on recommended dosage are published yearly by the Danish Health Authorities.

List of veterinary products

Several units have been proposed to quantify AM drug consumption for production animals (Callens *et al.*, 2012; Chauvin *et al.*, 2001; Eagar *et al.*, 2011; Timmerman *et al.*, 2006). In the Danish surveillance of AM consumption usage for production animals is mostly reported as:

- kg active compound AM consumed
- (number of) Animal Daily Doses (ADD)
- ADDs per 100 animals per day (percentage treated per day)

Quantification of drug consumption

ADD is defined as the daily maintenance dose per live animal for the main indication. Therefore ADD provides a measurement that takes potency of drugs into account. ADD enables reports on AM consumption to adjust for differences in dosage regimens depending on animal species and size. To account for the large variation between weights in production animals, the parameter standard weight was introduced in Vetstat. Standard weight is the estimated average weight at treatment assigned to all major production animal species according to age group (Table 1). ADD is the veterinary equivalent to the human measurement "defined daily dose" (DDD) (Wertheimer, 1986). DDD is an international standardized measurement defined by WHO (Anonymous, 2009), whereas ADD is still calculated differently across borders. In Vetstat ADD is calculated as:

Calculation of Animal Daily Dose (ADD)

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[2]For herds with more than 300 sows, 3000 finishers or 6000 weaners, information on animal numbers must be updated biannually.

$$ADD = \frac{Total\ amount\ of\ active\ compound\ AM\ sold/used(mg)}{dosage\ pr\ kg\ live\ animal(DMDkg) * standard\ weight\ of\ animal}$$

Calculation example:

100 mL of EthacilinVet. containing 300 mg benzylpencillinprocain/mL for use in cows (600kg)

$$ADD = \frac{(100mL\ product * 300mg/mL)}{15mg/kg * 600kg} = 3,33 ADD$$

Adjustment for population size

To enable adjustment for herd size when reporting AM consumption, the parameter "percentage animals treated per day" (or ADD per 100 animals per day) was introduced by the Danish authorities. The number of "pen places", presumably resembling live animals at any given time, is currently used as denominator. Data on number of pen places (animals present in herd) are automatically derived from the CHR-register.

ADD per 100 animals per day is calculated as:

$$ADD\ pr\ 100\ animals\ pr\ day = \frac{ADD\ used}{number\ of\ pen\ places * days\ in\ period} \times 100$$

Calculation example:

150 ADD (cows/bulls) used in a herd with 400 pen places in January (31 days).

$$ADD\ pr\ 100\ animals\ pr\ day = \frac{150\ ADD\ used\ (total\ in\ 31\ days)}{400\ pen\ places * 31\ days} \times 100 = 1,2$$

Equaling an estimate of 1,2% of cows treated per day during January.

User-access to Vetstat-data

Data on overall national AM consumption for all animal species and for pigs specified are presented online on the webpage of the Ministry of Food, Agriculture and Fisheries.

Detailed data on all entries into Vetstat are accessible to veterinarians and farmers on Vetstat's webpage vetstat.dk. Farmers can monitor all entries regarding their own herds. Veterinarians can monitor all entries submitted by themselves. Veterinarians can monitor all entries on herds with whom they have a Health Advisory Agreement (HAA)[3]. Automated graphic reports can be made on AM consumption for each individual herd reported as ADD per 100 animals per day.

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[3]HAA's are mandatory for Danish herds of a certain size (>100 cows or >200 heifers and steers. They cover rules on frequency of veterinary visits, treatment schemes and management.

Challenges and benefits of health data recording for food chain quality, management and breeding

Since spring 2012 it has been possible for any member of the public to obtain access to detailed data excerpts from Vetstat. Possible pitfalls when designing a system as Vetstat

Presently there is no automatic linking of animal species, age group and diagnostic group. This makes it possible to make an entry containing logically diverging values e.g.: animal species "cattle", age group "broilers" and diagnostic group "furunculosis". In 2011 1.4% entries reported by pharmacies on drugs for use in cattle herds either stated an invalid age group, diagnostic group or both.

Possible pitfalls when designing a system as Vetstat

Furthermore cases of erroneous data on prescribing veterinarian-ID are known to the authors. A validation process was introduced in 2003 (Jensen *et al.*, 2004), where prescribing veterinarian-ID is checked against the Danish veterinary authorities' list of registered veterinarians. Despite this, entries still occur where the entered veterinarian-ID does not correspond with the ID of the actual prescribing veterinarian. The authors speculate this might be due to typing errors by the reporting entity or misreading of the veterinarian-ID on handwritten prescriptions.

Vetstat only incorporates data on consumption submitted by the three reporting entities (pharmacies, veterinary practitioners, feed-mills). Reporting procedures have improved much since Vetstat was first implemented in 2000. This is important to keep in mind, especially when evaluating consumption over time. An increase in AM consumption according to Vetstat might not be a true increase in consumption, but rather a reflection of increased registration of consumption. Data registrations by pharmacies are considered complete. Since the 1980s all Danish pharmacies have employed a standardized IT-based reporting system, reporting all purchases of drugs to the Danish Health and Medicines Authority. The same cannot be said for data from veterinary practitioners. It is estimated that registrations on up to 25% of AM used in cattle practice were missing for several years following the launch of Vetstat (DANMAP, 2003). From 2010 to 2012, the estimate has been that 10% of AM used in veterinary cattle practice were not registered into Vetstat by the veterinary practitioners (DANMAP, 2012).

The lack of consistency in registrations by veterinary practitioners might be due to many factors, such as lack of entries being submitted by veterinary practitioners or due to rejection by the Vetstat database procedures[4]. Veterinary practitioners also had the drawback that they did not already utilize an existing, automatic reporting system when Vetstat was implemented, such as the pharmacies did.

In 2011 36% of the AM registered for use in cattle were purchased through veterinary practitioners (Figure 3). Contrary to this, less than 0,1% of the AM purchase for pigs were directly through veterinary practitioners. Therefore data validity on Danish pig AM consumption is considered better than that on cattle Am consumption.

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[4]Until 2011 entries submitted by veterinary practitioners lacking information on any of the required parameters were allocated to en error table in Vetstat for correction.

Effect of calculation routines on AM consumption reports

Data on the Danish AM consumption for cattle are published yearly by DANMAP - the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (DANMAP, 2012). To adjust for potential missing registrations by veterinary practitioners, DANMAP calculates AM consumption for cattle (kg active compound) as:

DANMAP cattle AM
= *AM sold directly for use in cattle herds from pharmacies*
+ *AM sold for use in cattle practice from pharmacies*

By applying this method, AM consumption is estimated relying solely on data registered by pharmacies. Registrations by pharmacies on AM sold for use in veterinary practice do not include information on animal species (figure 2). Therefore this method is not without flaws as:

1. AM used in mixed practice for cattle are not included.
2. AM used for non-cattle are included if used by veterinarians employed in cattle practice.

An alternative to the DANMAP method is solely to include data where animal species have been explicitly specified as "cattle". This method does not adjust for missing registrations by veterinary practitioners.

When comparing AM consumption according to these two methods there is a discrepancy of 4-15% (Table 2) (DANMAP, 2008, 2009, 2010, 2011, 2012).

This comparison highlights the importance of meticulous description of calculation routines when publishing numbers on AM consumption. DANMAP reports can be accessed at *www.danmap.org*.

Antimicrobial consumption in Danish cattle according to Vetstat data

All Vetstat data were assessed for entries where animal species "cattle" were given. The reported AM consumption for Danish cattle increased from 12.7 tons in 2007 to 13.7 tons in 2011 equivalent to 7. 9 and 8.7 grams AM per live cattle respectively. In 2011 AM reported by pharmacies for cattle constituted 64% of total reported AM kg consumption for cattle (Figure 3).

Table 2. AM consumption (kg active compound) for cattle 2007-2011 according to Vetstat and DANMAP respectively.

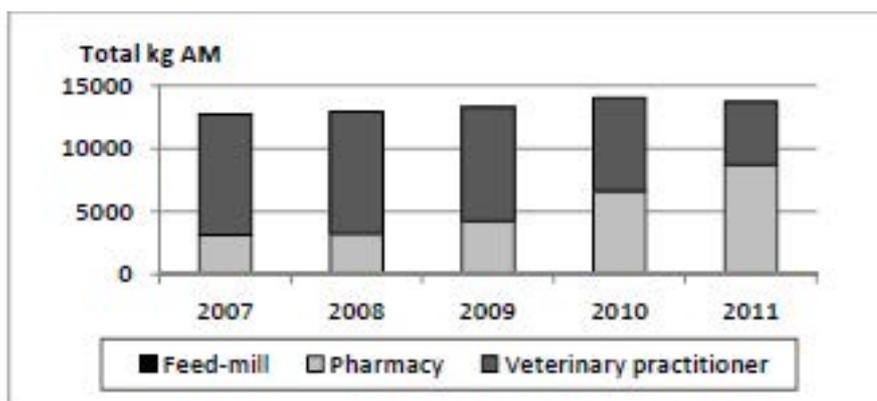|	Vetstat	DANMAP	Discrepancy (kg active compound AM)	Discrepancy in %
2007	12741	15000	2259	15.1
2008	12923	14500	1576	10.9
2009	13232	15000	1768	11.8
2010	14027	14636	608	4.2
2011	13671	14678	1006	6.9

Figure 3. AM consumption reported for use in cattle 2007-2011, shown as total kg active compound AM per year according to reporting entity. Feed mills account for less than 0,1% of consumption)

Figure 4 and 5 depicts the AM consumption in the different cattle age groups, reported as kg active compound and ADDs, respectively. The effect of adjusting for animal standard weight is obvious as the AM consumption for use in cows and bulls constitutes roughly 80% of the total amount of active compounds, whereas it constitutes about 45% % of the total ADDs.

Figure 5 also shows the total Danish cattle population, which has increased slightly with 1.5% from 2008 to 2011. Due to changes in reporting methods reliable numbers on cattle population were not available before 2008.

The AM consumption for cattle in 2011 resembles approximately 18.7 million ADDs, which would imply 3.4% cattle>2 years of age and 5.2% of cattle <1 year of age were treated daily. This implies a 5% decrease since 2007 in AM consumption measured as ADD. This decrease may be even larger, due to an increase in cattle population and a decrease in lacking registrations from veterinary practitioners.
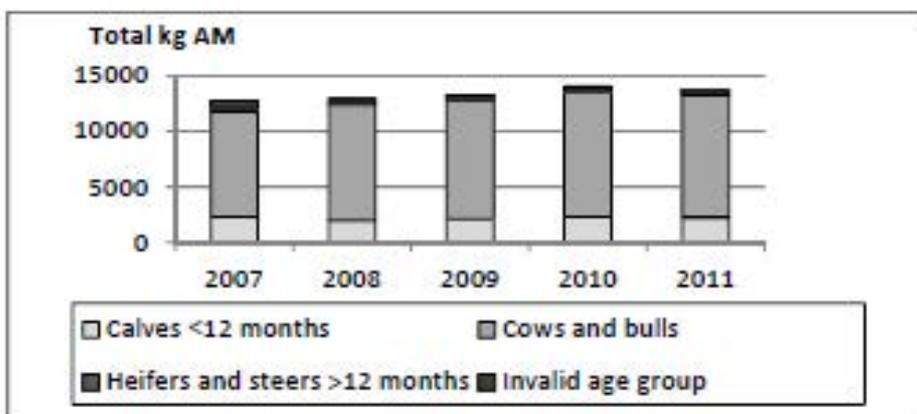

Figure 4. AM consumption reported for use in cattle 2007-2011, shown as total kg active compound AM per year according to age group.
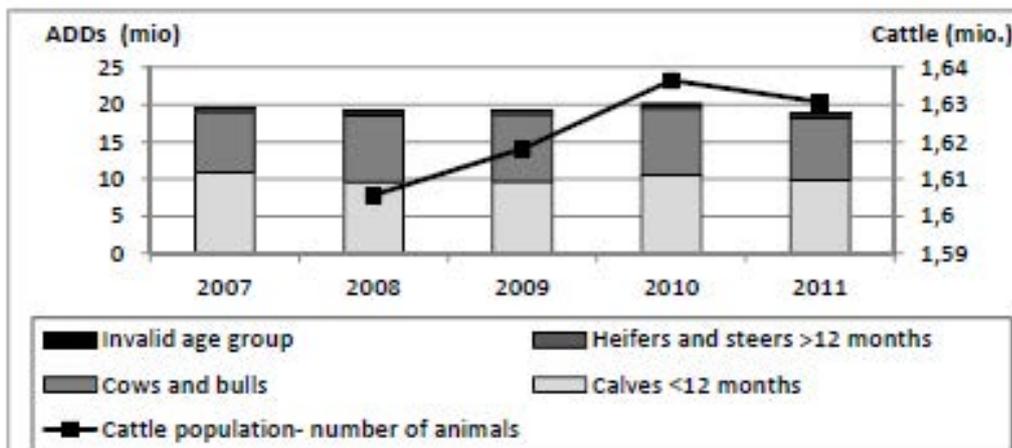
Figure 5. AM consumption reported for use in cattle 2007-2011, shown as ADD per year, according to age group and number of pen places from 2008-2011.
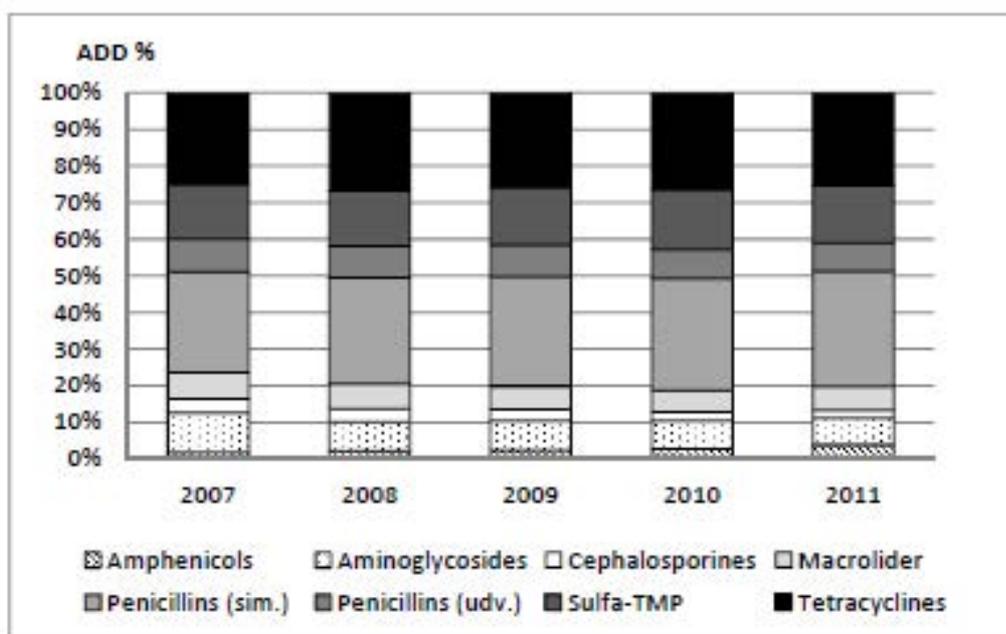

Figure 6. AM consumption reported for use in cattle 2007-2011, shown as percentage of ADD distributed according to ATC main group (Fluoroquinolones, lincosamides and pleuromutilins are not presented, as they each account for less than 1% of the consumption.

Pattern of AM consumption according to ATC main group has been relatively stable since 2007. The most used AM for systemic treatment in 2011 were narrow spectrum penicilllins (figure 6). Diseases related to the mammary glands were the predominant indication for AM treatment (29% of treatments) (Figure 7).
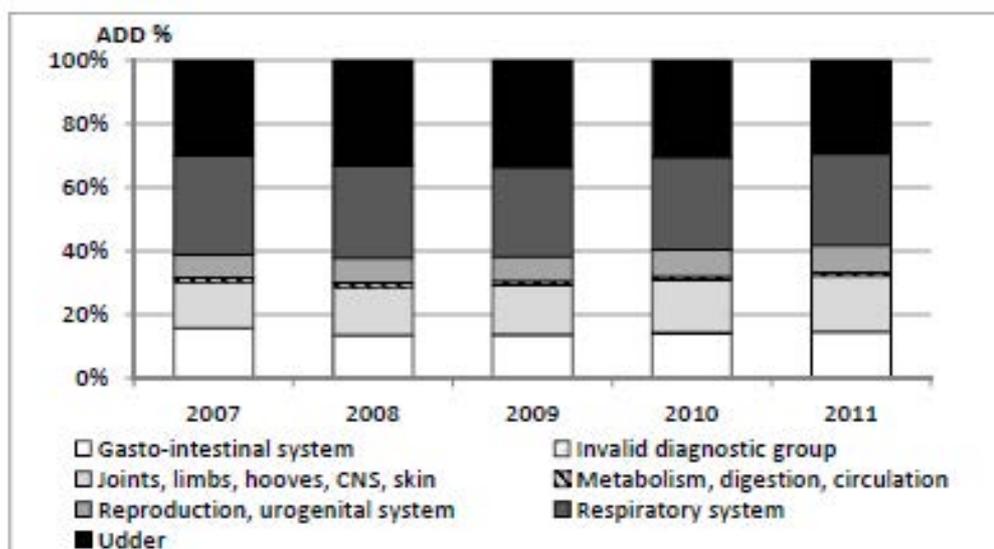
Figure 7. AM consumption reported for use in cattle 2007-2011, shown as percentage of ADD distributed according to diagnosis group.
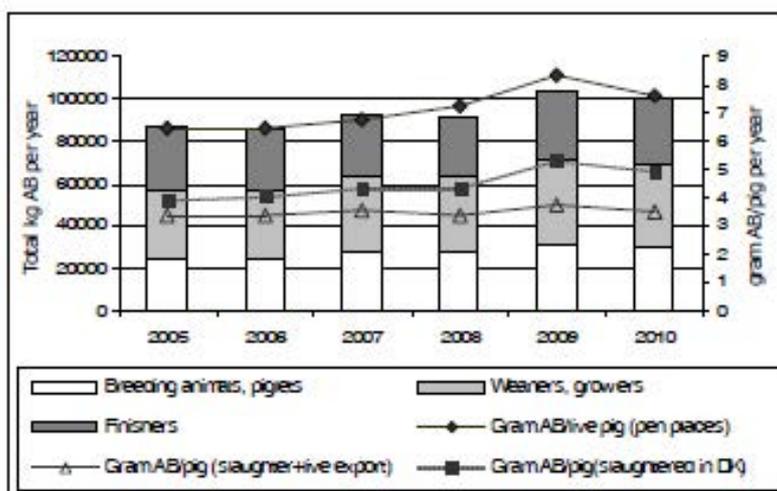

Figure 8. Danish consumption of AM for pigs 2005-2010. Measured in total amounts and as g/pig/year, using 3 different denominators

It is important to realize, that what holds true for DDD also applies to ADD ((Norway), 2012)). ADD does not necessarily reflect the prescribed-, used- or recommended daily dose. Drug consumption data presented as ADD only gives an estimate of consumption and not an exact picture of actual use.

AM consumption reports - Effect of animal population

To enable adjustment for population size when reporting AM consumption, Danish authorities presently use "number of pen places", presumably resembling live animals in herd at any time. This does not pose a large problem in the dairy industry, as turnover of animals per year is quite low (mortality rate of Danish cows in 2011 was 5.4% (Anonymous, 2012). But for herds with a large turnover of animals, such as fattening pig facilities, this may not be an accurate measure, as several generations pass the stable facilities each year.

When making international comparisons, it is also important, how number of animals produced each year are measured (e.g. with or without exported finishers). Pigs>30 kg that are exported for slaughter outside Denmark should be included, since they have received most of their AM treatment before export (measured in ADDs, the usage for weaners and growers constituted 77% of total usage in 2010). The export is especially important to take into consideration, when evaluating consumption over time as it increased 146% (3,1 to 7,8 million live pigs) from 2005 to 2010.

Many different takes on population estimation exists (Chauvin *et al.*, 2008; MacKenzie and Gould, 2005; Merle *et al.*, 2012). Figure 8 illustrates the pig AM consumption as gram active compound/pig/year from 2005-2010 applying three different population measurements:

1. Number of pen places.
2. Number of pigs slaughtered in Denmark.
3. Number of pigs slaughtered in Denmark + number of exported growers and finishers.

Data on number of pen places were collected from Statistics Denmark. Data on number of pigs produced were collected from Statistics - PIGMEAT including number of pigs slaughtered in Denmark and the number of pigs>30 kg, exported from Denmark each year. Student's t-test was used to test the difference between mean AM consumption/pig/year for 2005 and 2010.

Without adjusting for number of pigs, the consumption increased from 86.932 in 2005 to 100.066 kg in 2010 (i.e. 15%, p<0,05). Table 3 shows consumption/pig/year applying the three different measurements of pig population. The increase from 2005 to 2010 constituted 1.14g (17,7%), 1.0g (25,6) and 0.1g (3,9%)/pig/year, respectively. From 2005 to 2010 there was a significant increase in consumption/pig/year (P<0,001) when using "number of pen places" and "number of pigs slaughtered in Denmark". But the increase was not significant when measuring population as "pigs slaughtered in Denmark + number of exported growers and finishers".

Table 3. Danish consumption of AM/pig in 2005 & 2010 using 3 different denominators.

	Year		P- value
	2005	**2010**	
Gram AB/pen place	6.46	7.60	<0.001
Gram AB/pig slaughtered in DK	3.94	4.94	<0.001
Gram AB/pig slaughter+live export	3.40	3.51	0.3069

The authors conclude that population always should be included when reporting the AM usage. Also, there is an obvious risk of misclassification if the productivity is not taken into account.

Conclusions

In conclusion, Vetstat data offers a great opportunity to assess AM usage both at a national level and a herd level. But these data must used with caution. One must consider potential erroneous data, lacking registrations and changes in population, especially when evaluating AM consumption over time.

Acknowledgement

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