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ORIGINAL RESEARCH

Estimating antimicrobial usage based on sales to beef and dairy farms from UK veterinary practices

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Abstract

Background: Accurate estimation of antimicrobial use (AMU) is important in assessing reduction of agricultural AMU. This cross-sectional study aimed to evaluate several approaches for estimating AMU at the herd level and to report on AMU for beef and dairy farms in Scotland.

Methods: Pharmaceutical sales data for 75 cattle herds (2011–2015) were screened for antimicrobial products and aggregated by herd and year. Several denominators for usage estimates were calculated and compared for their suitability at the herd level.

Results: The median total mass of active ingredient sold per kg of bovine livestock was 9.5 mg/kg for beef herds and 14.3 mg/kg for dairy herds. The 'highest priority critically important' antimicrobials (HPCIA) were by total mass of active ingredient, 10.6% of all sales; by total defined daily dose veterinary (DDDVet), 29.8% and by DCDvet, 20.0%. These are the first estimates of AMU for beef cattle in the UK, and for cattle of any kind in Scotland.

Estimates of herd-level usage based on population correction unit (PCU) were sensitive to low values for PCU for specific herd-years due to their demographic composition.

Conclusion: Pharmaceutical sales data can provide useful estimates of AMU, but estimating usage per PCU is not appropriate for comparing groups of cattle with different demographic compositions or for setting herd-level targets. Total mass of active ingredient per kilogram of livestock is more stable and hence suitable than PCU-based methods for assessing AMU at the herd level.

INTRODUCTION

Antimicrobial resistance is a concern to animal and human health due to the risk of antimicrobial treatment failure.[1,2] Of primary concern is treatment failure in humans[3] and hence concern of possible transfer of resistance between animals and humans. Strategies for mitigating antimicrobial resistance in humans and animals have been recommended,[2] including defining country-level targets to reduce the use of antibiotics in agriculture. The UK government pledged to "reduce antibiotic use in livestock and fish farmed for food to a multispecies average of 50 mg/kg by 2018".[4]

In 2017, the Targets Task Force of the Responsible Use of Medicines in Agriculture Alliance (RUMA) set a target for the UK beef sector of either a 10% reduction on the 2016 figures, or of 10 mg/population correction unit (PCU) – whichever is lower on a mg/PCU basis.[5] For the UK dairy sector, the RUMA target for the total antimicrobial usage (AMU) is 21.0 mg/PCU by 2020.[5] The "population correction unit" is defined within Veterinary Medicines Directorate guidance as 'the standardised average mass in of all animals at time of treatment multiplied by the number of animals based on national statistics (live and/or slaughter);.[6] These PCU calculations were standardised and are typically used, for purposes of *national* level statistics, the most recent of which suggest a general downward trend for the UK, with headline figures of 17 mg/kg in dairy and 21 mg/kg in beef.[7]

We require good estimates of AMU to inform target setting and to assess progress towards those targets. Ideally, national targets would be translated into herd-level targets to facilitate both high-level national/strategic decisions and lower herd-level decisions. Targets need to be appropriate for the level at which they are applied, and different target types may be needed for different levels. Three relevant and common measures of AMU are the following:

- The total mass of active ingredient (a.i.) of antimicrobials administered per kg of animal,[8]
- The 'defined daily dose veterinary' (DDDvet): assumed average dose (i.e., total mass in mg of a.i.) per kg animal per day of treatment,[9]
- The "Defined Course Dose Veterinary" (DCDvet): assumed average dose (total mass of a.i.) per kg animal per treatment course.[9]

Estimates of AMU have been made for English dairy herds,[10] but, to our knowledge, there are no published estimates for beef cattle anywhere in the UK or for cattle of any kind in Scotland. Beef production in Scotland is dominated by a particularly extensive form of production.

Our aims were to evaluate several approaches for the measurement of AMU for their suitability at the herd level and to provide initial estimates of AMU at the herd level for Scottish cattle based on antimicrobial sales, by interrogating the sales records of one vet practice in Scotland.

METHODS

Data acquisition

The participating veterinary practice identified all commercial cattle farms (defined as those having more than 20 breeding cows) on its client list. Two farms were excluded because they were owned by members of the veterinary practice and thus considered atypical. The study size was determined by the available data. Pharmaceutical sales data were extracted from the practice database for each of these farms for each year between 2011 and 2015, inclusive. Farms were identified at the veterinary practice by County-Parish-Holding (CPH) number.

The numbers of beef and dairy cattle of different age classes (see the Supporting Information) on each of these farms at the time of the annual Agricultural and Horticultural Census in June of each year was extracted from data provided by the Scottish Government's Rural and Environment Science and Analytical Services Division (RESAS), with its permission. In order to maintain the anonymity of the farms, personnel in the participating vet practice office executed software that (1) extracted relevant demographic information from census data, (2) matched demographic data to pharmaceutical sales data based on the CPH number and (3) replaced the CPH number with an anonymized number. All potentially identifying information was withheld from researchers involved in the analysis.

Data cleaning

Demographic data

Herds were categorised as dairy or beef based on the veterinarian's knowledge of whether the herd was producing dairy products during the 2011–2015 period. We chose not to include a category 'mixed' to keep the comparisons simple. This is consistent with the Scottish Dairy Cattle Association's definition of a dairy herd: a 'farm that produces milk, from cows, for retail to a milk buyer for payment'.[11] We did not account for sheep, on the basis that where AMU for sheep has been measured, the estimates have been low in comparison to other livestock species.[12,13]

Pharmaceutical sales data

Any product containing a substance acting as an antibacterial agent (excluding disinfectants, antifungals and anthelmintics) was deemed to be an 'antimicrobial'. These products are listed in Table S3 (Supporting Information).

Antimicrobial sales records were retrieved via a sequence of filters illustrated in Figure Supp1 (Supporting Information). Records relating solely to species other than cattle or to non-antimicrobial products were discarded. Products with more than one target species including cattle were retained.

Defining the relevant characteristics of each product sold

Characteristics of each antimicrobial product were obtained and documented (see the Supporting Information). Unit prices were based on the practice's own data which pertained to the relevant time period.

Data processing

The quantity of antimicrobial active ingredient within each sale was estimated by dividing the price of that sale by the unit product price and multiplying by the quantity of that antimicrobial in the unit product. Quantities were aggregated as follows:

- Total mass of antimicrobial active ingredient (a.i.) used [excluding topical aerosols]
- DDDvet,[9] [excluding dry-cow intramammaries, topicals – both aerosol and non-aerosol]
- DCDvet,[9] [excluding topicals – both aerosol and non-aerosol]

Data analysis

Mass (mg) a.i. per denominator unit

For each herd-year, the total mass of antimicrobial a.i. per kg of animal – a ''primary indicator'[14] – was estimated based on the standard masses of animals described by the PCU.[6] Other denominators were also assessed, as described below and within the Supporting information: Table S1 and equations. All routes of antimicrobial administration were included for the calculation of total mass of a.i. per PCU except aerosol sprays.[10,15]

DDDvet and DCDvet

DDDvet units and DCDvet units are defined by EMA.[9] The ratio metrics (usage per measure of herd size) are calculated differently depending upon the administration route (Table S2 and equations in the Supporting Information)

Parenteral and oral antimicrobials
For parenteral and oral antimicrobials, we calculated the number of DDDvet and DCDvet per kg of adult cow by dividing the total DDDvets and DCDvets for each antimicrobial[9] in the packet(s) sold by the standard number of kg of all the adult cows (425 kg per cow)[16] in the herd. As the standardised mass of adult cows is unlikely to be appropriate (or even defined) for beef herds, we also used as our denominator the total mass of *all* cattle based on the standard set of masses[16] for both dairy and beef herds.

Intramammary antimicrobials
The DDDvet unit is defined by the unit dose of one dose per teat (commonly known as a 'tube'), and the DCDvet is the unit dose for one course for one teat (typically three 'tubes').[15] The standard denominator for both DDDvet and DCDvet for intra-mammaries is the number of adult cows. Note that for dry lactating cow intramammary therapy, there is no definition of DDDvet which is therefore not reported.[8,9]

Intrauterine antimicrobials
The DDDvet and DCDvet for intrauterine antimicrobials are defined as units of 'IUP' or intrauterine product (pessary or tube). We then divided this by the total number of adult cows in the herd for that year to get the number of DDDvets and DCDvets per adult cow.

For the calculation percentage of the total DDDvet or DCDvet that was 'highest priority critically important' antimicrobials (HPCIA), we summed the relevant numerator and divided by the summed denominator across all categories of records which shared the same definition of numerator and denominator to get the standard DDDvet or DCDvet. We then summed this calculated DDDvet or DCDvet from each of those two categories together. This was done for records that were HPCIA and compared to all records irrespective of their HPCIA status.

Topical/aerosol antimicrobials
Similarly topical products and aerosol spray products were not included in either DDDvet or DCDvet (dose undefined).

Denominator for beef and dairy herds

We used several approaches for calculating the PCU or other denominator mass: two for beef and three for dairy herds (Tables S1 and S2 and accompanying equations in the Supporting information), to facilitate comparison at the herd level and between these two sectors.

The EMA propose that the PCU for beef production be based on the number of animals going to slaughter.[16,17] In our case, this approach for calculating a PCU for beef herds was not directly applicable: we had data for animals *present*, rather than for those going to slaughter. Consequently for beef farms, we chose to use the following denominators:

- *DenB_slaught*: the sum of the PCU masses (see Table 3 of Appendix 2 in EMA, 2011,[16]) for cattle of both genders and both dairy/beef classifications in the age group 1–2 years, together with male cattle over the age of 2, which should approximately represent the mass of animals going to slaughter. This is the standard proposed by EMA.[16]
- *Den_cows*: To allow for the presence of beef animals on dairy farms (see below), we calculated the PCU for each herd-year in beef herds based on all cows over 2 years old of both dairy and beef breeds.
- *Den_all*: the sum of PCU masses of *all* bovines present in beef herds based on the standard PCU masses for each age class.[16]

For dairy herds, we used the following denominators:

- *PCUD_std*: The standard proposed by EMA[16] is the total PCU for dairy herds is based on the standard PCU for a 'livestock' dairy cow (425 kg)[16] multiplied by the number of dairy cows (with or without calves).
- *Den_cows*: To account for the presence of beef animals on dairy farms, we calculated the alternative total PCU (described above for beef herds) for each dairy herd-year, which was based on all cows over two years old of both dairy and beef breeds.

TABLE 1 Size profile of the herds in our study compared with that of Scottish herds as derived from the Scottish Government (tables C11, C12 (The Scottish Government 2017))

Number of dairy cows per herd[a]	Scotland Percentage holdings with dairy cows	Study farms Percentage holdings with dairy cows	Scotland Number of beef cows per herd[b]	Scotland Percentage holdings with beef cows	Study farms Percentage holdings with beef cows
1–4	38.9	12.8	1–4	20.7	8.4
5–19	6.4	2.0	5–19	24.1	18.6
20–49	4.1	5.9	20–49	22.3	33.5
50–74	5.9	25.1	50–74	11.3	16.0
75–99	6.7	25.1	75–99	7.7	8.4
100–149	13.9	12.8	100–149	7.8	10.3
150 &and over	24.1	16.3	150 and over	6.1	4.9

[a]Female dairy cattle aged 2 years or over with offspring.
[b]Female beef cattle aged 2 years or over with offspring.

- *Den_all*: Finally, to facilitate comparison with results from beef herds, we used the same denominator for dairy herds, which was the total mass (kg) of *all* bovine animals recorded on the farm for each herd-year and based on the standard PCU masses for each age class.[16]

In all calculations, any observation (herd-year) for which no animals were recorded at the time of the June census was removed from the calculation of the summary statistics. A single herd with no recorded animals in four out of five herd years as also removed from this calculation. Any herd-year for which there were no pharmaceutical sales at all was treated as missing rather than zero.

Data processing and analysis was carried out in R version 3.4.4[18] using core R plus packages *dplyr* and *ggplot2*, and Microsoft Excel.

Ethical approval

Following the submission of an SRUC ethical approval application form (02/04/2019), we were advised that due to the nature of the study no further ethical approval was required.

RESULTS

Pharmaceutical sales and herd demographic data were obtained for the years 2011–2015 for 39 beef and 36 dairy herds. There were several examples of dairy cattle in beef herds (33 out of the 193 beef herd-years) and of beef cattle in dairy herds (159 out of the 180 dairy herd-years).

Herd size

Compared to the range of herd sizes found in Scotland, in our study we had fewer large and small dairy herds. For beef herds we had fewer small herds but otherwise had a similar size distribution to Scotland as a whole (Table 1).

Consumption patterns of antimicrobials

In aggregate, the total consumption of antimicrobial among beef herds was 9.5 mg/kg of bovine animal and 14.3 mg/kg for dairy herds.

Mass (mg) a.i. per kg or PCU for beef and dairy herds

Patterns for mass of a.i. used per kg or PCU are shown in Table 2. In most cases, the mean was substantially higher than the median amount of a.i. used, indicating wide ranges and high maximums of AMU across herd-years for each of the different measures. The highest values of mass of antimicrobial per denominator came from herd-years with the lowest denominator values.

DDDvet and DCDvet

Due to the uncertainty in the denominator for the DDDvet and DCDvet, results are separated according to the calculation adopted, following the ESVAC/EMA guidelines (Table 3). Dairy herds used more DDDvet and DCDvet than beef herds in each of the respective comparisons where the same denominator is applied (Table 3). Usage was slightly higher (per kg of all animals) in dairy than in beef herds in the case of oral and parenteral administered products, and several times higher (per adult cow) in the case of intramammary and intrauterine products. The DDDvet was, in general, about three times higher than the DCDvet.

Administration route

For all routes of administration, dairy herds were sold more total antimicrobials (by mass, DDDvet or DCDvet per kg of bovines) than beef herds in this study (Figure 1(a)–(c)). As expected, both proportionately and absolutely, beef herds received very low quantities of antimicrobial via the intramammary route.

TABLE 2 Weight of active ingredient (mg of antimicrobial) per PCU or per kg, p.a. per herd or aggregated over all herd-years (and routes of administration) to give the total weight of active ingredient divided by the total PCU or kg of animal

	Beef PCU based on all animals 1–2 years old and males over 2 years old(*DenB_slaught*)[a]	BeefAll cows over 2 years old of both dairy and beef breeds (*Den_cows*)	Beefkg of animal based on all bovines(*Den_all*)	DairyPCU based on dairy cows alone(*PCUD_std*)[a]	DairyAll cows over two years old of both dairy and beef breeds *Den_cows*	Dairykg of animal based on all bovines(*Den_all*)
Mean	267.4	17.8	12.3	30.4	25.0	16.2
Median	76.5	14.0	9.48	23.8	19.8	13.7
Range	(2.1, 6280)	(0.156, 115)	(0.12, 93.8)	(4.0, 595)	(3.37, 424)	(2.33,141.7)
Aggregated over all herd-years	81.9	15.04	10.1	24.8	22.4	15.3

[a]Denotes the official EMA standard PCU. Herd years in which the denominator was zero have been excluded in the calculations.

Route of administration and antimicrobial class

Figure 2 presents the total mass of antimicrobials (per kg of all bovines) sold by herd type, antimicrobial class and route of administration. For all classes and routes, more antimicrobial was sold to dairy herds than to beef herds. The dominant route of administration was parenteral, and the two most dominant classes of antimicrobials were beta lactam (excluding third-/fourth-generation cephalosporins) and aminoglycoside.

Highest priority critically important antimicrobials

By mass, 10.6% (1.42 mg/kg of bovine animals) of the total antimicrobial sold was classified as highest priority critically important antimicrobial for human medicine HPCIA[19] and by DDDvet and DCDvet the corresponding percentages were 29.8% and 20.0%. HPCIA sales were dominated by sales of Macrolides to dairy herds. The total mass of HPCIA was, for beef, 0.59 mg/kg of bovine animal (*Den_all*), and for dairy, 1.91 mg/kg. Colistin, another HPCIA, was not sold to any of the contributing herds during the study period. The total mass of parenteral HPCIA per PCU (*PCUD_std*, Supporting information Tables S1 and S2) for dairy herds was 0.56 mg/PCU (Table 4). The total number of DCDvet HPCIA intramammary use antimicrobials in our study was 0.62 per dairy cow.

DISCUSSION

Principal findings

Farmers are being encouraged to reduce AMU at national and global levels.[5,20] Given difficulties in obtaining consumption data, sales data act as a proxy. Attempts have been made to estimate sales data for veterinary antimicrobials at international,[21] national[22] and individual herd levels.[10,12,23–25] Our paper complements these and provides dairy and beef herd-level data for Scotland.

We found that herd size and total sales were strongly correlated, dairy herds were sold more antimicrobial (AM) per PCU than beef, and dairy were sold considerably more intramammary products than beef herds. The DDDvet was, in general, about three to five times higher than the DCDvet (Table 3), which concords with definitions and previous results.[10]

With such a complex set of stages to process data, there is a risk of unobserved processing errors. It was therefore encouraging (although far from definitive) to find that there was a strong correlation between herd size and total sales, that dairy herds were sold more AM per PCU than beef, and that dairy were sold much more intramammary products than beef herds.

We also note the following similarities between Figure 2 in our study and a similar one of English dairy farms[10] (although our Figure 2 expresses the estimates of AMU per kg of all bovines to enable comparison between dairy and beef estimates):

- Most of the antimicrobials (by mass per kg of all bovines) sold to dairy herds were injectable/parenteral.
- Of the injectable/parenteral and intramammary antimicrobials, the greatest mass per kg of all bovines was contributed by aminoglycosides and beta lactams (excluding third-/fourth-generation cephalosporins). Beta lactams were recorded as being highly used in similar studies of dairy farms.[26,27]

Measures of antimicrobial used (the numerator)

Others have discussed the advantages and disadvantages of different metrics of AMU.[8] When comparing populations to one another or to the overall mean or median, the choice of metric can be very important and lead to different conclusions, such as a change in relative ranking.[8]

Some antimicrobials require less mass of active ingredient per treatment: among the antimicrobials in our data, the DDDvet (mg/kg) varied by more than one order of magnitude between products (0.3–41 mg/kg). This potential large sensitivity of any comparison

TABLE 3 The mean, median, range of ratios over herd years and the ration of the aggregate numerator and denominator over all herd years of estimates of mg a.i., DDDvet and DCDvet per PCU calculated for beef and dairy herds and broken down by route of administration. NB DDDvet is not defined for dry cow intramammary therapies and is therefore signified with ND

Beef	**Oral**			**Parenteral**			**IMM LCT**	**IMM DCT**	**Intrauterine**
Denominator/ PCU	**PCU based on all animals 1–2 years old and males over 2 years old (*DenB_slaught*)a**	**per kg of all bovine animals (*Den_all*)**	**per kg of all adult cows (*Den_cows*)**	**PCU based on all animals 1–2 years old and males over 2 years old (*DenB_slaught*)a**	**per kg of all bovine animals (*Den_all*)**	**per kg of all adult cows (*Den_cows*)**	**per adult cow[a]**	**per adult cow[a]**	**per adult cow[a]**
Mass of a.i. (mg)									
Mean	24.622	2.063	3.096	246.952	10.77	15.478	93.363	552.301	96.298
Median	4.366	0.447	0.656	71.352	8.081	11.761	54.433	175.56	54.11
Range	(0.173, 284)	(0.014, 37.2)	(0.018, 52.52)	(2.104, 6112)	(0.117, 90.1)	(0.156, 110)	(4.904, 568)	(1.32, 2545)	(3.037, 376)
Aggregated over all herd-years	14.981	1.639	2.399	70.143	8.756	12.973	75.61096	383.653	81.49
DDDvet									
Mean	1.288	0.107	0.152	24.234	1.035	1.487	0.267	ND	0.052
Median	0.183	0.017	0.026	6.01	0.779	1.124	0.172	ND	0.032
Range	(0.004, 18.7)	(0.001, 2.457)	(0.001, 3.469)	(0.481, 680)	(0.038, 10.141)	(0.051, 12.413)	(0.016, 1.403)	ND	(0.006, 0.216)
Aggregated over all herd-years	0.825	0.090	0.132	6.799	0.851	1.260	0.216	ND	0.044
DCDvet									
Mean	0.287	0.023	0.033	7.346	0.313	0.449	0.089	0.278	0.026
Median	0.045	0.004	0.006	1.778	0.241	0.342	0.057	0.088	0.016
Range	(0, 3.931)	(0, 0.515)	(0, 0.728)	(0.138, 198.903)	(0.01, 3.191)	(0.014, 3.906)	(0.005, 0.468)	(0.002, 1.272)	(0.003, 0.108)
Aggregated over all herd-years	0.18	0.020	0.029	2.064	0.258	0.382	0.072	0.194	0.022

Dairy	**Oral**			**Parenteral**			**IMM LCT**	**IMM DCT**	**Intrauterine**
Denominator/ PCU	**PCU based on mass of all dairy cows (*PCU_std*a)**	**per kg of all bovine animals (*Den_all*)**	**per kg of all adult cows (*Den_cows*)**	**per kg all dairy cows (*PCU_std*a)**	**per kg of all bovine animals (*Den_all*)**	**per kg of all adult cows (*Den_cows*)**	**per adult cow**	**per adult cow**	**per adult cow**
Mass of a.i. (mg)									
Mean	7.239	3.821	6.984	21.035	11.128	16.535	526.842	803.279	65.388
Median	2.305	1.447	2.093	16.164	10.117	14.615	431.649	792.317	33.364
Range	(0.01, 345)	(0.004, 115)	(0.007, 345)	(3.07, 515)	(1.80, 39.1)	(2.60, 77.1)	(18.8, 2358)	(25.8, 3052)	(2.26,404)
Aggregated over all herd-years	4.649	2.972	4.308	17.5	10.8	15.8	499	848	63.3
DDDvet									
Mean	0.238	0.155	0.224	2.177	1.192	1.762	1.771	ND	0.051
Median	0.096	0.061	0.094	1.705	1.052	1.499	1.568	ND	0.037
Range	(0, 2.624)	(0, 1.735)	(0, 2.624)	(0.242, 47.71)	(0.142, 5.009)	(0.205, 6.449)	(0.21, 5.974)	ND	(0.005, 0.27)
Aggregated over all herd-years	0.258	0.164	0.239	1.938	1.198	1.752	1.710	ND	0.050
DCDvet									
Mean	0.05	0.033	0.047	0.647	0.350	0.518	0.590	0.545	0.026
Median	0.02	0.013	0.02	0.509	0.320	0.455	0.523	0.535	0.019
Range	(0, 0.55)	(0, 0.364)	(0, 0.550)	(0.077, 14.957)	(0.045, 1.436)	(0.066, 1.994)	(0.07, 1.991)	(0.043, 1.526)	(0.002, 0.135)
Aggregated over all herd-years	0.055	0.035	0.051	0.567	0.350	0.512	0.570	0.560	0.025

[a]Denotes the preferred EMA 2011 standard PCU. Herd-years in which the denominator was zero have been excluded in the calculations.

TABLE 4 Total usage of antimicrobials classed as HPCIA, as sold to dairy herds in this study based on RUMA targets. Numerator and the respective denominator are selected to allow comparison with the RUMA baseline estimates and setting of targets in 2017 (RUMA 2017)

Dairy herds	RUMA baseline	RUMA 2020 target	Our estimate
HPCIA parenterals (mg/PCUD_std)	1.075	0.538	0.56
HPCIA intra-mammaries (DCDvet/dairy cow)	0.332	0.166	0.62

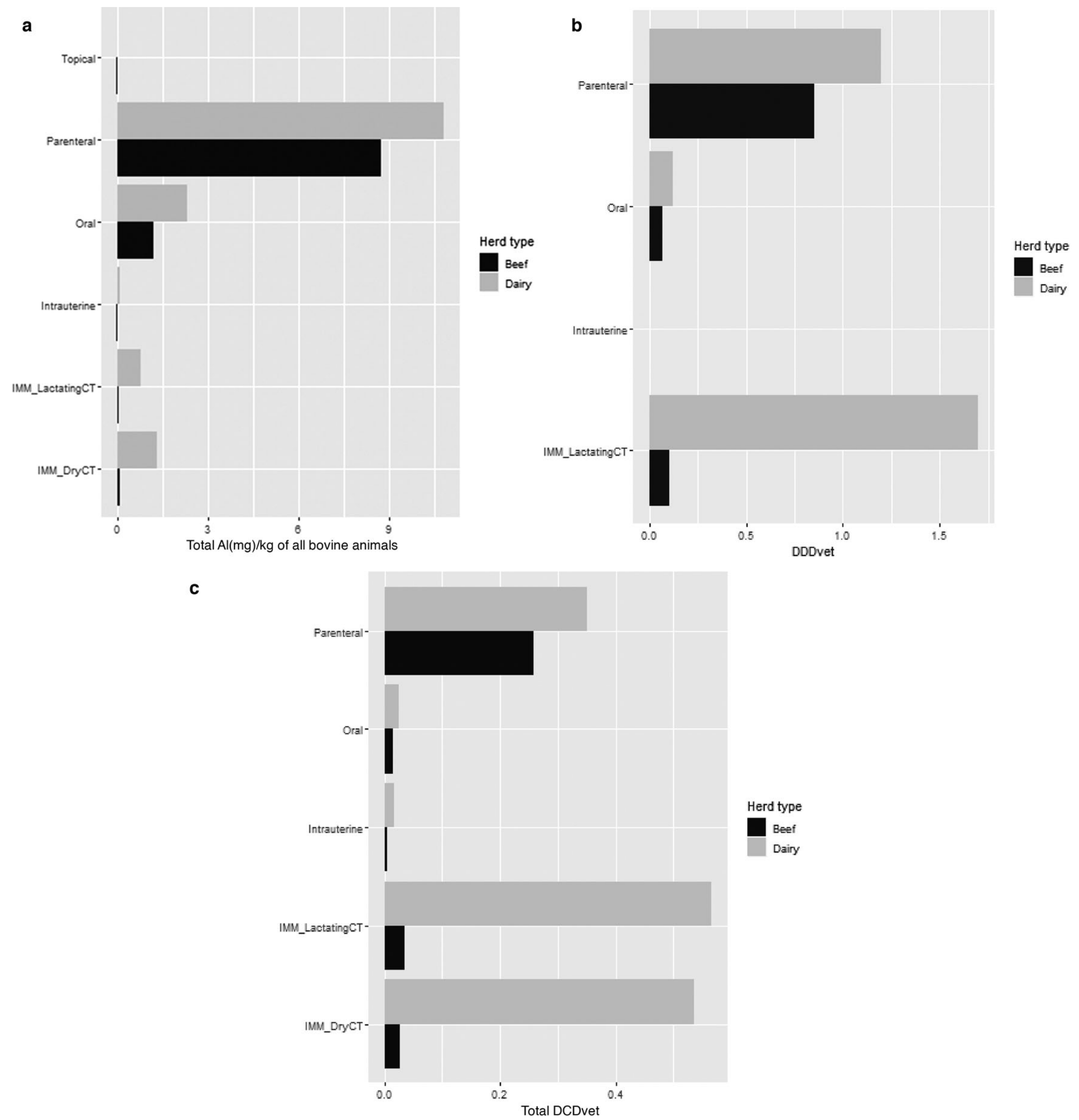

FIGURE 1 (a) Total sales of active ingredient (mg) per kg of all bovine animals broken down by route of administration and herd type. 'CT' represents 'cow therapy'. (b) Total DDDvet broken down by route of administration and herd type. In the case of parenteral, topical and oral routes of administration the denominator is the total kg of all bovine animals. In the case of the intra-mammaries (both dry and lactating cow therapy) the denominator is number of adult cows. "CT" represents "cow therapy". (c) Total DCDvet broken down by route of administration and herd type. In the case of parenteral, topical and oral routes of administration the denominator is the total kg of all bovine animals. In the case of the intra-mammaries (both lactating cow therapy) the denominator is a number 'of adult cows. 'CT' represents 'cow therapy'

between groups of animals, if the antimicrobials are different between the animal groups, depending on the metric used, means that no single comparison is 'correct'. Such comparisons between groups where the antimicrobials are very different should be treated with care.

It appears that measurement of AMU is a fast-moving discipline and still requires further standardisation and consistency over time. For example, it is not clear that there is a single standard for the weight of an adult dairy cow with values of 425, 500 and 600 kg being used.[17,28–30] In addition to differences between authors, there are also changes over time, including changes in antimicrobial classification with HPCIAs for some including macrolides[19,43] while another recent classification has relabelled

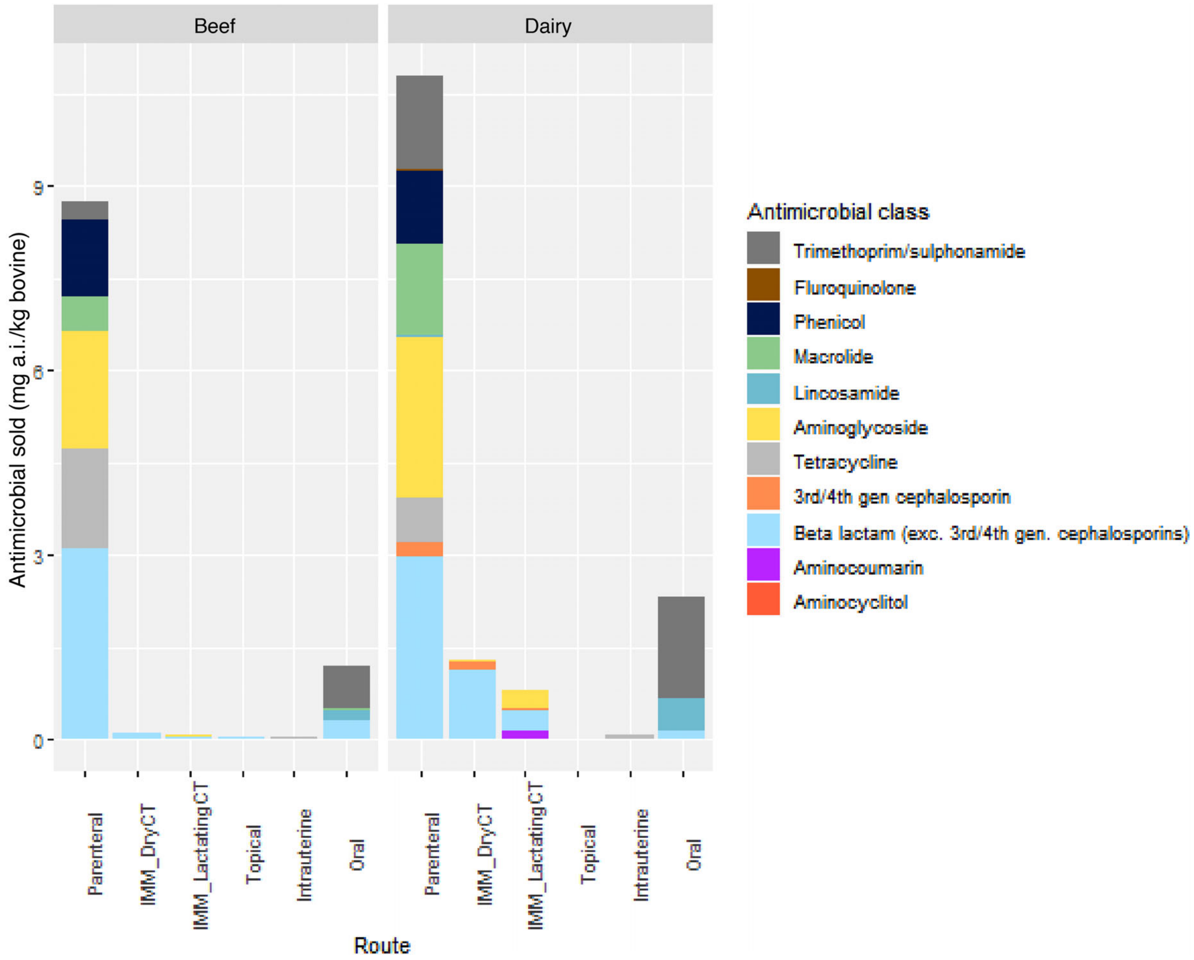

FIGURE 2 Breakdown of total weight of antimicrobials sold (mg a.i. per kg of bovine animal) by herd type, route of administration and antimicrobial class. CT refers to 'cow therapy'

their highest priority category as 'Category B' or 'Restrict'.[31,32]

Choice of denominator (PCU or total mass of bovine animal)

Several concerns regarding the calculation of the denominator are exposed by our study, particularly when applying definitions of denominators created for national-level estimates to individual herds:

- For beef herds, in the absence of appropriate data on the slaughter population, we were obliged to consider proxies for this denominator as well as denominators that might allow for reasonable comparison with dairy herds.
- The standard masses per animal of each demographic type is considered inaccurate in many situations: consider, for example, the standard mass for an adult cow (at the time of treatment) of 425 kg (see the Supporting Information) compared to an estimate of 650 kg for a high output dairy cow housed year-round[33] and alternative estimates of mass 500 and 600 kg cited previously.[8] Any simplification of 'herd size' for the purposes of standardisation will result in such inaccuracies, and we accept them in return for the benefits of comparison provided by standardisation.
- Demographic data at the individual herd-level can be more variable over time than demographic data at the national level. Therefore, data such ours, based on a snap-shot of individual herd demographics, which may not be representative of an entire year, may inappropriately exaggerate variation in our estimates of usage and recent work recommends averaging of liveweight over time to ameliorate this.[32]

Our results demonstrated high variation in estimates of usage per PCU between herd-years and that they are particularly sensitive to the value of the denominator. Due to this sensitivity, we have concerns about estimates that utilise denominators based on snap-shots of herd demographics for comparing small (e.g. herd-level) groups of animals that are different in demographic composition.[34] Published estimates of AMU per PCU (or other mass of animal) tend to be based on PCU calculated either from questionnaires,[35–37] or existing databases.[10,23,24,38] Details of exactly what the demographic data represent or how calculations are made are not always explicitly stated.[26,27,39,40] The data and methods used for such estimations should be clearly described to enable appropriate comparisons.

It is likely that these difficulties are less important when estimation is done at a national level. RUMA stated that 'the ESVAC methodology is required to calculate antibiotic use at a national level. However, the Beef Antimicrobial Use Working Group has identified that this method is not best suited for on-farm benchmarking and that there is a need to establish a separate standard protocol'.[5] Such questions are being considered by industry,[41,42] and recent work recommends standards that include proposed solutions to the fact that animal numbers vary through the year ('important that the weight of antibiotic used (in mg) is interpreted relative to the average live-weight of animal population').[32]

Estimates in context

The UK's contribution to the international effort in reducing AMR and AMU includes targets for AMU in agriculture.[5] The RUMA task force targets are a 10% reduction or 10 mg/kg of animal (whichever is lower) for beef and 21 mg/kg of animal for dairy – both by 2020. Whether the group of farms in our study satisfied these targets (in advance) depends on the chosen assumptions in the calculation. Our estimates of AMU in total for both beef and dairy and HPCIA injectables in dairy compare favourably to (2017) RUMA 2020 targets. HPCIA intra-mammaries were substantially higher than the RUMA 2020 target, mainly due to the sale of macrolides reflecting recent evidence from elsewhere.[43] It suggests that the RUMA targets are achievable at least for injectables in these herds. It is encouraging from a public health viewpoint to note that, for this practice at least, a small proportion of the antimicrobials sold were Highest Priority Critically Important (HPCI): we estimated 10.6% by mass of antimicrobials sold were HPCI and 29.8% and 20.0% by DDDvet and DCDvet, respectively. This usage was predominantly in the dairy herds, and, within dairy herds, it was primarily through the usage of macrolides followed by cephalosporins. Therefore, any targeting to reduce HPCIA usage in cattle might start with macrolides and cephalosporins in dairy herds. This already is being addressed through mastitis control programmes promoted by Agriculture and Horticulture Development Board (AHDB)[44] and quality assurance schemes required by dairy companies (e.g. Red Tractor Quality Assurance[45]). Programmes to reduce disease, such as the above,[44] have a wider benefit because they are highly effective ways of reducing AMU in general – not just targeted antimicrobials.

Limitations

There are several limitations of our approach concerning our use of antimicrobial sales data and the source of these data:

- The data come from one veterinary practice, which may not be typical of other Scottish practices.
- Data are based on sales rather than direct usage. We cannot determine how much antimicrobial sold went unused (whether discarded, used in other livestock or stored for use in subsequent years), or whether antimicrobials were obtained from other sources.
- These data describe antimicrobial sales for a particular time period (2011–2015). They likely do not represent current (2020) sales. Nonetheless, these data are likely to be useful for future comparison/benchmarking.
- Our estimates were based on the sales cost of the item according to a 2016 price list. We assumed that the prices of products did not change appreciably during the period of interest, and that the relationship between cost of a sale and the amount of product sold in that sale was proportional.
- It is possible that some herds had other livestock (in particular sheep) which may have received some of antimicrobials contributing to our dataset and therefore were assumed to have been given to cattle. If this occurred then it would provide an overestimate of the AMU on that farm. We think it likely this did occur, we cannot currently estimate the size of this effect but assume that it is not large because of the consumption of antimicrobials by sheep is considered to be very low as indicated by comparing sales of sheep only products with sales specific to other species.[46] Future studies will need to seek to account for usage of products (licensed for more than one species) by species other than the target species (e.g. 'Alamycin LA 300') ideally by separating the usage for the different species or by excluding farms that have sheep and accepting a different consequent bias.[7]
- We have included certain antimicrobials such as those that can be used through the 'Cascade' for off-licence use in footbaths (e.g. Tylan solution), which may be used in such quantities that they can be strong determinants of total usage (by mass) at the herd level.[8,10] To include them seems proper, but they may disproportionately affect total usage in specific herd-years.

Other limitations affect the herd-level demographic data used in this study:

- Standardised definitions are not always consistently referred to within the literature (e.g. standard weight of an adult dairy cow or the definition of a DCDvet for intramammary tubes in dry cows).
- The distinction between beef and dairy herds is not always clear. Our definition of a dairy herd meant that some dairy herds had some beef animals within them and vice versa. This concords with the Scottish Dairy Cattle Association's definition,[11] but does not account for mixed herds, which is likely to have affected the calculated PCU for some herds.
- Herd demographics were represented by a single snap-shot at a particular point in time each year. The implications of this are discussed above. The use of cattle movement data[47] to more accurately represent herd demographic dynamics may be more suitable.

- For beef herds, we made further assumptions regarding the livestock which went to slaughter. This limitation reflects the difficulties that arise when trying to compare different sectors whose definition of PCU rely on different data. As above, the use of cattle movement data may ameliorate this difficulty.

Recommendations

Based on this study, we recommend that billing data continue to be considered a valuable resource for estimating AMU, and that attempts to standardise the recording of billing data within, and between, practices be progressed.[41]

We recognise that the definitions of PCU were created for national-level estimates and suggest that comparisons based on estimated denominators such as PCU should only be made between groups of animals that have similar demographic composition.[34] A more appropriate definition of PCU for use at the individual herd level, and which allows for the existence of herds that include both dairy products and beef animals, is needed for herd-level comparison and benchmarking.

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CONFLICT OF INTEREST

The co-authors know of no conflicts of interest, financial, professional or otherwise relating to the collection and presentation of these results.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

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