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# A quantitative analysis of antibiotic usage in British sheep flocks

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## Abstract

The aim of this study was to examine the variation in antibiotic usage between 207 commercial sheep flocks using their veterinary practice prescribing records. Mean and median prescribed mass per Population Corrected Unit (mg/PCU) was 11.38 and 5.95 respectively and closely correlated with Animal Defined Daily Dose (ADDD) 1.47(mean), 0.74(median) ($R^2$ = 0.84, p<0.001). This is low in comparison with the suggested target (an average across all UK livestock sectors) of 50mg/PCU. In total, 80% of all antibiotic usage occurred in the 39% of flocks where per animal usage was greater than 9.0 mg/PCU. Parenteral antibiotics, principally oxytetracycline, represented 82% of the total prescribed mass, 65.5% of antibiotics (mg/PCU) were prescribed for the treatment of lameness. Oral antibiotics were prescribed to 49% of flocks, 64% of predicted lamb crop/farm. Lowland flocks were prescribed significantly more antibiotics than hill flocks. Variance partitioning apportioned 79% of variation in total antibiotic usage (mg/PCU) to the farm level and 21% to the veterinary practice indicating that veterinary practices have a substantial impact on overall antimicrobial usage. Reducing antibiotic usage in the sheep sector should be possible with better understanding of the drivers of high usage in individual flocks and of veterinary prescribing practices.

## Introduction

Antibiotic usage in farmed species is under scrutiny because of increasing concern surrounding antimicrobial resistance, with imprudent patterns of prescribing and use representing a potential risk to human and animal health (O'Neill, 2015).

Antibiotic usage is measured across the EU at a national level using the metric of total mass (mg) of any and all antibiotic active ingredients per Population Corrected Unit (mg/PCU). The PCU denominator is calculated as a standardised figure for each farmed species for breeding and slaughtered animals (EMA, 2013). There is significant variation between countries, with the UK's usage at 62.1 mg/PCU ranked 15th out of 26 EU countries in order of highest antibiotic usage (EMA, 2013).

The UK government has identified reducing antibiotic usage as a priority and has adopted the mg/PCU metric to measure usage across all livestock sectors (UK Government, 2016) with a target for UK livestock production set at 50mg/PCU. The UK is the 4th largest livestock producer in the EU as calculated by PCU biomass (EMA, 2013) and the sheep industry in the UK is the largest in the EU. The sheep sector is also the largest single sector of UK livestock agriculture, representing 40% of the PCU biomass (EMA, 2013). For this reason, antibiotic usage in the UK sheep industry has a disproportionate impact on the total mg/PCU figure for the whole UK livestock sector.

Species or sector specific targets are also expected to be set (UK Government, 2016), for which a detailed understanding of current usage patterns is required in order to make informed decisions in this area. To understand how to reduce antibiotic usage in each sector, we need to understand the farm level usage, variability between farms within a species and reasons for use within farm.

The aim of this study was to collate information from a large number of British sheep farms, primarily to evaluate the magnitude and variation in antibiotic usage and secondarily to assess factors that impact on farm level antibiotic usage.

# Methodology

## Farm selection criteria

Two hundred and seven anonymised flock records were collated from a convenience sample of eight veterinary practices that were able to contribute sales and prescription records for all antibiotic products supplied to a minimum of ten sheep farm enterprises which met specific selection criteria. Practices were recruited with client farms located in the following regions: West Wales, Mid Wales, Central Scotland and the following English regions: South West, South East, West Midlands, East Midlands and North West. Each practice provided details of all antibiotic products and quantity prescribed to all their sheep farming clients during the study period of August 2015-July 2016 along with flock level information on breeding flock size, flock type (categorised as Hill (18), Upland (25), Lowland (164)) and management system (Organic (11), Conventional (196)). A single, recent year was selected for analysis to reduce recall bias in the recording of the breeding ewe flock size, which were used as the denominator for antibiotic calculations. Data were requested from farms that were sheep only holdings with a minimum of 100 breeding ewes; to avoid the risk of antibiotics being used in other species the study was restricted to farms exclusively with sheep. A minimum breeding ewe flock size was used to reduce the potential bias associated with unnecessarily large pack sizes of antibiotic products being supplied for small flocks, where unused product could represent a large proportion of the purchased total. The threshold also represented a reasonable cut off for commercial vs leisure/hobby flocks. The flock size ranged from 100 to 4000 ewes, with a mean and median size of 529 and 300 respectively. The threshold was selected based upon the maximum number of doses per product unit available in the UK.

## Calculation of antibiotic usage per population correction unit (PCU)

The mass of antibiotic active ingredients per PCU was calculated for each prescribed product using the manufacturer supplied product specification and the ESVAC standard methodology (EMA, 2015) using approximate average body weights of adults (75kg) and weighted average weight for slaughtered lambs drawn from the Eurostat census. To calculate the lamb component of the PCU the mean rearing % of lambs per ewe (143.5%) in the reference period was estimated using the UK levy board benchmarking data (AHDB 2016) as a coefficient of the standard ESVAC lamb weight value (20kg). This metric was applied to all flocks in the study.

The average ESVAC ewe and lamb weights were considered reasonable estimates for lowland flocks by the authors, however breeds used in hill farming in UK systems are generally smaller and less fecund than their lowland counterparts. To account for this potential bias, a sub-analysis was conducted where a separate 'Hill-PCU' was used as the denominator for antibiotic usage in hill flocks specifically. This was calculated based on a mature ewe body weight of 55kg, a lamb average body weight of 16kg and a rearing percentage of 115% (Welsh Farm Survey, 2016).

## Calculation of antibiotic usage by Defined Daily Doses (DDDvet), Defined Course Doses (DCDvet) and Animal-Defined Daily Dose (ADDD).

Antibiotic usage at flock level was estimated using standardized methods as follows. The number of Defined Daily Doses (DDDvet) and Defined Course Doses (DCDvet) as Animal Defined Daily Dose (ADDD) per farm for the one year reference period were estimated for each farm. The breeding female population was used as the flock denominator and a standardized body weight of adult sheep of 75kg and was applied to convert the mg/kgBW into a per head unit in line with the standardised methodology set out by the ESVAC (EMA/710019/2014)(EMA, 2015). For oral and parenteral products DDDvet and DCDvet were calculated for each antibiotic product using either; (a) the licenced recommended maintenance dose for sheep where available, (b) the licenced recommended maintenance dose for cattle or pigs [dependent on the species licencing of the product] where the product used was not licenced for sheep but prescribed under the Veterinary Medicines Directorate 'cascade'. Topical preparations were excluded from the calculation of DDDvet and DCDvet in line with the ESVAC methodology. All products and preparations, including topical and oral preparations, were included in the mg/PCU metric. The ADDD metric was generated for comparison with mg/PCU and was calculated as previously described (Bos et al., 2013) and used for comparison of antibiotic usage in dairy herds (Kuipers, Koops, & Wemmenhove, 2016). An additional Lamb DCDvet metric was calculated for oral antibiotics licenced exclusively for neonatal lambs where dose was independent of body weight. These products were assigned a lamb DCDvet per animal rather than mg/kg body weight. In this study, the dose rates for these products were calculated on a fixed volume per animal as directed by manufacturer recommendations, rather than mg/kg bodyweight. The number of lamb DCDvet doses was then divided by the breeding ewe population per farm to generate an index of lamb doses per breeding ewe per flock.

## Statistical modelling

A Linear regression model was used to assess the correlation between mg/PCU, ADDD (DDDvet and DCDvet) using MiniTab17 (Minitab 17 Inc, 2015). A multivariable regression model was developed with antibiotic use (mg/PCU) as the response variable. A multi-level structure was used to account for correlations in antibiotic use between farms, within a veterinary practice. The number of breeding ewes, farm type (organic, conventional) and farm stratification (Lowland, Upland, Hill) were forced into the model. Based on the a priori hypotheses of this study, all variables were retained in the model. The model was built using MLwiN version 2.36 (Charlton, et al, 2017) and parameter estimates generated using iterative generalised least squares (IGLS). Model fit was assessed by examining q-q plots of residuals. The mg/PCU of antibiotic calculated for each farm were transformed to meet the assumptions of the multivariable regression model. The optimal transformation (mg/PCU to the power 0.28) was calculated using the *boxcox* function in the MASS package in R (Venables, W. N. & Ripley, 2002). Variance partition coefficients (VPCs) were calculated using the final model to evaluate the proportion of unexplained variance occurring at both the farm and veterinary practice level. To facilitate interpretation of the final model, predictions were calculated by fixing explanatory variables at their mean value except the variable of interest. Predictions and their corresponding confidence interval estimates were back transformed to the mg/PCU scale.

### Antibiotic use by disease

Analysis of the disease for which each antibiotic product was prescribed was possible for 24 flocks from one practice that routinely and accurately collected this information. Diseases were categorised for comparison of antibiotic usage by antibiotic class in mg/PCU. Disease incidence rates were estimated for the two most common prescribed reasons for antibiotic usage, using the DCDvet metric and the following assumptions: licenced dose rate was used for each dose, 75kg ewe body weight for each administered dose, all doses administered to ewes not lambs, zero wastage of antibiotic product.

## Results

### Distribution of total antibiotic usage per farm and comparison of metrics.

Flock usage of antibiotics during the reference period ranged from 0 mg/PCU to 116.9 mg/PCU, with a mean of 11.38 (sd = 15.35)  and median of and 5.95 (IQR = 2.47 – 13.95) mg/PCU respectively. 4.3% of flocks recorded no antibiotic prescriptions during the reference period, while 1.9% of flocks recorded over 50 mg/PCU (Figure 1). In total, 80% of all antibiotic usage occurred in the 39% of flocks where per animal usage was greater than 9.0 mg/PCU

Antibiotic usage at the farm level, using the ADDD metric, calculated using the DDDvet method indicated mean daily doses per animal of 1.47 (sd = 2.1)  and a median of 0.74 (IQR = 0.299 – 1.97). Mean and median usage as calculated by DCDvet per ewe per flock were 0.39 (sd = 0.53) and 0.20 (IQR = 0.17, 0.26) respectively.

Correlation between mg/PCU and ADDD using DDDvet for farms in this study was $R^2 = 0.84$ ($P<0.001$). The correlation between mg/PCU and ADDD using DCDvet was $R^2 = 0.77$ ($P<0.001$). There was no significant correlation between Lamb DCDvet and any of the other metrics.

## Distribution of antibiotic usage by antibiotic group

The mass of antibiotic products prescribed were ranked by antibiotic class (Table 1). The most commonly prescribed antibiotic was oxytetracycline, which comprised 57.4% of the total, followed by penicillin (including extended spectrum penicillins) 23.7%, aminoglycosides 10.7%, lincomycin 4.7%, macrolides 1.7%, fluoroquinolones 0.5% and florfenicol 0.5%, with the remaining 0.9% being made up of cephalosporins, sulphonamides, trimethoprim and thiamphenicol.

## Distribution of antibiotic usage by route of administration

Parenterally administered products represented 84.4% of the total mass used, whilst topical preparations represented 12.3% and oral represented 3.3% of the total mg/PCU (Table 1).

*Table 1 Percentage distribution of antibiotic prescriptions by mass (mg/PCU), antibiotic class and administration route per class across all farms.*

| Antibiotic class | Administration route (% of each class) | | | % of Total mass of all classes |
|---|---|---|---|---|
| | Oral | Parenteral | Topical | |
| **Oxytetracycline** | | 91% | 9% | 57.4% |
| **Penicillin (inc extended spectrum)** | | 98% | 2% | 23.6% |
| **Aminoglycoside** | 29% | 66% | 6% | 10.7% |
| **Lincomycin** | | | 100% | 4.7% |
| **Macrolides** | | 60% | 40% | 1.7% |
| **Florfenicol** | | 100% | | 0.5% |
| **Fluoroquinolones** | | 38% | 62% | 0.5% |
| **Other** | 25% | 55% | 21% | 0.9% |

## Comparison of antibiotic group and route of administration between 1st and 4th quartile (high and low users)

A comparison was made between the antibiotic usage of the upper quartile of flocks (Q1) (High users >13.95mg/PCU) and lower quartile flocks (Q4) (Low users < 2.47 mg/PCU). All the antibiotic classes were represented in the Q1 group of flocks, however the Q4 group used fewer antibiotic classes (oxytetracycline, penicillin (including extended spectrum), aminoglycosides, lincomycin). The total usage of all of these individual classes was significantly lower in Q4 compared to Q1. There was no significant difference in the proportional usage of antibiotic classes i.e. oxytetracycline was still the predominant antibiotic used, followed by penicillins, or in administration route.

## Seasonality of antibiotic usage by antibiotic group

Antibiotic prescriptions were distributed throughout the year with a significant increase in spring along with a significant relative increase in the mg/PCU of penicillins and aminoglycosides (Figure 2). Oxytetracycline usage also increased in the spring but to a lesser extent than the increase observed with penicillin and the aminoglycosides. February was the only month in which oxytetracycline was surpassed by penicillins as the most commonly prescribed antibiotic class. All of the oral aminoglycoside antibiotics (neomycin and spectinomycin) were prescribed during the spring months, which coincides with the majority of lambing periods in UK flocks.

## Oral antibiotic usage in lambs

In this study, 47% (95% CI: 41% - 62%) of flocks used oral antibiotics licenced for treatment/prophylaxis of colibacillosis in lambs. A further 2% of flocks, (4 farms from 2 practices) were prescribed oral antibiotic tablets. Of the lowland flocks sampled, 77% (95% CI: 42% - 90%) were prescribed oral antibiotics, whereas 44% (95% CI: 41% - 69%) of upland flocks and 25% (95% CI: 17% - 50%) of hill flocks were prescribed oral antibiotics. Licenced oral antibiotic products in this study were explicitly only approved for use in neonatal lambs. In those flocks using oral antibiotics, the mean number of lamb oral antibiotic doses prescribed per ewe per flock was 1.23 (95% CI: 0.034, 5.181) and median of 0.92 (95% CI: 0.8, 1.2) doses per ewe per flock.

## Topical antibiotic preparations

Topical antibiotic preparations were assigned to one of three catagories for comparison of the percentage prescribed total mass (mg/PCU) across all farms: ophthalmic preparations (4%), aerosol sprays (45%) and soluble powders (51%). Ophthalmic preparations were prescribed to 22% of farms, aerosol sprays were prescribed to 47% of farms and soluble powders were prescribed to 7% of farms. DDDvet and DCDvet metrics were not established for topical preparations in line with EMA standard methodology.

## Farm Stratification

Considerable variation was observed in antibiotic usage between farms both within and between farm stratification categories (Figure 3). The distributions of mg/PCU within all categories of farm were positively skewed.

## Multivariable analysis: Influence of veterinary practice, management system and farm stratification on antibiotic use

Accounting for influence of practice in the multi-level model structure, lowland farms were shown to use significantly more antibiotics ($mg/PCU^{0.28}$) than hill farms (p=0.02), principally due to higher usage of parenteral oxytetracycline. When a 'Hill-PCU' coefficient (accounting for the lower body weights and lamb output) was applied to the antibiotic usage of hill flocks as opposed to the standard PCU coefficient appropriate to lowland flocks, a significantly lower antibiotic usage in hill flocks was still identified (p = 0.03). There was a non-significant trend for organic farms to use less antibiotic than conventional farms (p=0.06). In the final model, 21% of the unexplained variation in mg/PCU$^{0.28}$ occurred between veterinary practices, with the remaining 79% of variation being between farms. Additional detail on model results are provided in supplementary material.

## Distribution of antibiotic usage by clinical diagnosis

A subset analysis of antibiotic class prescription patterns by clinical diagnosis was conducted on the data supplied by one veterinary practice with unusually detailed records of all antibiotics prescribed. Analysis of these 24 flocks data revealed that lameness accounted for 65.5% of antibiotics prescribed by this practice (Table 2) and oxytetracycline was the most commonly prescribed antibiotic accounting for 63.5% of the total, followed by penicillins (26.8% of total). Penicillins were prescribed for the widest range of clinical diagnoses (9 of 11 disease categories, Table 2), while oxytetracycline was prescribed for 4 of 11 categories and 85.1% of all oxytetracycline was prescribed for treatment of lameness (Table 2). The mean proportion of oxytetracycline prescribed for the treatment of lameness per farm was 91% (95% CI: 81%, 99%).

*Table 2. Antibiotic prescription patterns by diagnosis from a subset of 24 flocks supplied by one veterinary practice with unusually detailed prescription records. The proportions of antibiotics per class prescribed for each diagnosis are stated as a percentage of the total prescribed for that antibiotic class. The number of flocks prescribed a given class for a given diagnosis is stated in brackets. The Lameness category includes Contagious Ovine Digital Dermatitis, Footrot and Interdigital Dermatitis.*

| Treatment Diagnosis | Aminoglycosides | Penicillins (including extended spectrum) | Macrolides | Oxytetracycline | Lincomycin | % Total mg/PCU by cause |
|---|---|---|---|---|---|---|
| **Abortion** | | | | 5.4% (1) | | 3.2% |
| **Colibacillosis** | 43.4% (11) | | | | | 2.2% |
| **Lambing (inc dystocia, prolapse)** | | 29.4% (18) | | | | 9.7% |
| **Lameness (inc CODD, FR, ID)** | 24.6% (1) | 34.5% (13) | 75.6% (10) | 85.1% (23) | 100.0% (4) | 65.5% |

| | | | | | | |
|---|---|---|---|---|---|---|
| **Listeriosis** | | 0.3% (1) | | | | 0.1% |
| **Mastitis** | | 10.3% (4) | | | | 3.4% |
| **Metritis** | | 0.4% (1) | | | | 0.1% |
| **Ophthalmic** | | 1.7% (5) | | 9.2% (4) | | 6.0% |
| **Pneumonia** | | 0.4% (1) | | 0.3% (1) | | 0.3% |
| **Polyarthritis** | 32.0% (2) | 18.8% (9) | 24.4% (4) | | | 8.2% |
| **Not recorded** | | 4.3% (5) | | | | 1.4% |
| **% Total mg/PCU by antibiotic class** | 2.0% | 26.8% | 6.3% | 63.5% | 1.3% | |

Incidence of lameness treatments and treatments associated with lambing were estimated using the DCDvet for each flock (Table 3). DCDvet based estimates of lameness incidence between farms indicate a wider and higher range of treatment rates for lameness with a median of 29.6 ewe treatment DCDvet per 100 ewes per year.

*Table 3 Disease incidence estimates for lameness and lambing associated events based upon prescribed antibiotic DCDvet values for parenteral antibiotics prescribed for each.*

| | **Mean** | **Median** | **Range** |
|---|---|---|---|
| **Parenteral treatments for lameness** | 42.7 ewe treatment DCDvet per 100 ewes per year | 29.6 ewe treatment DCDvet per 100 ewes per year | 9.6 – 67.0 |
| **Parenteral treatments for lambing associated events (including dystocia, prolapse)** | 7.8 ewe treatment DCDvet per 100 ewes per year | 6.8 ewe treatment DCDvet per 100 ewes per year | 3.2 – 10.3 |

## Discussion

The results of this study suggest that antibiotic use in all sectors and management systems of the UK sheep industry is very low in comparison with the overall average of 56mg/PCU recorded across all

UK livestock sectors in 2015 (UK government VARSS 2015). The relatively low usage of antibiotics in the sheep sector should not give rise to complacency. This study highlights a number of areas where potential improvements in our use and monitoring of antibiotics can be made.

If antibiotic usage is to be reduced in line with the stated EU and UK policy statements (UK Government, 2016) then it would be logical to target those diseases which drive highest usage with a 'Refine, Reduce, Replace' strategy, whilst keeping in mind the other priorities, principally animal welfare. In identifying the most appropriate strategy for minimising any potential antibiotic resistance selection risk, the metric used needs to be appropriate. It would be counterproductive if a targeted adoption of one metric, led inadvertently, to antibiotic use patterns that did not reflect the best evidence based clinical practice or neglected high risk antibiotic use.

It should be noted that the dominance of parenteral oxytetracycline and to a lesser extent penicillins identified in this study resulted in a close correlation between the two main metrics for antibiotic usage; Population Corrected Unit (PCU) and Animal Defined Daily Dose ADDD (DCDvet/DDDvet). The close correlation between mg/PCU and ADDD (DDDvet/DCDvet) in the sheep sector may be very helpful in simplifying monitoring of antibiotic usage, however the use of oral aminoglycosides in neonatal lambs and the use of soluble antibiotic powders for topical use in footbaths or hand sprays to control lameness (particularly contagious ovine digital dermatitis (CODD)) present two important challenges that may be obscured by the scale of oxytetracycline use. Both of these practices have the potential to subject a larger proportion of the flock, as well as the wider farm environment, to antibiotic resistance selection, than targeted individual parenterally administered treatments.

Overall, 79% of the variation in antibiotic usage observed between flocks was attributable to differences between farms. These are likely to include a combination of biological and management differences, which influence the force of infection and genetic differences in disease susceptibility to infection. However, the between farm variation in antibiotic use will also likely be influenced by the priorities, understanding and attitudes of the farmers and shepherds responsible. Previous studies have demonstrated differences in attitude to population health management between sheep and pig farmers (Garforth, Bailey, & Tranter, 2013). In the context of antibiotic usage this study has demonstrated that flock type (Hill, Upland, Lowland) was significantly associated with different levels of antibiotic use and the basis for these differences warrant further investigation.

There was an important further 21% of variation attributable to the veterinary practice serving the individual flocks after the effects of stratification, region, flock size and management system were accounted for. This suggests there is an important influence of practice prescribing policy and practice culture on the quantity of antibiotics prescribed for sheep. Reasons for these differences cannot be elucidated from the current study and this would be a worthwhile topic for future research. Surveys that rely on the voluntary contribution of data from participants (veterinary practices in this case) are subject to bias and it is unclear the extent to which this convenience sample is representative of the national flock. With the current absence of a universal, robustly audited, mandatory reporting system of antibiotic use/prescription, these study findings represent initial data that may indicate current prescription patterns in the UK sheep industry. Further studies that incorporate true random sampling would be of value.

The subset analysis of antibiotic prescriptions per disease process from one practice (24 flocks) suggested that the pattern of antibiotic usage across the 24 flocks was comparable to the dataset as a whole in terms of overall usage per flock, relative usage by antibiotic classes and seasonality of usage. It would therefore seem reasonable to conclude that some useful estimates of the disease diagnosies underpinning antibiotic usage may be drawn from this subset of data. Principally the treatment of lameness was the most common reason for the use of antibiotics (mainly oxytetracycline) in sheep flocks, accounting for approximately 65 % of total mg/PCU. This result is not surprising given the prevalence of footrot, interdigital dermatitis and contagious ovine digital dermatitis. However, since important variation between practices in prescribing policies was also identified in this study, it should also be recognised that records from one veterinary practice may not be representative of practices in general.

Prompt parenteral antibiotic treatment (PAT) forms part of the accepted best practice guidelines for the control of footrot (Kaler et al, 2010) and has been shown to reduce the prevalence of footrot in flocks. In many upland and hill flocks, where grazing management is more extensive and PAT is not practical, regular periodic treatment with parenteral antibiotics has also been suggested to be effective in reducing lameness prevalence (Angell & Duncan, 2015). The authors suggest that some of the significant variation observed in this study between lowland and hill flocks in the usage of oxytetracycline may be due to the greater difficultly in adopting PAT protocols for lameness management in comparison to their lowland counterparts. Infection pressure and risk of clinical disease may also vary between these hill and lowland farms.

Whilst lameness prevalence is referred to widely (J. R. Winter, Kaler, Ferguson, Kilbride, & Green, 2015), there is little published data on the incidence rates of lameness in commercial flocks under typical management conditions. The extrapolated treatment rate calculated in this study from the subset of 24 flocks with detailed diagnosis data on each antibiotic product unit is an attempt to use readily available data to provide a crude estimate of treatment rate as a proxy for disease incidence. Accepting that the treatment rate measure used makes several key assumptions as detailed previously, the high median treatment rates of 29.6 cases per 100 ewes per year and wide range between farms may represent a reasonable benchmark when considering appropriate strategies for lameness control.

Whilst the use of parenteral oxytetracycline would seem most plausibly attributed to its perpetual use in the control of infectious lameness a small seasonal increase observed in February and March could be attributed, at least in part, to the prophylactic or metaphylactic use in the control of *Chlamydophila abortus.* This use of oxytetracycline was estimated in this study at 5% of flocks (table 2) per year and by others as high as 10% of flocks per year (Lovatt et al, unpublished data).

Oral aminoglycosides are licenced for the treatment and/or prophylaxis of enteric *E.coli* infections in neonatal lambs. The ESVAC methodology for calculating DDDvet and DCDvet values for oral antibiotics dramatically underestimate the number of individuals and thus the proportion of the population that are treated. For this reason it seems logical that neonatal antibiotic preparations should be recorded as a 'per animal' dose rather than as mg/kg body weight. In this study, 49% of farms were prescribed oral antibiotics. Extrapolating from the UK benchmarked mean rearing percentage of lambs per ewe (143.5%), the mean and median doses per lamb reared per flock using oral antibiotics is approximately 0.86 and 0.64 respectively.

The most common aminoglycoside antibiotic preparation prescribed in this study is also licenced for use in piglets. In piglets, the exposure of the developing gastrointestinal flora to antibiotics has been shown to have enduring effects on the microbiota (Schokker et al, 2015). It is unclear if similar results would be expected in ruminant species. It has been shown that there is significant variation in microbiota between calves from different beef herds (Weese & Jelinski, 2017) and early life exposure of calves to antibiotics was hypothesised as a potential contributory factor. More research is required to understand the dynamics of the microbiota development in lambs and what affect peri-natal antibiotic treatment may have on antimicrobial resistance as well as their long term health.

Topical use of antibiotics presents a different but no less important challenge. Topical antibiotic preparations are excluded from ESVAC DDDvet/DCDvet metrics, however in the sheep and cattle industries, these products are commonly used both in antibiotic footbaths and also as topical sprays, primarily for the treatment of pathogens causing lameness. A wide range of soluble antibiotic products including macrolides, aminoglycosides, lincomycin and fluoroquinolones were prescribed to a small proportion of flocks (7%). In the authors' experience, these products, licenced for oral administration to pigs, poultry and calves, are prescribed overwhelmingly for the treatment and control of lameness caused by CODD. The use of such preparations by this route for treating lameness is a well-established clinical approach for CODD in sheep and the cattle equivalent condition, digital dermatitis, in the UK and internationally (Laven & Logue, 2006; A. C. Winter, 2011).In the case of CODD in particular, there is no published evidence to support this form of use, whilst the evidence to support the use of antibiotic footbaths to control of digital dermatitis in cattle is weak. The lack of an evidence base to guide decisions on dose rate and effective application protocols raises the possibility that sub-therapeutic dosing may be common in this clinical scenario, whilst spent footbath solutions are commonly discharged into slurry or the environment. It must be recognised that in addition to the causative pathogens, a wide variety of other bacterial species on the foot and in the soil environment will also be exposed as a result of the use of these antibiotic products in this way.  This is an undesirable and potentially imprudent use of antibiotics, which is difficult to justify unless substantially better welfare outcomes can be demonstrated compared to targeted treatment with parenteral antibiotics, which is known to be highly efficacious (Duncan et al. 2011, 2012, Angell et al,  2014, Angell & Duncan, 2015). CODD is estimated to affect approximately 35% of UK flocks (Angell et al, 2014) Assuming a similar prevalence of CODD for the flocks in this study, it can be inferred that the majority of CODD affected flocks are not using antibiotic footbaths to control this disease on a regular basis.

It cannot be assumed that low antibiotic usage correlates with low disease or good welfare and there is a great danger in conflating the two measures. Low, targeted usage of antibiotics in all veterinary species is desirable but this must be balanced with concern for animal welfare and sustainable productivity. This study has demonstrated significant variation in antibiotic usage between farms and between veterinary practices. Further research is required to understand the biological, managemental and physiological drivers of antibiotic prescription and use among sheep farmers and their prescribing veterinary surgeons in order to achieve a sustainable reduction in antibiotic use.

## Figures

*Figure 1  Distribution of antibiotic usage in total mg/PCU from 207 individual sheep flocks in England, Wales and Scotland compiled from prescribing records of eight veterinary practices over a 12 month period from 1st August 2015 to 31st July 2016.*

*Figure 2  Percentage of total antibiotic usage mg/PCU per month for all flocks by antibiotic class.*

*Figure 3 Distribution of flock antibiotic usage in mg/PCU by farm stratification. Box indicates the interquartile range. Whiskers indicate upper and lower quartiles excluding outliers calculated as those > 1.5 IQR from Q1/Q2 or Q3/Q4 boundary. Median is identified by horizontal line, mean is identified by black diamond.*

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