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Supplementary Material - Evaluation of Metrics for Benchmarking Antimicrobial Use in the United Kingdom Dairy Industry

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S1: Details of the farm management practices and medicine review process

Here we provide brief descriptions of the management practices of the six farms discussed in the main paper and in Figure 2. The six farms are part of an ongoing research project at University of Bristol looking at antibiotic use.

Veterinary sales data were collected with permission from four different practices in the South West of England, and with signed consent from the relevant farmers to access this data. One veterinary practice was unable to provide the medicine sales for one of the farms (Farm A); consequently the medicine review for that farm was based on extensive on-farm records recorded using the farm management program 'Uniform Professional' (www.uniform-agri.com).

Total mgs of each antimicrobial sold to each farm (or used in the case of Farm A) over 12 months was collated into Excel spreadsheets for analysis. Note that with veterinary sales data it is assumed that all medicines that are sold to the farmer are used in the period of review, whereas on-farm records should only consist of what was used. The period of review varied slightly for each farm but was always 12 months within the dates August 2015- February 2017.

Data on course lengths and daily doses, particularly for lactating cow intramammary tubes, were collected from on-farm records and with discussion with the farmer. The modal course length in days for injectable products and the modal number of tubes in a course for intramammary products was used to calculate DCDfarm. Daily dose for lactating cow intramammary products was collected in the same way and was invariably 1 or 2 tubes per day. Daily doses for injectable products was taken from the UK Summary of Product Characteristics documentation for those products.Farms A and B are high-yielding, indoor Holstein herds; Farms C and D are extensive grazing, block-calving, crossbred herds; Farms E and F are average-sized, average-production Holstein-Friesian herds. Further detail is given in Table S1. These six farms were a convenience sample and are not expected to represent all the different variations of medicine use on UK dairy farms. It is impossible to tell how much more variation in treatment regimens exist compared to recommended guidelines.

Table S1: Details of the six farms used to illustrate the metrics in Figure 2 (main text) and Figure S1.

Farm	Number of cows and breed	Number of calves	Milk yield (L/year)	HP-CIAs	Medicine review dates	Management	Specific notes on medicine use
A	500 Holsteins	0	11,000	No	Feb 2016 - Feb 2017	Herd is milked three times a day. Herd is housed all year round. The farm rears their own heifers. Calves are reared off-site on a separate farm (hence medicine use on calves is not included in the analysis). The farm employs more than a dozen stockmen and night milkers.	The highest antibiotic usage was for mastitis (mastitis rate = 68%). This farm does not use macrolides. Main treatment options were cefalexin/kanamycin and penethemate/ dihydrostreptomycin/ framycetin intramammary tubes, frequently supplemented with the use of injectable penethemate. Long courses and off-label use was common. This farm does not use Macrolides. The farm does selective dry cow therapy and used 1.7 g of antibiotic/cow/year of intramammary products.
B	165 Holstein-Friesians	115	11,000	Yes	Dec 2015 - Dec 2016	The farm uses robotic milkers and is a family farm. The farm rears their own dairy calves as well keeping beef stock to fatten. Herd is housed all year round.	The antibiotic usage was split between adults and calves. Antibiotics were used occasionally for footbaths on the farm. Several different intramammary products were used for mastitis with modal course length of 3 milkings, sometimes along with injectable tylosin (mastitis rate= 26%). The farm does selective dry cow therapy and used 0.8 g of antibiotic/cow/year of intramammary products.
C	265 crossbreds	96	6,500	Yes	Nov 2015 - Nov 2016	Herd is milked twice daily and is a family farm. Herd calves in autumn in a tight block, rears their own calves and sells or culls bull calves at 2-3 weeks old. Herd is extensive grazing.	The antibiotic usage was mainly for mastitis (mastitis rate = 11.7%) and treating sick calves. The farm does selective dry cow therapy and used 0.4 g of antibiotic/cow/year of intramammary products.
D	250 crossbred/ Friesians	156	6,000	Yes	Dec 2015 - Dec 2016	Herd is milked twice daily and is a family farm. Herd calves in spring in a tight block, rears their own calves and sells or culls bull calves at 2-3 weeks old. Herd is extensive grazing.	The antibiotic usage was mainly for mastitis (mastitis rate = 9%). The farm does selective dry cow therapy and used 0.9 g of antibiotic/cow/year of intramammary products. The focus for this farm is cutting costs and being as low input as possible.
E	100 Holstein-	24	9,000	Yes	Nov 2015 -	Herd is milked twice daily and is a	The antibiotic usage was mainly for mastitis (mastitis rate =

	Friesians				Nov 2016	family farm. Herd calves from July to February and rears their own calves, running a beef herd as well as sheep alongside the dairy herd.	~40%) and respiratory disease in calves. The farm does selective dry cow therapy and used 1.3 g of antibiotic/cow/year of intramammary products was used.
F	90 predominantly Holsteins	21	8,575	Yes	Dec 2015 - Dec 2016	Herd is milked twice daily and run by one farmer and two part-time workers. Herd calves throughout the year, rears their own heifers and sells or culls bull calves at 3 weeks old. Herd grazes over summer months.	The antibiotic usage was mainly for mastitis (mastitis rate = 43%) and calves (an outbreak of respiratory disease occurred in the 12 months where a whole batch of calves were treated). The farm does selective dry cow therapy and used 0.7 g of antibiotic/cow/year of intramammary products.

S2: Details of assumptions for the calculation of metrics in Figure 2

This section gives further details of the calculations and assumptions made in calculating the metrics for the six farms in Figure 2 of the main text. Calculation of each metric was performed in R (https://www.r-project.org/) using the formulae described in Table 5 of the main text.

Farm-level data (doses rates and course lengths at which medicines were administered on that particular farm) were used for all calculations of DDDfarm and DCDfarm, except for dose rate for injectables, where the figure from the UK Summary of Product Characteristics (or the median if a range of figures was suggested) was assumed to be used on the farm. Farm medicine records for intramammary tubes and intrauterine treatments show how many/treatments tubes per day were given to each animal. Additionally, it was not possible to determine actual, or even farmer-estimated, cattle weights. Therefore, the following standard weights were used: 600 kg for adults and 100 kg for calves (<12 months old) (1). These weights were also used for total mg/kg calculations. Farm records indicated for each product whether it was predominantly used in adult or calves (<12 months of age). To make DDDfarm and DCDfarm more accurately represent AMU, actual farm daily dose rate for injectable products on each farm (as opposed to median values) along with weights and numbers of animals treated on each farm would be needed. If these additional data plus accurate information on cattle weights were used in these calculations, it is expected that this would increase the difference between DDDfarm, DDDUK and DDDvet metrics (and similarly for DCD metrics).

As there are currently no standards defined by European Surveillance of Veterinary Consumption (ESVAC) group for including dry cow therapy (DCT) in DDDvet calculations (2), all DCT products were given a DDDvet value equal to their DCDvet value on the assumption that a course of DCT products is administered in a single dose.

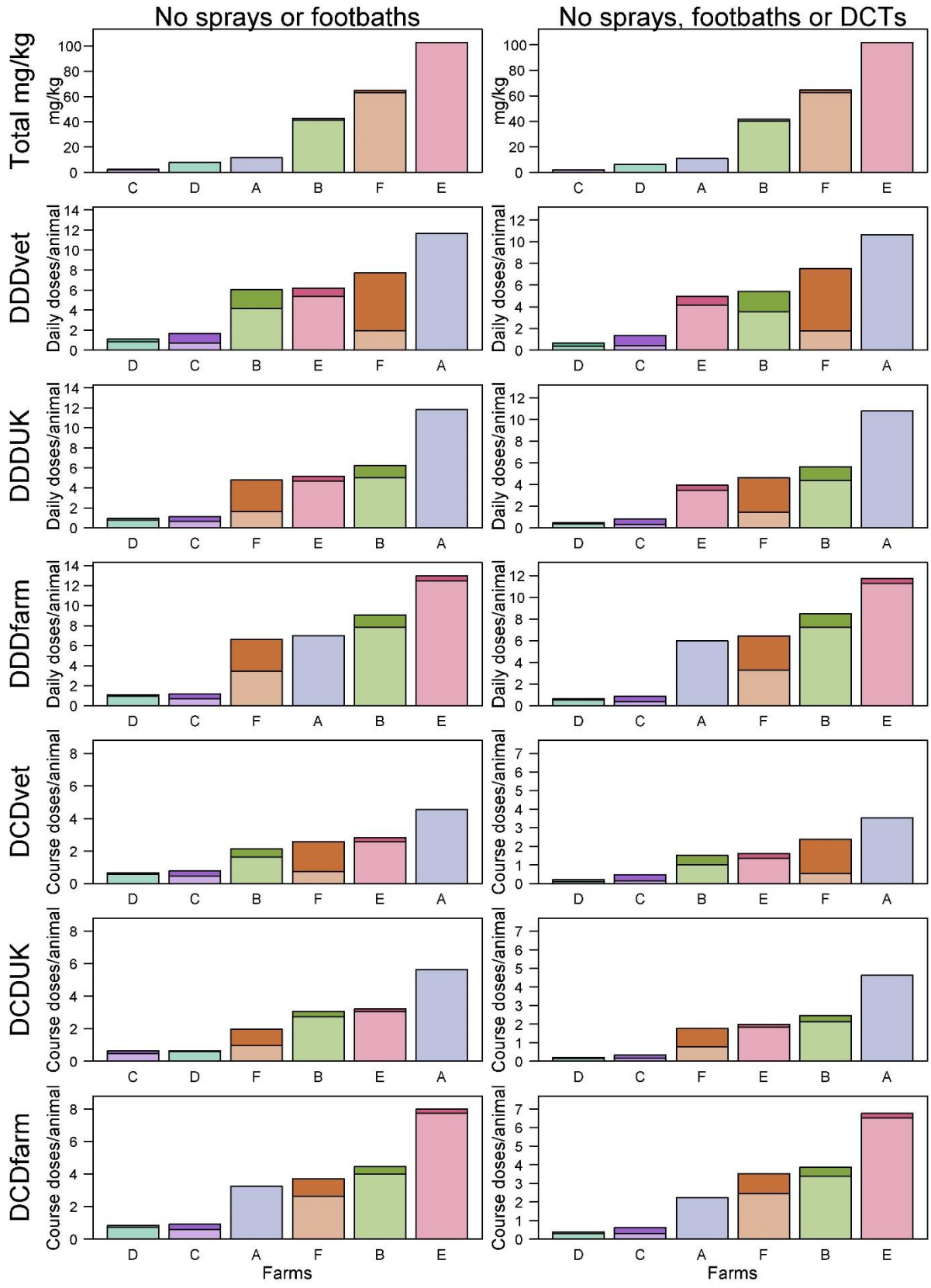
DDD and DCD at the UK and farm level for long-acting macrolides were calculated using the Summary of Product Characteristics (SPC) mg/kg figure, but their long duration of activity was not accounted for due to the paucity of information on duration factors and current lack of clarity on how to complete these calculations. Drugs without a published DDDvet value were excluded from the DDDvet calculation.

No topical antibiotic sprays or antibiotics used in footbaths were included in any of the metrics in Figure 2 of the main text.

It should also be noted that ionophores (a group of medicines used in cattle, e.g. monensin (Kexxtone) which is used as a slow-release product, indicated for the prevention of metabolic disease) have not been included in the metrics. There still exists uncertainty about the use of these substances in agriculture and their impact on AMR (3), especially their impact on human medicine as they are not currently used in humans. However, ignoring these substances should be done with caution as this uncertainty does not indicate that the livestock industries do not need to be concerned with the use of medicines in this class. Other medicines such as halofuginone (an alkaloid used to treat protozoal diarrhoea in calves) and diclazuril (a triazine derivative used to treat coccidiosis in calves) were also excluded from the calculations for Figure 2. Because of the risk of co-selection of AMR, these authors recommend that these medicines be recorded and monitored on farms, but they may be reported as separate entities and may require separate targets going forward.

In order to see the effect of these exemptions, the metrics were also calculated for each farm in turn as: excluding topical sprays and antibiotics used in footbaths (as shown in Figure 2) and excluding topical sprays, antibiotics used in footbaths and DCT (Figure S1). Including DCT makes little difference in the mg/kg metric because of the relatively low amount of active ingredient these tubes contain. However, including DCT does change the ranking of some farms for daily dose metrics (e.g. Farm E uses more than Farm B in DDDvet and DCDUK, Farm E uses more than Farm F in DDDUK and DCDvet).

Figure S1: The seven metrics (total mg/kg, DDDvet, DDDUK, DDDfarm, DCDvet, DCDUK, DCDfarm) shown as: left column - excluding sprays and footbaths (as shown in Figure 2 of the main text); right column - excluding sprays, footbaths and DCT. The darker sections of the bars are the HP-CIAs (as defined by the WHO and EMA (4-6)).



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