Supporting Information

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SI Text

Protocol S1: Three-Step Procedure to Calculate Coefficients of Antimicrobial Consumption per Population Correction Units

Step 1. OECD countries with published estimates of overall antimicrobial consumption were used to train a linear regression model to predict the overall consumption of antimicrobials in milligrams in other OECD countries (AmOECD) as a function of the log-transformed stock of animals (Fig. S3). The model was weighted by the total size of the livestock sector (PCUs) in each country. To avoid overestimating antimicrobial consumption, we excluded the United States from the training set, since it is known to have uncharacteristically high consumption of antimicrobials compared with other OECD countries.

Step 2. A Bayesian linear regression model was fitted to the total consumption of antimicrobials AmOECD, to estimate consumption per PCU for each type of livestock in intensive production systems in 37 countries (all OECD countries, as well as four candidate-OECD countries, except the United States). The prior distributions used for the regression coefficients were assumed to be Gaussian, with means and SDs corresponding to the animal-specific antimicrobial consumption per PCU that could be obtained for 10 countries (Australia, Belgium, Denmark, France, Japan, Korea, The Netherlands, New Zealand, Sweden, and the United Kingdom). The relative importance of cattle, chickens, or pigs in explaining the variability in total antimicrobial consumption was quantified using the difference in the Bayes factor value between a full model including all animal types and a model excluding the animal type of interest.

Step 3. For each country, a value for antimicrobial consumption per PCU in intensive production systems was sampled from the estimated posteriors distribution. The corresponding coefficients for extensive systems were calculated using a randomly sampled scaling ratio ranging from 0.05 to 0.5 times the value sampled for intensive systems. The procedure was repeated 50 times for each country to compute an SD and average coefficient value for each type of livestock. An overall confidence interval for global antimicrobial consumption in food animals was calculated by combining the SD of the antimicrobial consumption predicted in each country in relation to the share of each country in the global antimicrobial consumption.

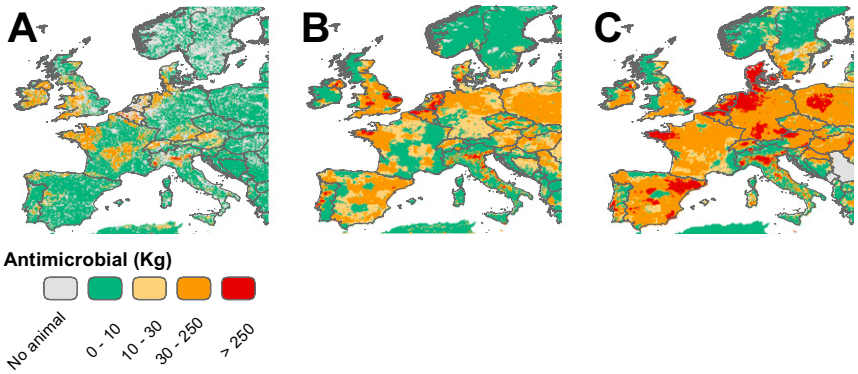

Fig. S1. Antimicrobial consumption in livestock in the European Union in 2010 for cattle (*A*), chickens (*B*), and pigs (*C*).

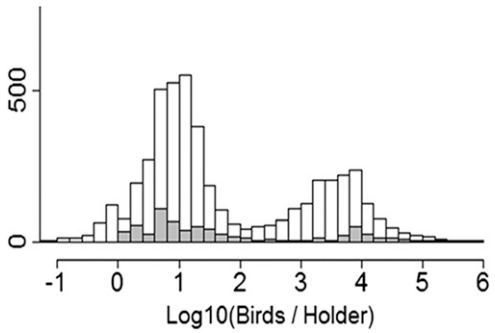

Fig. S2. Distribution of farm sizes in Thailand. The bimodal distribution shows that farms are distributed in two distinct groups corresponding to different production systems: A large number of farms have a median size of 10 birds, whereas another large group of farms host between 5,000 and 10,000 birds.

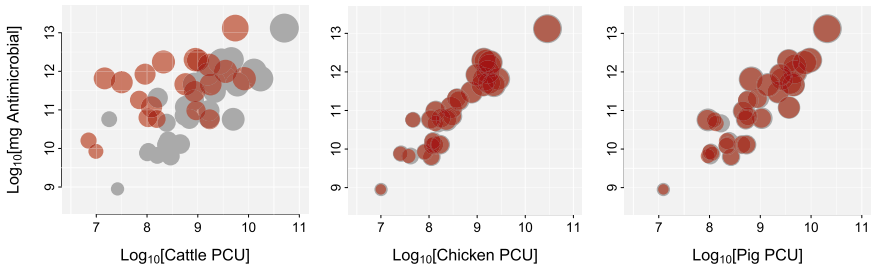

Fig. S3. Association between national antimicrobial consumption obtained from national reports (Table S1) and population correction units (kilograms of meat) in OECD countries in 2010 for cattle, chicken, and pigs. Gray dots represent the total production, and red dots represent intensive production alone.

Table S1. Data used to inform the model presented in this study

Country	Cattle, mg/PCU	Chickens, mg/PCU	Pigs, mg/PCU	Annual sales cattle, kg	Annual sales chickens, kg	Annual sales pigs, kg	Total annual sales, kg	Year	Data source	URL
Australia	–	–	–	133,300*	406,400	104,200	644,000	2009–2010	APVMA	archive.apvma.gov.au/publications/reports/docs/antimicrobial_sales_report_march-2014.pdf
Austria	–	–		–	–	–	63,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	–	–	26.1[†]	–	–	–		2010	Trauffler et al. (1)	veterinaryrecord.bmj.com/content/early/2014/07/22/vr.102520.full.pdf+html
Belgium	–	–	–				299,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	–	–	–	24,800	26,079	156,869		2009–2010	BelVet-SAC[‡]	www.belvetsac.ugent.be/pages/home/BelvetSAC_report_2013%20finaal.pdf
Bulgaria	–	–	–	–	–	–	46,200[§]	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Cyprus	–	–	–	–	–	–	57,200[§]	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Canada	–	–	–	–	–	–	1,450,776[¶]	2012	Correspondence with Jean Szkotnicki (CAHI)	–
Czech Republic	–	–	–	–	–	–	71,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Denmark	–	–	–				119,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	–	–	–	14,636	477[#]	100,527	115,010	2010	DANMAP	www.danmap.org/~/media/Projekt%20sites/Danmap/DANMAP%20reports/Danmap_2010.ashx
Estonia	–	–	–	–	–	–	7,600	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Finland	–	–	–	–		–	13,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
					38.4[‖]			2010	Correspondance with Dr. Hannele Nauholz (ETT)	–
France				–	–	–	997,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	19.11	107.53	147.37	–	–	–		2010	ANSES**	https://www.anses.fr/sites/default/files/documents/ANMV-Ra-Antibiotiques2010.pdf
Germany	–	–	–	–	–	–	2,002,000[§]	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Hungary	–	–	–	–	–	–	206,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Iceland	–	–	–	–	–	–	900	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Ireland	–	–	–	–	–	–	96,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Italy	–	–	–	–	–	–	1,928,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf

Table S1. Cont.

Country	Cattle, mg/PCU	Chickens, mg/PCU	Pigs, mg/PCU	Annual sales cattle, kg	Annual sales chickens, kg	Annual sales pigs, kg	Total annual sales, kg	Year	Data source	URL
Latvia	–	–	–	–	–	–	6,600	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Lithuania	–	–	–	–	–	–	16,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Japan	–	–	–	59,490	89,782	506,549	655,820.50	2010	MAFF[††]	www.maff.go.jp/nval/iyakutou/hanbaidaka/pdf/h22hanbaidakabessatu.pdf
Korea	–	–	–	57,443	204,472	581,507	843,422	2010	QIA[‡‡]	lib.qia.go.kr/Search/Detail/90953?key=%EC%B6%95%EC%82%B0%20%ED%95%AD%EC%83%9D%EC%A0%9C%20%EB%82%B4%EC%84%B1%EA%B7%A0%20%EA%B0%90%EC%8B%9C%EC%B2%B4%EA%B3%84%20%EA%B5%AC%EC%B6%95
The Netherlands	–	–	–				461,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	–	–	–	193,920	42,740	174,700	411,370	2010	Bondt et al. (2)[§§]	www.sciencedirect.com/science/article/pii/S0167587712002346
New Zealand	–	–	–	8,000	24,000	24,000	57,043	2010–2011	MPI[¶¶]	www.foodsafety.govt.nz/industry/acvm/documents/reports.htm
Norway	–	–	–	–	–	–	6,300	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Poland	–	–	–	–	–	–	479,000	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Portugal	–	–	–	–	–	–	181,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Slovakia	–	–	–	–	–	–	–	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Slovenia	–	–	–	–	–	–	8,400	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Spain	–	–	–	–	–	–	1,746,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Sweden	–	–		–			13,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	–	–	14.5[##]	–		3,780		2009	SVA	www.sva.se/upload/Redesign2011/Pdf/Om_SVA/publikationer/Swedres_Svarm2013.pdf
	–	–		–	44.5[‖‖]		14,117	2010	SVA	www.sva.se/upload/Redesign2011/Pdf/Om_SVA/publikationer/1/Svarm2010.pdf
Switzerland	–	–	–	–	–	–	58,121***	2010	SwissMedic	https://www.swissmedic.ch/marktueberwachung/00135/00136/00181/index.html?lang=en
United Kingdom							456,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	6	204	204	11,000	302,000	299,000	390,000	2010	VMD[†††]	https://www.vmd.defra.gov.uk/pdf/VARSS.pdf
United States	–	–	–	–	–		13,542,030	2011	FDA[‡‡‡]	www.fda.gov/downloads/ForIndustry/UserFees/AnimalDrugUserFeeActADUFA/UCM338170.pdf
	–	–	–	–	–	1,270,000		2006–2009	Apley et al. (3)[§§§]	www.nppc.org/wp-content/uploads/Swine-in-feed-use-estimates.pdf

Antibiotic sales for use in other poultry birds are included in most of the chicken-specific data (i.e., "Chickens, mg/PCU" or "Annual sales chickens") presented in this table. Although this may potentially result in overestimation of antibiotic use in chickens only, we believe this approximation is reasonable considering chicken production generally represents the majority of poultry production in most countries. Chicken-specific sales data were obtained for Belgium, Denmark, Finland, and Sweden only. The data collection search procedure involved both contacting relevant government ministries and agencies regarding available data sources and a systematic search of existing published studies on PubMed. In the initial stages of our search for species-specific sales/consumption data, we contacted the agencies listed as data sources for the 25 European countries presented in the European Surveillance of Veterinary Antimicrobial Consumption report (4) as well as all veterinary medicines authorities listed by the Heads of Medicines Agencies website (for further information, see www.hma.eu/vdirectory). All national reports listed in Annex 6 of the ESVAC report were accessed for species-specific data (4). For the remaining OECD countries not listed in the ESVAC report, a systematic search for the relevant government ministry or agency was performed on Google using the following terms in conjunction with a country name: "(Ministry OR Agency) AND (Agriculture OR Health)," "Veterinary Medicines (Directorate OR Authority)," "Medicines Directorate," "Drug Controller," "Food and Drug Administration," "Veterinary Association," "Food Safety," and "(Antimicrobial OR Antibiotic) (Consumption OR Sales) Surveillance." We then contacted ministries/agencies from search results and would either receive data directly from the agency/ministry contacted, be informed that data are not available, or be directed to another ministry/agency. A limitation of this search procedure was the use of English search terms when many countries' ministries/agencies list their names in native languages. However, the relevant agencies for all OECD countries were contacted regarding the availability of data. The search for existing published studies on PubMed used the following terms in conjunction with a country name: "Veterinary (Antibiotic OR Antimicrobial) (Consumption OR Sales)" and "(Antibiotic OR Antimicrobial) (Consumption OR Sales) AND (Food Animals OR Livestock)." ANSES, Agence National de Sécurité Sanitaire (France); APVMA, Australian Pesticides and Veterinary Medicines Authority (Australia); BelVet-SAC, Belgian Veterinary Surveillance of Antibacterial Consumption (Belgium); CAHI, Canadian Animal Health Institute (Canada); DANMAP, Danish Program for surveillance of antimicrobial consumption and resistance in bacteria from animals, food and humans (Denmark); EMA (or ESVAC), European Medicines Agency (or European Surveillance of Veterinary Antimicrobial Consumption) (Europe); ETT, Association for Animal Disease Prevention (Finland); FDA, US Food and Drug Administration (United States of America); MAFF, Ministry of Agriculture, Forestry and Fisheries (Japan); MARAN, Monitoring of Antimicrobial Resistance and Antibiotic Use in Animals in the Netherlands (Netherlands); MPI, Ministry for Primary Industries (New Zealand); QIA, Animal and Plant Quarantine Agency (Korea); SVA (or SVARM), National Veterinary Institute (or Swedish Veterinary Antimicrobial Resistance Monitoring) (Sweden); SwissMedic, Swiss Agency for Therapeutic Products (Switzerland); VMD, Veterinary Medicines Directorate (United Kingdom).

*Sales data for cattle and sheep were pooled together—therefore, this figure likely represents an overestimation of use in cattle. Total annual sales data includes sales for food-producing animals only (sales for use in companion animals were excluded).

†Use data were given in milligrams antibiotic per biomass (kilograms) produced per year. In the study from which this data point was extracted, electronic drug application records from farmers from 75 conventional pig farms were revised and checked for their plausibility. The registered drug amounts were verified by comparing the farmers' records with veterinarians' dispensary records.

‡Species-specific annual sales data were extrapolated using a model based on data from Persoons et al. (5), Callens et al. (6), and Pardon et al. (7).

§Total annual sales (in kilograms active ingredient) for 2010 was back-calculated from 2011 ESVAC (European Medicines Agency) data because 2010 data were not available. This calculation was performed by dividing the 2011 ESVAC data by the median of the ratio of 2011 ESVAC data to 2010 ESVAC data for all countries with data available for 2011 [i.e., 1/median(ESVAC 2011/ESVAC 2010)].

¶Total annual sales data includes sales for food-producing animals only (sales for use in companion animals were excluded).

#Annual sales data for chickens includes only broilers, breeding and rearing broilers, and layers—this figure does not include any other poultry birds.

‖Annual sales data for chickens includes only broilers—this figure does not include any other poultry birds.

**Data given in milligrams of antimicrobial per kilogram live weight of food animal treated and therefore is equivalent to milligrams per PCU.

††Data were disaggregated into the annual sales volume-specific antibiotics. Therefore, total sales volume for all antibiotics was calculated by summing across all antibiotics. Data on antihelmintics and antiprotozoals was also collected but not included in these figures.

‡‡Data were translated by Chang-Yong Choi of the Research Institute for Agriculture and Life Science at Seoul National University.

§§Species-specific annual sales data were derived from use data collected in a MARAN sample survey. Total annual sales refers only to cattle, poultry, and pigs. Please note that the data for cattle is the sum of use for "Cattle" (29,930 kg) and "Veal Calves and Young Beef" (163,990 kg).

¶¶MPI presented sales data for poultry and pigs pooled together. These data points were disaggregated into species-specific constants by assuming a constant consumption per PCU to generate species-specific coefficients used in the priors.

##Data are presented as milligrams per kilogram slaughtered pig. To convert units to mg/PCU live animal, this data point was multiplied by 1/0.7 where 0.7 represents the ratio of live weight to carcass weight for pigs. In other words, 1 kg of live pig was raised for every 0.7 kg of pig meat produced.

‖‖Annual sales data for chickens includes only broilers—this figure does not include any other poultry birds. "In 2010, the total sales where *Gallus gallus* was given as species was 44.5 kg of which 78% were aminopenicillins" (SVARM 2010).

***Total annual sales data include sales for food-producing animals only (sales for use in companion animals were excluded).

†††VMD presented milligrams per PCU data for pigs and poultry pooled together. Annual sales data by species was presented in the following categories: "Cattle Only Products," "Pig Only Products," "Poultry Only Products," "Pig and Poultry Combined Products," and "Multi Species Products in Food Animals Only." "Poultry Only" and "Pig and Poultry Combined" product sales were summed to yield our sales estimate for poultry. We performed the analogous procedure to derive our sales estimate for pigs. We excluded sales of "Multi Species Products in Food Animals" in an attempt to prevent overestimation of antibiotic use. Species-specific consumption was derived from this data by assuming the coefficients for consumption per PCU were identical.

‡‡‡Total annual sales data includes sales for food-producing animals only (sales for use in companion animals were excluded). The FDA presented 2011 sales data for domestic consumption disaggregated by antimicrobial class. Therefore, our estimate is the sum of sales of all antimicrobial classes for domestic consumption only.

§§§Apley et al. (3) presented data as "National Estimates of Total Kilograms of Swine In-Feed Antimicrobials for All Production Cycles in a Year by Antimicrobial and Reason." Therefore, our estimate is the sum across all antimicrobials and reasons.

1. Trauffler M, Griesbacher A, Fuchs K, Köfer J (2014) Antimicrobial drug use in Austrian pig farms: Plausibility check of electronic on-farm records and estimation of consumption. *Veterinary Record* 175(16):402.
2. Bondt N, Jensen VF, Puister-Jansen LF, van Geijlswijk IM (2013) Comparing antimicrobial exposure based on sales data. *Prev Vet Med* 108(1):10–20.
3. Apley MD, Bush EJ, Morrison RB, Singer RS, Snelson H (2012) Use estimates of in-feed antimicrobials in swine production in the United States. *Foodborne Pathog Dis* 9(3):272–279.
4. European Medicines Agency (2013) Sales of veterinary antimicrobial agents in 25 EU/EEA countries in 2011 - Third ESVAC Report. Available at: www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000302.jsp. Accessed March 10, 2015.
5. Persoons D, et al. (2012) Antimicrobial use in Belgian broiler production. *Prev Vet Med* 105(4):320–325.
6. Callens B, et al. (2012) Prophylactic and metaphylactic antimicrobial use in Belgian fattening pig herds. *Prev Vet Med* 106(1):53–62.
7. Pardon B, et al. (2012) Prospective study on quantitative and qualitative antimicrobial and anti-inflammatory drug use in white veal calves. *J Antimicrob Chemother* 67(4):1027–1038.