

Global trends in antimicrobial use in food animals

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Demand for animal protein for human consumption is rising globally at an unprecedented rate. Modern animal production practices are associated with regular use of antimicrobials, potentially increasing selection pressure on bacteria to become resistant. Despite the significant potential consequences for antimicrobial resistance, there has been no quantitative measurement of global antimicrobial consumption by livestock. We address this gap by using Bayesian statistical models combining maps of livestock densities, economic projections of demand for meat products, and current estimates of antimicrobial consumption in high-income countries to map antimicrobial use in food animals for 2010 and 2030. We estimate that the global average annual consumption of antimicrobials per kilogram of animal produced was 45 mg·kg⁻¹, 148 mg·kg⁻¹, and 172 mg·kg⁻¹ for cattle, chicken, and pigs, respectively. Starting from this baseline, we estimate that between 2010 and 2030, the global consumption of antimicrobials will increase by 67%, from 63,151 ± 1,560 tons to 105,596 ± 3,605 tons. Up to a third of the increase in consumption in livestock between 2010 and 2030 is imputable to shifting production practices in middle-income countries where extensive farming systems will be replaced by large-scale intensive farming operations that routinely use antimicrobials in subtherapeutic doses. For Brazil, Russia, India, China, and South Africa, the increase in antimicrobial consumption will be 99%, up to seven times the projected population growth in this group of countries. Better understanding of the consequences of the uninhibited growth in veterinary antimicrobial consumption is needed to assess its potential effects on animal and human health.

antimicrobials | livestock | mapping | drug resistance | linear regression

Antimicrobials are widely used for disease prevention and growth promotion in food animals. In the United States, antimicrobial use in food animals is estimated to account for ~80% of the nation's annual antimicrobial consumption (1), a significant fraction of which involves antimicrobials that are important in human medicine in the treatment of common infections and also necessary to perform medical procedures such as major surgeries, organ transplantation, and chemotherapy (2).

This widespread use of antimicrobials in livestock contributes—by means of natural selection—to the emergence of antimicrobial-resistant bacteria (ARBs) and has significant public health implications: ARBs of animal origin can be transmitted to humans through the environment (3) and food products (4) and to agricultural workers by direct contact (5). Although direct causality is difficult to establish because of the ecological nature of antibiotic selection pressure, studies have shown a close association between the prevalence of livestock-associated ARBs in animals and in humans (6), as well as between the levels of antimicrobial use in animals at a population level, and the prevalence of ARBs in animals (7) and in humans (8). A recent study from seven European countries (Norway, Sweden, Denmark, Austria, Switzerland, The Netherlands, and Belgium) showed a strong correlation between consumption levels for eight classes of antimicrobials (9) and the prevalence of antimicrobial-resistant commensal *Escherichia*

coli in pigs, poultry, and cattle. Several works additionally suggested that repeated exposure to low doses of antimicrobial agents—the context in which growth-promoting antimicrobials and prophylactic are administered—creates ideal conditions for the emergence and spread of ARBs in animals (10).

In low- and middle-income countries, rising incomes have driven an unprecedented growth in demand for animal protein (11) and, as a result, the global biomass of animals raised for food now exceeds the global biomass of humans (12). In Asia, daily animal protein intake grew from 7 grams per capita per day to 25 grams per capita per day (12) between 1960 and 2013 while the proportion of the diet coming from rice and wheat progressively decreased, primarily among higher-income adults (13). To meet this demand, countries such as Brazil, Russia, India, China, and South Africa (BRICS) have shifted toward highly cost-efficient and vertically integrated intensive livestock production systems. Because these production systems necessitate antimicrobials to keep animals healthy and maintain productivity, rising incomes in transitioning countries are effectively driving an increase in antimicrobial consumption and thereby antimicrobial resistance. Meanwhile, multiresistant ARBs have been isolated in food animals in BRICS countries (14, 15) and throughout the developing world where the use of antimicrobials for growth promotion remains largely unregulated (16).

The challenges of the nutritional transition to animal protein-based diets and the rise of antimicrobial resistance are thus closely linked: The use of antimicrobials as growth promoters

Significance

Antimicrobials are used in livestock production to maintain health and productivity. These practices contribute to the spread of drug-resistant pathogens in both livestock and humans, posing a significant public health threat. We present the first global map (228 countries) of antibiotic consumption in livestock and conservatively estimate the total consumption in 2010 at 63,151 tons. We project that antimicrobial consumption will rise by 67% by 2030, and nearly double in Brazil, Russia, India, China, and South Africa. This rise is likely to be driven by the growth in consumer demand for livestock products in middle-income countries and a shift to large-scale farms where antimicrobials are used routinely. Our findings call for initiatives to preserve antibiotic effectiveness while simultaneously ensuring food security in low- and lower-middle-income countries.

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and therapeutics to support the growing demand for meat is placing ever greater selection pressure for resistant strains of bacteria to evolve. Whereas trends in antibiotic consumption in humans are now being tracked in most high-income and some middle-income countries through databases on antibiotic sales (17, 18), antimicrobial consumption in livestock has received comparatively little attention. Expert opinion suggests that global consumption of antimicrobials in animals is twice that of humans (19). However, the underlying data from the veterinary sector supporting these claims are weak and lack standardization. Without reliable evidence to estimate global antimicrobial consumption in livestock, the links between antimicrobial consumption and resistance patterns are poorly quantified, and efforts and policies to optimize antibiotic use in animals are poorly targeted.

This study addresses these gaps in our understanding of antimicrobial use in animals. We use statistical models combining maps of livestock densities and reports of antimicrobial consumption in high-income countries to estimate and map the global consumption of antimicrobials in food animals for 2010. We then project antimicrobial consumption trends for the year 2030 based on growth projections of the consumption of livestock products.

Results

Overall Antimicrobial Consumption Trends. Global consumption of antimicrobials in food animal production was estimated at 63,151 ($\pm 1,560$) tons in 2010 and is projected to rise by 67%, to 105,596 ($\pm 3,605$) tons, by 2030. Two thirds (66%) of the global increase (67%) in antimicrobial consumption is due to the growing number of animals raised for food production. The remaining third (34%) is imputable to a shift in farming practices, with a larger proportion of animals projected to be raised in intensive farming systems by 2030. In Asia alone, as much as 46% of the increase in antimicrobial consumption by 2030 is likely due to shifts in production systems. By 2030, antimicrobial consumption in Asia is projected to be 51,851 tons, representing 82% of the current global antimicrobial consumption in food animals in 2010.

In 2010, the five countries with the largest shares of global antimicrobial consumption in food animal production were China (23%), the United States (13%), Brazil (9%), India (3%), and Germany (3%) (Fig. 1). By 2030, this ranking is projected to be China (30%), the United States (10%), Brazil (8%), India (4%), and Mexico (2%). Among the 50 countries with the largest amounts of antimicrobials used in livestock in 2010, the five countries with the greatest projected percentage increases in antimicrobial consumption by 2030 are likely to be Myanmar (205%), Indonesia (202%), Nigeria (163%), Peru (160%), and Vietnam (157%). China and Brazil are among the largest consumers of antimicrobials currently but are not the countries with

the most rapid projected increases in antimicrobial consumption. This indicates that these two countries have already initiated a shift toward more intensified livestock production systems using antimicrobials to maintain animal health and increase productivity. Antimicrobial consumption for animals in the BRICS countries is expected to grow by 99% by 2030, whereas their human populations are only expected to grow by 13% over the same period (20).

Consumption by Type of Livestock. The global estimates of antimicrobial consumption presented in this study are based on species-specific coefficients of antimicrobial consumption per population correction unit (PCU). Using a Bayesian regression framework, we estimated the posteriors distributions for these coefficients for intensively farmed animals (Fig. 2). The mean of the posterior for antimicrobial consumption in cattle was generally lower (45 mg/PCU) than for chickens (148 mg/PCU) and pigs (172 mg/PCU). The difference in Bayes' factors between a complete regression model including cattle, chickens, and pigs and regression models including two types of animals were, respectively, 1.32 for a model including just chicken and pigs, 78 for a model including just cattle and pigs, and 1.72×10^9 for a model including just cattle and chickens. This indicates that dropping chicken and pigs from the regression models resulted in a significant loss of predictive power to estimate the overall antimicrobial consumption, and that the number of pig PCUs best explained the differences in overall antimicrobial consumption between countries. The higher dispersion of the posterior distribution of chicken production compared with that of pig production suggests that intensive chicken production showed a wider range of intensity of antimicrobial use across countries than did pork production.

Geographical Patterns. Antimicrobial consumption displayed important geographic heterogeneity across continents. In South and Southeast Asia, antimicrobial consumption hotspots include the southeast coast of China, Guangdong and Sichuan provinces, (Fig. 3, *Top*), the Red River delta in Vietnam, the northern suburbs of Bangkok, and the south coast of India and the cities of Mumbai and Delhi. In the Americas, the highest consumption of antimicrobials was observed in the south of Brazil, the suburbs of Mexico City, and midwestern and southern United States. The only notable hotspots of antimicrobial consumption in Africa were the Nile delta and the city of Johannesburg and its surrounding townships. The uncertainty bounds associated with the spatial predictions of antimicrobial consumption are presented in Fig. 3 (*Bottom*). In general, the SDs of the coefficients of antimicrobial consumption per PCU were moderate in regions where intensive farming practices are common and food animals are densely populated. Higher uncertainty in the model prediction was observed in Central Asia, Ethiopia, Canada, and eastern India, for example.

When disaggregated by food animal species, the geographical distributions of antimicrobial consumption display distinct spatial patterns according to regional production patterns. Fig. S1 shows these patterns within the European Union. Most of the antimicrobial consumption associated with chicken production is found in Flanders (Belgium), The Netherlands, the British Midlands, Brittany (France), and the Po Valley (Italy). Consumption in pork production is largely concentrated in northern Germany, Denmark, The Netherlands, northern France, northern Belgium, Madrid and the autonomous region of Cataluña in Spain, and the Po Valley. Comparatively, the geographic intensity of antimicrobial consumption in cattle production was low across Europe because of the lower use of antimicrobials per PCU and the lower animal densities characteristic of cattle, compared with chicken and pig.

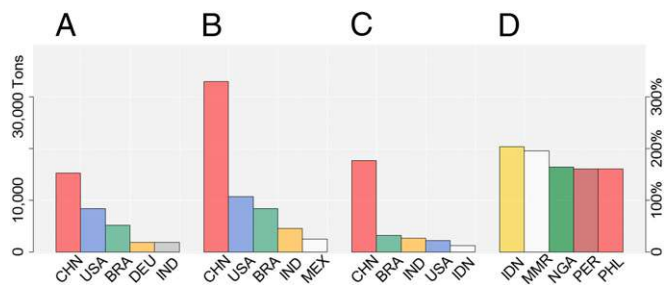


Fig. 1. (A) Largest five consumers of antimicrobials in livestock in 2010. (B) Largest five consumers of antimicrobials in livestock in 2030 (projected). (C) Largest Increase in antimicrobial consumption between 2010 and 2030. (D) Largest relative increase in antimicrobial consumption between 2010 and 2030. CHN, China; USA, United States; BRA, Brazil; DEU, Germany; IND, India; MEX, Mexico; IDN, Indonesia; MMR, Myanmar; NGA, Nigeria; PER, Peru; PHL, Philippines.

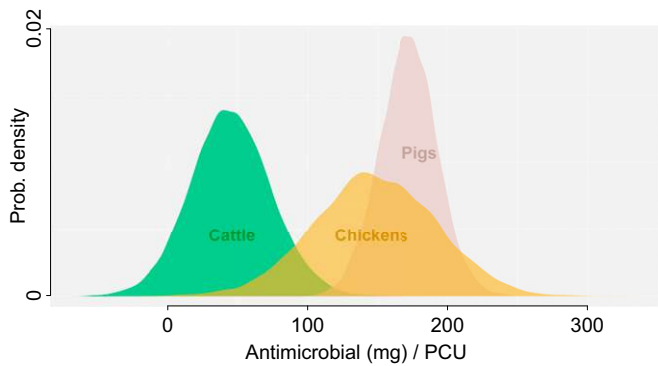


Fig. 2. Posterior distributions for estimates of antimicrobial consumption in cattle, chickens, and pigs in OECD countries.

In Asia, antimicrobial consumption in chicken and pigs is expected to grow by 129% and 124%, respectively, by 2030 (Fig. 4). However, the total acreage of areas where antimicrobial consumption is currently greater than $30 \text{ kg}\cdot\text{km}^{-2}$ will grow by 4% for pork and 143% for chicken. This has potentially important logistical implications for surveillance programs to track the emergence of ARBs over larger portions of land. The extreme growth in consumption for chickens is primarily the result of the expansion of this sector in India alone, where areas of high consumption ($30 \text{ kg}\cdot\text{km}^{-2}$) are expected to grow 312% by 2030.

Discussion

In this study, we use statistical models to map the global consumption of antimicrobials in food animals for 2010 and 2030. This is the first study that we are aware of that attempts to quantify antimicrobial consumption in food animals at a global scale.

As with any model-based study, our analysis is subject to assumptions and limitations. Data on antimicrobial use in livestock are scarce, stemming from both the lack of publicly funded surveillance systems and the reluctance of food animal producers, animal feed producers, and veterinary pharmaceutical companies to provide comprehensive reports of antimicrobial consumption or sales. For this study, estimates of antimicrobial consumption could be obtained for only 32 countries, all of which were high income. These data were first interpolated among other high-income countries and subsequently extrapolated to estimate antimicrobial consumption in intensive production systems of low- and middle-income countries. This modeling strategy was necessarily chosen as a result of the lack of systematic and reliable reports on antimicrobial sales in middle- and low-income countries. The underlying assumption implicit to this modeling strategy is that because they are highly standardized, intensive farming operations use similar quantities of antimicrobials across high-, middle-, and low-income countries. Additionally, several European countries used to train the statistical model have experienced declining sales of antimicrobials for animal consumption, ranging from 0.4% to 28% between 2010 and 2011 (21), and several Organization for Economic Co-operation and Development (OECD) countries are currently engaged in initiatives aiming at reducing antibiotic use in livestock production (22). Additionally, patterns of antimicrobial consumption in middle-income and high-income countries differ in many respects. In most instances, the absence of clear legislative framework on the use of antimicrobials in livestock production in most middle- and low-income countries may result in increased irrational consumption. Our estimates of antibiotic consumption in 2010 may thus represent an overestimation of the current consumption levels. However, several of our assumptions may also result in underestimating the global antimicrobial consumption. First, among the countries used to train the statistical models, 25 are subject to

a ban on antimicrobial use for growth promotion, and two are subject to a partial ban (Australia and New Zealand) (16). Second, the United States, where withdrawal of antimicrobials for growth promotion is voluntary, was excluded from the model-fitting procedure to prevent its comparatively larger statistical weight from artificially increasing the significance of the linear regression. Individual US state estimates could have helped overcome these issues, but these were not available. As a result, we likely underestimate consumption of antimicrobials in livestock in the United States. Additionally, because this information was missing in the majority of countries used to train the statistical models, this study does not evaluate antimicrobial consumption on a compound-specific basis. Finally, the total volume figures do not account for choices of drugs, potential differences in drug potencies, resistance selection pressures, or use for treatment in human medicine. A potential caveat of this study is that ionophores—compounds that are used only in animals—are reflected in our estimates of the global antimicrobial consumption because these are generally pooled with medically important antimicrobials in national reports of total antimicrobial sales. As a result, our estimates of antimicrobial consumption may not always reflect differences in exposures to antimicrobials among countries.

The introduction of a binary distinction between extensively and intensively raised livestock masks a variety of production processes prevalent globally but is relatively well documented for poultry production systems in Asia (Fig. S2) (23) and was recently validated for Thailand (24). For pigs, production systems of intermediate size (semiintensive) may represent a nonnegligible share of production, but these were not treated as an individual category for this study. Our simplifications were chosen over more speculative and arbitrary modeling assumptions that could have introduced additional uncertainty and potentially affected the projected trends for growth in antimicrobial consumption. The estimates presented in this study should therefore be seen as conservative estimates of antimicrobial consumption in food production, barring major changes in the global regulatory framework of these substances over the next 2 decades.

Globally, intensive livestock farming has increased food production at a low cost per unit produced, but perhaps at an unrecognized price paid in increased antimicrobial resistance. Linking antimicrobial consumption in animals to drug-resistant infections of humans is inherently complex owing to the ecological nature of the selection pressure for drug-resistant pathogens as well as the existence of indirect routes of transmission through the environment. However, in recent years, a growing body of

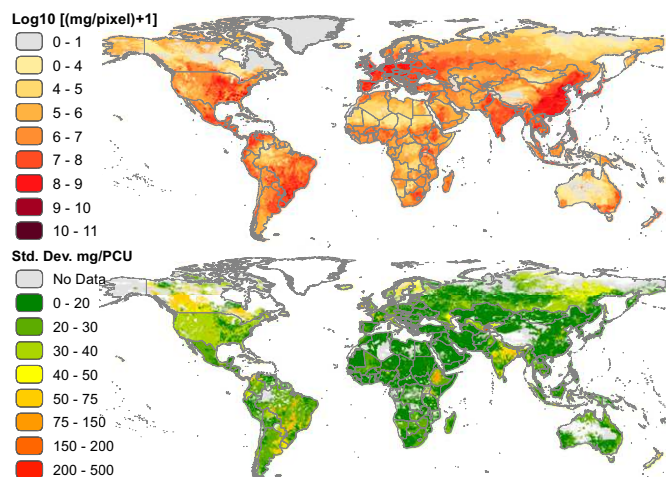


Fig. 3. Global antimicrobial consumption in livestock in milligrams per 10 km^2 pixels (Top) and average SD of estimates of milligrams per PCU (Bottom).

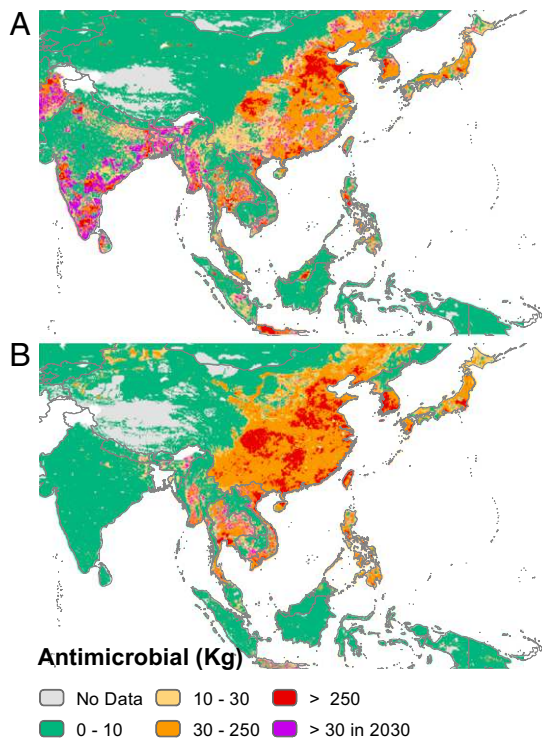


Fig. 4. Antimicrobial consumption in chickens (A) and pigs (B) in 2010. Purple indicates new areas where antimicrobial consumption will exceed 30 kg per 10 km² by 2030.

evidence has accumulated that strengthens the hypothesis that the routine (25) use of antimicrobials in intensive animal production systems constitutes a waste of natural resources (26)—antimicrobial effectiveness—that is of crucial importance in human medicine. Intensive farming practices have not only been associated with antimicrobial resistance in animals, humans, and meat but also with numerous other livestock diseases such as highly pathogenic avian influenza H5N1 (27) and porcine reproductive and respiratory syndrome (28). Beyond animal health and antimicrobial resistance, other negative externalities associated with poorly regulated intensive farming include water and soil pollution (29), loss of biodiversity (30), and decline of meat nutritional quality (31). All of these have severe consequences that potentially outweigh long-term benefits of increased productivity.

Mapping the antimicrobial consumption in livestock provides a baseline estimate of its global importance. Similar mapping exercises have been conducted for other major public health issues, such as malaria (32) or tuberculosis (33). Leading a comparable initiative for antimicrobial consumption provides several insights. First, it provides an objective data-driven estimate of the potential magnitude of antimicrobial consumption at the global scale, whereas previous estimates were based on expert opinions (34). Second, it identifies regions at higher risk of emergence of drug-resistant pathogens—places where surveillance and intervention efforts should be targeted. Third, this baseline estimate can be used to evaluate the progress (35) of future antimicrobial stewardship efforts. Finally, this approach can be adapted to predict antimicrobial consumption in the future using updated maps of livestock, and thus continuously update projections for the evolution of antimicrobial resistance in livestock and humans.

If regulatory action is not taken, our projections suggest that global antimicrobial consumption in food animals will grow by at least 67% by 2030. This corresponds to a compound annual

growth rate of 2.60%, a rate comparable to the compound annual growth rate for consumption of antibiotics in humans for the period 2000–2010 (2.84%) (18) but almost threefold the projected annual growth rate of the human population (0.98%) from 2010 to 2030. In 2001, Wise estimated the annual antimicrobial market at 100,000–200,000 tons (34), but Wise’s methodology is unknown to us. Under the plausible hypothesis that global human antimicrobial consumption is likely smaller or at best equivalent to animal consumption, and that human consumption grew by 36% between 2000 and 2010 (17), we find that our estimate for antimicrobial consumption in 2010 (63,151 tons) is surprisingly consistent with the expert opinion estimate (34). Finally, up to one third of the increase in antimicrobial consumption in animals between 2010 and 2030 will be imputable to a shift toward intensive production systems where antimicrobials are used routinely in subtherapeutic doses for disease prevention and growth promotion, rather than for disease treatment (16, 36, 37).

In 2010, China was the largest antimicrobial consumer for livestock, and we estimate that its livestock industry will use up to 30% of the global antimicrobial production by 2030. Another country contributing to a large share of the overall growth in antimicrobial consumption in food animals, if current trends continue, is India—a country already confronted with antibiotic overuse in human medicine and an extremely high (and increasing) prevalence of ARBs (e.g., ~95% of adults in India carry bacteria resistant to β -lactam antimicrobials) (38). Widespread resistance may be more consequential for India than for other countries because India’s bacterial disease burden is among the highest in the world, and therefore antimicrobials play a critical role in limiting morbidity and mortality (39). Currently, India has no regulatory provisions for the use of antimicrobials in cattle, chicken, and pigs raised for domestic consumption, nor do the majority of middle-income countries for which substantial growth in antimicrobial consumption over the next 15 y is predicted (16). Recent studies in various regions of India have discovered antimicrobial residues in food animal products (such as chicken meat and milk) (40), indicating that antibiotic use in food animal production is widespread and current regulation is nonexistent for domestic production. Limiting antimicrobial consumption in both humans and livestock may present a formidable challenge for Indian public health authorities, but it might also be an opportunity for the country to take a regional lead in tackling this problem. For instance, neighbors such as Pakistan, Bangladesh, Nepal, and Sri Lanka are likely to be guided and influenced by regulatory action in India, given the interconnectedness of the region’s pharmaceutical commerce (41).

The role of aquaculture has not been investigated in the present study. However, this industry may represent a large share of the antimicrobial consumption for an increasing number of countries in Southeast Asia. For instance, studies of antimicrobial consumption in fish farming in Chile (42) and shrimp farming in Vietnam (43) demonstrate that aquaculture is associated with extremely high rates of antimicrobial consumption per PCU [up to 1,400 mg/PCU reported for salmon farming in Chile (42)]. As the aquaculture industry grows (44) and shifts toward more-efficient production systems, it could constitute a major source of antimicrobial contamination of the aquatic environment over the coming decades.

The analysis presented here is based on the very limited available evidence on antimicrobial consumption in livestock production. We provide somewhat crude estimates of present and projected antimicrobial consumption in food animals in 2030. Our estimates of absolute values for the global antimicrobial consumption should therefore be viewed with caution. Antimicrobial consumption levels in middle- and low-income countries were extrapolated from consumption levels in intensive production systems in high-income countries. This methodology may result in significant uncertainties when evaluating the global

antimicrobial consumption level in livestock production. However, working under the hypothesis that our methodology is subject to a systematic error over the period 2010–2030, we project that, in relative terms, the consumption of antimicrobials in food animals will grow significantly by 2030 owing to an important increase in demand for meat in middle- and low-income countries. This indicates a potentially growing contribution of these countries to the global burden of antimicrobial resistance. In fast-growing Asian countries, this will constitute a serious challenge because these countries are currently experiencing the most rapid increase in demand for meat products (45), but regulations on antimicrobial use (for the domestic market) are still lacking and surveillance information on antimicrobial consumption is either nonexistent or not publicly available. Despite its regional nature, this process will unavoidably drive a global increase in the prevalence of ARBs through trade and transport networks, with potentially important consequences for human health. This rise of ARBs seems potentially reversible for certain compounds: Withdrawal of antimicrobials for growth promotion in several European countries led to a decrease in the prevalence of ARBs, but the duration needed for reversal is unclear and the subject of ongoing investigation (7, 46).

Given the potential costs of inaction, this study, among others, calls for urgent and concerted action in all countries, which is needed to limit the overuse and abuse of antimicrobials in food animal production (2, 18, 47). These actions should include (i) implementation of a publicly funded international surveillance network of antimicrobial consumption in food animals in countries undergoing rapid intensification in the livestock sector, (ii) collaboration with veterinary drug manufacturers and animal feed producers to cross-validate estimates of consumption with sales data, (iii) implementation of an international agenda to harmonize regulatory frameworks among countries, and (iv) the ultimate phasing out of antimicrobial use for growth promotion, based on the successful experience in the European Union and the new biological (48, 49) and economic (50, 51) evidence challenging the purported benefits of antimicrobial use in food animal production.

Methods

In the absence of systematic and harmonized data on antimicrobial consumption in livestock, we use indirect means to estimate antimicrobial consumption (in milligrams of active ingredient per kilogram of animal) for cattle, pigs, and chickens raised in both extensive and intensive farming systems in 228 countries. In our study, intensive production refers to high input–high output systems that, compared with extensive systems (backyard production), achieve greater economies of scale and efficiency while also possibly using mechanized labor, operating with high animal densities, and using specialized breeds with rapid weight gain and high feed conversion ratios. The coefficients calculated for each type of livestock and for each system were subsequently applied to high-resolution maps of livestock population densities to predict the geographic distribution of antimicrobial consumption in food producing animals for the years 2010 and 2030.

Antimicrobials. Data on antimicrobial consumption in food animals were obtained from government veterinary agencies, agriculture ministries, scientific reports and publications, and personal communications with academic researchers; all data are included in Table S1. Data were collected by contacting relevant government ministries or agencies and through a systematic search of studies on PubMed. The search terms and a detailed description of the data collection process are given in Table S1. The majority of countries either do not collect or do not release data on veterinary antimicrobial consumption. Across countries, data on antimicrobial consumption were found in three formats: (i) estimates of overall antimicrobial consumption, (ii) estimates of consumption by livestock species, and (iii) estimates of consumption per PCU disaggregated by species type (e.g., chickens, cattle, and pigs). PCUs are used to compare population and production of different types of livestock across countries and correspond to 1 kg of living or slaughtered animal (21). For example, a herd of 10 pigs each weighting 100 kg corresponds to 1,000 PCUs. Assuming that antimicrobial consumption in chickens, cattle, and pigs represents the majority of antimicrobial consumption

in food-producing animals, the total consumption of antimicrobials was calculated for each country by pooling the estimates collected in case *ii* or by multiplying the per PCU figure by the total national PCU for each type of livestock in case *iii*. When data could not be obtained for the reference year 2010, the antimicrobial estimates obtained for another year were adjusted using the ratio of overall antimicrobial consumption between 2010 and the corresponding year. Estimates of total antimicrobial consumption could be obtained for 32 countries, including 28 member states of the OECD and four candidate-OECD countries (Cyprus, Latvia, Lithuania, and Bulgaria).

Animal Census. To calculate estimates of antimicrobial consumption per PCU that could be applied at the pixel level to generate total antimicrobial consumption maps, we estimated national PCUs as a function of the number of living animals. Thus, total PCUs in a country or a pixel for livestock type *k* in the production system *s* were defined as follows:

$$PCU_{k,s} = An_{k,s} \cdot (1 + n_{k,s}) \cdot \left(\frac{Y_k}{R_{(CW/LW),k}} \right)$$

where An_k is the number of living animals, $n_{k,s}$ is the number of production cycles in each production system (extensive or intensive), Y is the quantity of meat per animal (carcass weight) obtained for each country from FAOSTAT, and $R_{(CW/LW),k}$ is the killing-out percentage (or dressing percentage)—that is, the ratio of carcass weight to live weight of an animal—obtained from literature estimates (52). The last term of this equation can be interpreted as the animal weight reconstructed from country-specific productivity figures.

To reflect differences in productivity, distinct values were used for the number of production cycles in extensive ($n_{c,Ext}$) and intensive ($n_{c,Int}$) production systems. Working under the assumption that extensive farming represents the bulk of livestock production in low-income countries, n_{Ext} was estimated from the median number of production cycles in the quartile of countries characterized by the lowest gross domestic product (GDP) per capita (World Bank estimates). This value was considered identical in all countries on the basis that backyard productivity displays little variability across low-income countries (the ratio of SD to the mean in the lower GDP per capita quartile was 0.65 for cattle, 0.44 for chickens, and 0.91 for pigs). The number of production cycles in intensive systems was calculated by imputation as $n_{c,Int} = (S - n_{Ext} \cdot An_{Ext}) / An_{Int}$, where S is the total number of animals slaughtered in 2010.

Statistical Models. Antimicrobial consumption per PCU for each type of livestock in extensive and intensive systems was estimated using Bayesian regressions through a three-step procedure described in *S1 Text* and *Fig. S3*.

Mapping Predictions. To generate spatially explicit estimates of antimicrobial use, the estimates of consumption per PCU in each country were multiplied by the corresponding PCU values in each pixel. The uncertainty of the mapped prediction was quantified by weighting the respective SD for each livestock coefficient by the relative PCU for each pixel. Maps of chickens and pigs, disaggregated by extensive and intensive production systems for the year 2010, were obtained from Gilbert et al. (24). For cattle, maps of population densities disaggregated between extensive and intensive were generated from the total population densities obtained from Robinson et al. (53). We used a threshold of five cattle head per kilometer to allocate animals to a map of intensively raised cattle. The map of extensively raised cattle was generated by subtracting the intensively raised from the total number of head in each pixel. Livestock densities in 2030 were estimated based on a projection of meat consumption in 2030 (45). Assuming a constant value for the compound annual growth rate from 2000 to 2030, this value was used to calculate the ratio of meat consumption $R_{30/10}$ between 2010 and 2030,

$$R_{30/10} = \frac{An_{2030}}{An_{2010}} = \left(\frac{An_{2030}}{An_{2000}} \right)^{\frac{2}{3}}$$

where An is the number of animals in each pixel. The projected livestock densities for 2030 were estimated by multiplying animal densities per pixel in 2010 by $R_{30/10}$. For pigs and chickens, we used the model developed by Gilbert et al. (24) that quantifies the country-level proportion of extensively raised chicken and pig stock as a function of GDP per capita in purchasing power parity. On the national level, the proportion of chickens or pigs raised intensively showed a good correlation with this metric because the development of cost-efficient, large-scale farms typically requires substantial investments and influx of capital.

The proportion of animals raised in extensive production systems was calculated by replacing the current GDP values in the model by those of the year 2030, obtained from linear projection of GDP estimates from the International Monetary Fund for the period 1980–2018. For cattle, in the absence of reliable global estimates for shift in production structure, the proportion of animals raised extensively and intensively was assumed to be identical for 2010 and 2030. All maps were resampled at 0.08333 decimal degree resolution (~10 kilometers at the equator).

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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 (Am_{OECD}) 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 Am_{OECD} , 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 as-

sumed 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.

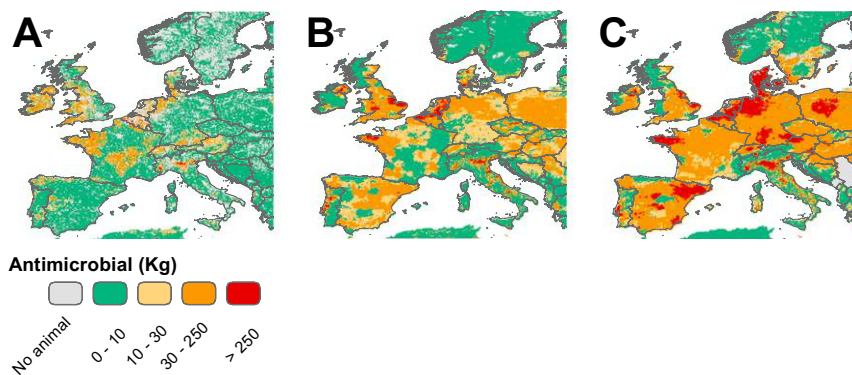


Fig. S1. Antimicrobial consumption in livestock in the European Union in 2010 for cattle (A), chickens (B), and pigs (C).

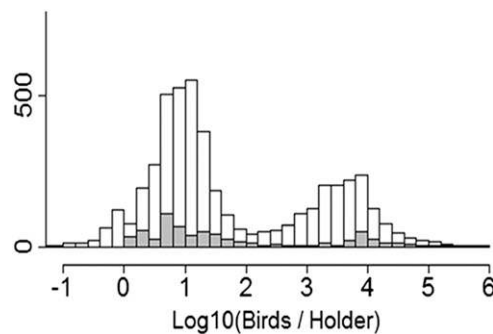


Fig. S2. Distribution of farm sizes in Thailand. The bimodal distribution shows that farms are distributed in two distinct groups corresponding to different production systems: A large number of farms have a median size of 10 birds, whereas another large group of farms host between 5,000 and 10,000 birds.

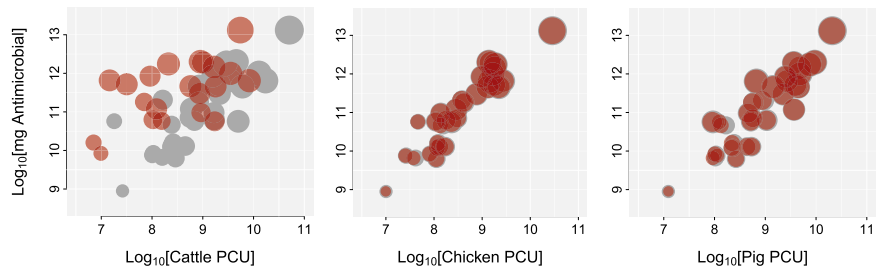


Fig. S3. Association between national antimicrobial consumption obtained from national reports (Table S1) and population correction units (kilograms of meat) in OECD countries in 2010 for cattle, chicken, and pigs. Gray dots represent the total production, and red dots represent intensive production 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
Belgium	-	-	26.1 [†]	-	-	-	299,000	2010	Trauffler et al. (1)	veterinaryrecord.bmj.com/content/early/2014/07/22/vr.102520.full.pdf+html
Bulgaria	-	-	-	24,800	26,079	156,869	299,000	2009–2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.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	-	-	-	14,636	477 [#]	100,527	119,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Denmark	-	-	-	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
France	19.11	107.53	147.37	-	38.4	-	997,000	2010	Correspondence with Dr. Hannele Nauhholz (ETT)	-
France	-	-	-	-	-	-	997,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Germany	-	-	-	-	-	-	2,002,000 [§]	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/nvail/yakutou/hanbaidaka/pdf/h22hanbaidakabessatu.pdf
Korea	-	-	-	57,443	204,472	581,507	843,422	2010	QIA ^{††}	lib.qja.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
New Zealand	-	-	-	193,920	42,740	174,700	411,370	2010	Bondt et al. (2) ^{§§}	www.sciencedirect.com/science/article/pii/S0167587712002346
Norway	-	-	-	8,000	24,000	24,000	57,043	2010–2011	MPI ^{¶¶}	www.foodsafety.govt.nz/industry/acvm/documents/reports.htm
Poland	-	-	-	-	-	-	6,300	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Portugal	-	-	-	-	-	-	479,000	2011	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
Slovakia	-	-	-	-	-	-	181,000	2010	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
Switzerland	-	-	-	-	-	3,780	14,117	2009	SVA	www.sva.se/upload/Redesign2011/Pdf/Om_SVA/publikationer/Swedres_Svarm2013.pdf
United Kingdom	6	204	204	11,000	302,000	299,000	390,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
United States	-	-	-	-	-	-	13,542,030	2011	FDA ^{†††}	https://www.vmd.defra.gov.uk/pdf/VARSS.pdf
	-	-	-	-	-	1,270,000	2006–2009	Apley et al. (3) ^{§§§}		www.nppc.org/wp-content/uploads/AnimalDrugUserFeeActADUFA/UCM338170.pdf
	-	-	-	-	-	-	58,121 ^{***}	2010	SwissMedic	www.swissmedic.ch/marktueberwachung/00135/00136/00181/index.html?lang=en
	-	-	-	-	-	-	456,000	2010	EMA	www.ema.europa.eu/docs/en_GB/document_library/Report/2013/10/WC500152311.pdf
	-	-	-	-	-	-	44.5	2010	VMD ^{†††}	https://www.vmd.defra.gov.uk/pdf/VARSS.pdf
	-	-	-	-	-	-	14.5 ^{##}	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/vdindex). 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 (Food Animals OR Livestock)," ANSES, Agence Nationale 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., $1/\text{median}(\text{ESVAC } 2011/\text{ESVAC } 2010)$].

[¶]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, breeding and rearing broilers, and layers—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 antihelminthics 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. Trauffer 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/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.