COSTS AND BENEFITS OF ANTIMICROBIAL USE IN LIVESTOCK

AUDE TEILLANT, RESEARCH ASSISTANT, PRINCETON ENVIRONMENTAL INSTITUTE, PRINCETON UNIVERSITY, USA

Antimicrobial use in food-animal production is rising rapidly, driven by the increasing demand for animal protein and livestock globally. The volume of antimicrobials used in livestock outstrips that used for disease treatment in humans and creates significant selection pressure for the evolution of antimicrobial resistance. This article overviews the available data on the use of antimicrobials in livestock, the public health questions it raises, and the specific issues of the economic value of antimicrobial growth promoters (AGPs) to producers and consumers.

The discovery of antimicrobials is one of the most significant achievements of modern medicine and has substantially contributed to a reduction in the burden of common infectious diseases of humans and livestock globally. Antimicrobials are used in various applications including human and animal medicine, food production, plant agriculture and industrial applications. In food-producing animals they are typically used for three purposes: therapeutic reasons (cure a disease), prophylactic reasons (prevent a disease) and as growth promoters (sub-therapeutic quantities of antimicrobials increase animal growth rates and improve feed efficiency).

Rapid income growth in low- and middle-income countries has increased demand for animal protein *(1–3)*. This increasing demand is being met by a shift toward intensive livestock production systems that depend on antimicrobials to keep animals healthy and operate efficiently *(4)*.

The widespread use of antimicrobials in human medicine and in agriculture comes at a cost: it has created selection pressure and fostered the emergence and spread of antimicrobial-resistant pathogens worldwide. Resistant microbes and resistance genes can circulate among humans, animals, food, water and the environment and there is greater awareness of the deep connections between animal and human health. Moreover, trade, travel and migration are carrying resistant organisms globally at an unprecedented pace, and highlight the need for cooperation between countries and sectors for controlling the spread of antimicrobial resistance *(5)*. At the Ministerial Conference on Antimicrobial Resistance that took place in the Netherlands in June 2014, a global call was made to take action on antimicrobial resistance, acknowledging it as a global threat to effective prevention and treatment of infections *(6)*.

Since many antimicrobials commonly used in sub-therapeutic concentrations are the same as or similar to antimicrobials used in human medicine, there is global concern that drug-resistant organisms may pass from animals to humans and present a serious threat to public health *(7)*. This article presents an overview of the available data on the use of antimicrobials in livestock, the public health questions it raises, and the specific issues of the economic value of antimicrobial growth promoters (AGPs) to producers and consumers.

Overview of antimicrobial use in livestock

➤ *There are major knowledge gaps about the extent of antimicrobial use in livestock globally*

Surveillance systems monitoring the quantity of antimicrobials used in food-producing animals exist in relatively few countries (including European Union countries, the United States, Canada, Australia, Japan, South Korea and New Zealand). According to a survey conducted by the World Organisation for Animal Health (OIE) in 2012, only 27% of the OIE member countries had an official system for collecting quantitative data on antimicrobial use in livestock *(8)*. Data on the use of antimicrobials is lacking in areas where the food production is increasing rapidly, such as China, India or Brazil.

In the United States, antimicrobials are used primarily in swine and poultry production, and to a lesser extent in dairy cows, sheep, and companion animals. Antimicrobials are also widely used in feedlot cattle *(9)*. In the rest of the world, most antimicrobials are used for growth promotion and prophylaxis in intensive pig and poultry operations. The only publicly available information on the quantity of antimicrobials used in food animals in the United States are aggregate data on annual sales and distribution obtained from antimicrobial drug sponsors. These data have been published by the US Food and Drug Administration (FDA) for the years 2009 to 2013. An estimated 14,788 tons of antimicrobials were sold for use in animals (both food-producing animals and companion animals for disease treatment and sub-therapeutic use) in 2013 in the United States, including 4,434 tons of ionophores, a class of antimicrobials used only in veterinary medicine *(10)*. The total quantity of medically important antimicrobials sold or distributed for use in food-producing animals increased by 20% between 2009 and 2013. In comparison, an estimated 3,290 tons of antimicrobials were sold during 2011 for human use *(11)*.

The European Surveillance of Veterinary Antimicrobial Consumption report, which covers 26 EU countries and approximately 95% of the food-producing animal population in the European Economic Area, reported sales of 8,046 tons of veterinary antimicrobials in 2012. The intensity of antimicrobial use in animals (defined as the annual sales divided by the estimated weight of livestock and of slaughtered animals) fell overall by 15% between 2010 and 2012 in Europe *(12)*.

➤ *With no major changes in policy, global consumption of antimicrobials could rise by two-thirds by 2030*

In the absence of data on global antimicrobial use in livestock, a recent study has used indirect means to estimate consumption for cattle, pigs and chickens raised in both extensive and intensive farming systems in 228 countries *(13)*. Global consumption of antimicrobials in food animal production was estimated at 63,151 (±1,560) tons in 2010 in this study, and is projected to rise by 67%, to 105,596 (±3,605) tons by 2030. The biggest increases are likely to be in larger emerging economies, and especially important for poultry, as demand is more important and growing faster than for other livestock products. In hotspots like India for instance, areas of high consumption (30 kg per km^2) for industrial poultry production are expected to grow 312% by 2030. Whereas these projection numbers are highly indicative and should not be considered as a prediction, these results show that excessive antimicrobial consumption will become a more global, if not uniform, problem in the coming years and consequently a concern for all.

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Antimicrobial use in livestock: The public health question

Numerous studies have demonstrated that food animals on farms using low levels of AGPs harbour a higher percentage of resistant bacteria than farms that do not use AGPs *(14)*. Increased resistance to certain drugs in both animals and humans coincides with their use in food-animal production. For instance, increased resistance to fluoroquinolones in both humans and animals is temporally associated with the introduction of fluoroquinolones in veterinary medicine, primarily for the treatment of respiratory diseases in poultry *(15,16)*. Additionally, studies comparing resistance prevalence in both humans and animals before and after AGP bans have documented significant decreases in resistance, primarily in vancomycin-resistant enterococci isolated from farm animals and healthy ambulatory people following the ban of avoparcin as a growth promoter *(17,18)*.

Increasing levels of resistance in bacteria isolated from food-producing animals and retail meat sources have been reported by the National Antimicrobial Resistance Monitoring System *(19)*. FDA reported that resistance to third-generation cephalosporins rose among isolates from retail ground turkey between 2008 and 2011, and among certain salmonella serotypes in cattle between 2009 and 2011 *(19)*.

Most important from a public health perspective, extensive research has documented the spillover of resistance genes and resistant pathogens from food animals into human populations via three primary pathways:

- (1) the release of antimicrobial-resistant bacteria into the environment *(20)*;
- (2) resistance transmission through the food chain *(21);*
- (3) the acquisition of resistant strains through direct contact with food animals *(22)*.

How much these processes contribute to resistance of human pathogens to antimicrobials is still unclear. Nevertheless, a report from the Centers for Disease Control and Prevention (CDC) states, "Because of the link between antimicrobial use in food-producing animals and the occurrence of antimicrobial-resistant infections in humans, antimicrobials should be used in food-producing animals only under veterinary oversight and only to manage and treat infectious diseases, not to promote growth" *(23)*.

The economic cost of withdrawing antimicrobial growth promoters from the livestock sector

In 1986, Sweden became the first country to ban antimicrobial growth promoters (AGPs) – initially because of consumer's concern about antimicrobial residues in food – and require veterinary prescription of therapeutic doses for treating or preventing disease *(24)*. Concerns about increasing antimicrobial resistance led to bans on AGPs in the European Union in 2006. In the United States, AGPs are not banned, but the FDA recently issued guidelines for the veterinary drug sponsors to voluntarily withdraw medically important antimicrobials from growth promotion *(25)*. In 2014, the Canadian government published a strategy mimicking the voluntary FDA approach on phasing out AGPs.

Some other OECD countries have a ban on AGPs (for instance, Mexico, South Korea and New Zealand). AGPs are not banned in most of the non-OECD countries which are major meat (poultry, pig and cattle) producers, such as China, Brazil, Russia Federation, Argentina, India, Indonesia, Philippines and South Africa *(26)*.

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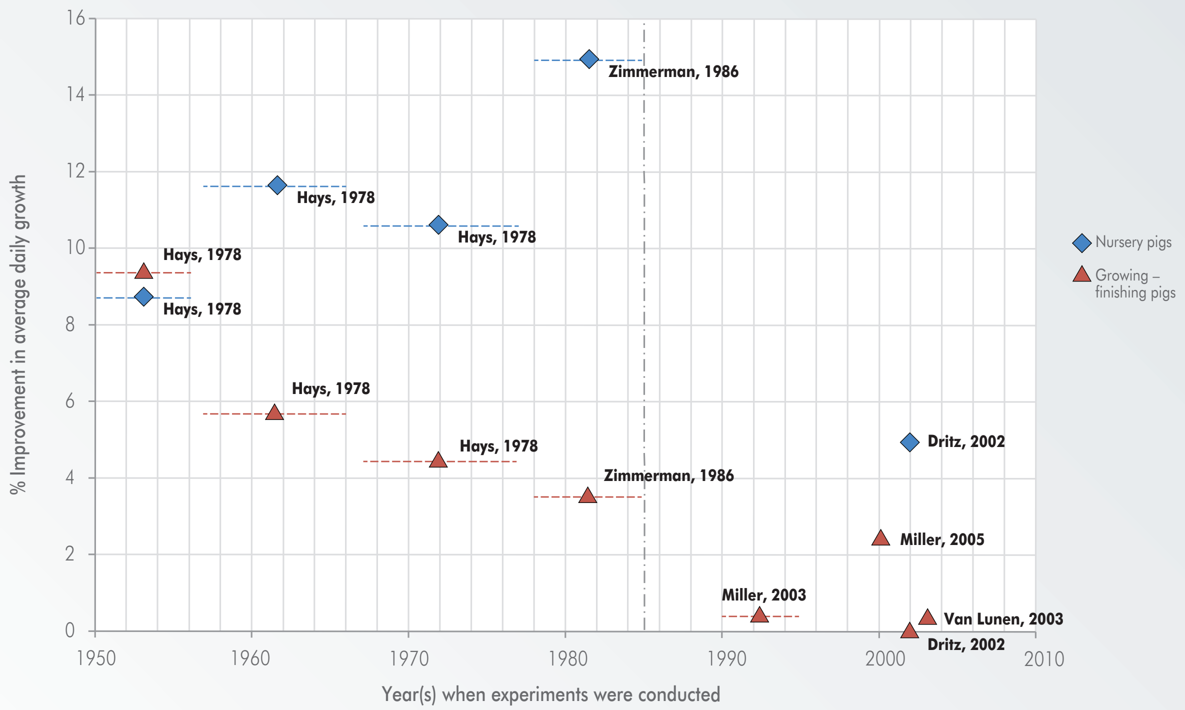
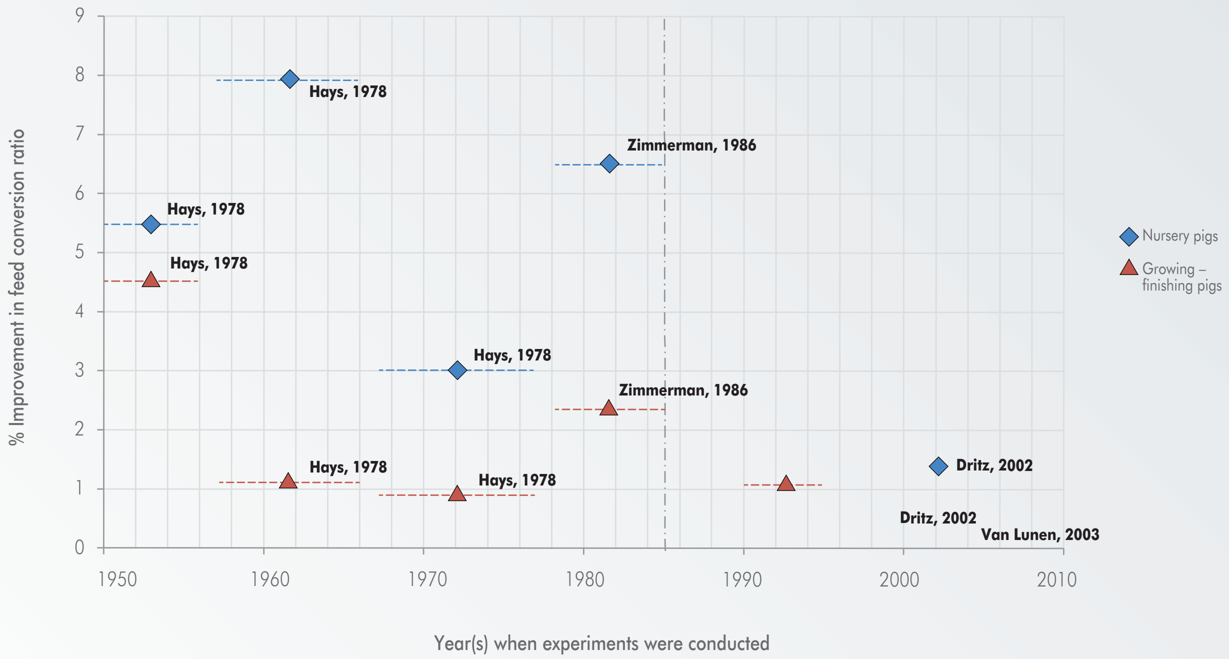
Policy-making on the use of antimicrobials in the livestock sector requires a clear understanding of the benefits and the costs of antimicrobial use in livestock to society. Since the preponderance of antimicrobial use is for growth promotion in livestock, it is important to accurately quantify the economic contribution of this mode of antimicrobial consumption. In the next section, we summarize recent

Figure 1: Percentage improvement in average daily growth of pigs fed antimicrobials over time



Note: The x-axis refers to the year when the experiments were conducted. Hays, 1978 and Zimmerman, 1986 are reviews of studies conducted over a given time period. The horizontal lines represents the period during which the experiments were conducted.
Source: Data compiled from Hays (1978), Zimmerman (1986), Miller (2003), Dritz (2002), Miller (2005), Van Lunen (2003).

Figure 2: Percentage improvement in feed conversion ratio of pigs fed antimicrobials over time



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evidence on the economics of AGP use in the livestock industry and the potential economic consequences for producers and consumers of phasing out AGPs.

➤ *The growth response to Antimicrobial Growth Promoters (AGPs) is small in optimized production systems*

The discovery that antimicrobials fed in sub-therapeutic concentrations to livestock can hasten their growth and prevent disease came just as farmers in the United States were struggling to keep pace with demand for food and animal protein *(27,28)*. Antimicrobial use for growth promotion and disease prevention soon became an integral part of a new agricultural production model, despite early warnings about the potential risks of developing resistance *(29)*.

In spite of 50 years of antimicrobial use as growth promoters, recent and reliable data on the effect of AGP use on productivity are lacking. There is considerable variability in the growth response to sub-therapeutic antimicrobials, according to the species, the age of animals, their genetic potential, and the specific hygiene and management conditions. While studies conducted before the 1980s reported improvement in the growth rate and feed efficiency of pig, poultry and cattle fed sub-therapeutic antimicrobials as high as 5–15%, studies conducted in the United States, Denmark and Sweden after the 2000s point to more limited effects (Figs. 1 and 2). In pigs, less than 1% improvement or not statistically significant improvement have been reported recently, except for nursery pigs in which improvement in growth rate can still reach 5% *(30)*.

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Table 1 provides a comparison of three studies on the effects of AGPs on broiler production: one animal-level experimental study of the removal of AGP in two United States broiler farms *(31)*, one farm-level observational study

Table 1: Comparison of production and economic effects of AGP restrictions in the poultry industry, United States and Denmark

	US animal-level experimental research (31)	US farm-level observational research (32)	Denmark observational research pre (1994–1997) and post (1998–2000) ban on AGPs (33)
Change in feed conversion ratio, value (percentage change)	Site 1: +0.016 (0.8%*) Site 2: +0.012 (0.6%*)	No HACCP: +0.08 (4%) HACCP: +0.05 (2.6%)	+0.016 (0.9%)
Average weight differential grams (percentage change)	Site 1: −13.6 g (0.6%*) Site 2: −18.1 g (0.8%*)	2–7% production decline without AGPs when controlling for labor, capital and other inputs, not statistically significant	+ 53 g
Mortality rate	Differential: Site 1: −0.2% Site 2: −0.14%	With AGP: 3.95% No AGP, no HACCP: 5.01% No AGP, HACCP: 3.95%	Pre-ban: 4.1% Post-ban: 4.0%
Cost-effectiveness	Cf. Graham et al. study, based on Engster data: Net effect of using AGP = lost value of $0.0093 per chicken (savings in cost of AGPs more than compensate for decrease in production)	Growers using no AGPs and with HACCP receive 2.1% more fees per kg than growers using AGPs, suggesting higher costs of production in absence of AGP Non-AGP premium that would be paid to growers by integrators: $22.5 million	Calculations suggested that savings in cost of APG almost exactly offset cost of decreased feed efficiency Potential substantial costs associated with modifications to production systems (not evaluated)

Source: Emborg et al. (2001), Engster et al. (2002), Graham et al. (2007), MacDonald & Wang (2011)
Abbreviations: HACCP, hazard analysis and critical control points (food safety plan).

** The baseline values of feed conversion ratio and average weight were not provided in (31). We assumed that baseline feed conversion ratio = 1.95 and average market liveweight = 2.27 kg to calculate the percentage change in feed conversion ratio and average weight.*

based on US Department of Agriculture (USDA) poultry national survey *(32)*, and one observational study with data from before and after the ban on AGPs in Denmark *(33)*. Similarly to what is observed in recent studies on the growth response to AGP in hogs, recent results in poultry suggest limited effect of withdrawing AGP on growth performance (Table 1).

A common explanation for these results is that the growth response to antimicrobials is less important when nutrition, hygiene practices, the genetic potential of animals and health status of the animal herd or flock are optimal. With drastic changes in the animal industry over the last 30 years in the OECD countries, all of these key parameters have changed, potentially explaining the decrease in the efficacy of AGPs.

➤ *Projected effects of restricting sub-therapeutic antimicrobial use on livestock production globally vary widely*

In a recent report produced for the OECD, the potential loss of production and meat value following a ban on AGPs was estimated in two scenarios: a scenario where the growth response to AGPs is still high (based on growth response data from the 1980s), and a scenario with a low growth response to AGP (based on data from the 2000s) *(26)*. In this study, it was projected that the cumulative loss of global meat production resulting from a worldwide ban on AGPs would result in a decrease by 1.3% to 3% from its current level (1980s vs 2000s scenarios), corresponding to a global loss in meat production value between US$ 13.5 and US$ 44.1 billion in the two scenarios respectively *(26)*.

➤ *The economic impact of a ban on AGPs could be limited in high-income industrialized countries but higher in lower* *income countries with less optimized production systems*

Studies from Denmark and Sweden, as well as recent estimates in the United States, suggest limited economic effects of phasing-out AGPs *(34–36)*. However, such limited economic effects may not be applicable in every country or every operation within a country. It is likely that countries which have modern production systems applying good hygiene and production practices would see limited productivity and economic effect of phasing out AGPs *(32,36,37)*. However, countries with less optimized production systems could observe larger productivity and economic effects. The cost of investing in improved hygiene practices and their indirect benefits are difficult to estimate but potentially significant.

Conclusion

There are major data gaps on the use of antimicrobials in livestock globally. Data on the quantity and patterns of antimicrobial use will be essential to evaluate the efficacy of potential policy options. The most controversial use of antimicrobials in livestock is their use as growth promoters. Our review of the economics of AGPs indicates that the magnitude of the growth response to antimicrobials in the swine and poultry industry appears to have decreased over time, even if recent data are relatively sparse. Based on the Danish and Swedish cases, maintaining production after AGPs are phased out would involve substitution practices such as improved hygiene management and biosecurity measures. However, the cost of investing in improved production systems is unknown and could be significant for some producers. In the long-term, investing in more biosecurity measures could improve the productivity of the industry by reducing the spread of all infectious diseases, including those that cannot be controlled with antimicrobials, and by preserving the efficacy of antimicrobials to prevent and treat animal disease. Restricting antimicrobial use in food animals and decreasing antimicrobial resistance reservoirs in animals could have major public health benefits, even if such benefits are difficult to quantify. •

Aude Teillant is a Research Assistant at the Princeton Environmental Institute, Princeton University, USA. She works on antimicrobial resistance and the economics of antimicrobial use in livestock and co-authored the recently published first OECD report on antibiotics use in husbandry. Before joining Princeton University, Aude Teillant worked for three years as a policy officer in the Policy Planning Unit (CAS) of the French Prime Minister. She holds a MD in biology from the École Normale Supérieure de Cachan, France, and a Master's degree in Sustainable Development from Sciences Po Paris, France.