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Introduction

Antimicrobials are of fundamental importance for modern medicine. They have substantially reduced the number of fatalities and sufferings from bacterial infections. Antimicrobial treatment of infected individuals also reduce transmission of bacteria and thereby the incidence of disease outbreaks. In addition, without efficient antimicrobials, many surgical interventions would be high-risk procedures (ECDC, 2008; Aminov, 2017; Cook and Wright, 2022; WHO, 2023).

However, bacteria develop resistance to antimicrobials if exposed to them (Bronswaer et al, 2003; WHO, 2005; ECDC, 2008; Page and Gautier, 2012; O'Neil et al, 2015a; Cook and Wright, 2022). Resistant bacteria have a competitive advantage in an environment with frequent use of antimicrobials. Therefore, the effectiveness of antimicrobials decreases with the amount used, if broad-spectrum antimicrobials are used, if antimicrobials are used in sub-therapeutic doses, or if they are used over longer periods (Goossens et al. 2005; Aminov and Mackie, 2007; Aminov, 2017). Moreover, due to travel and trade, bacteria that become resistant in one country can, similar to infectious diseases, rapidly spread to other countries.

The societal costs for antibiotic resistance are high

Antimicrobial resistance is considered a global problem with significant costs to society (World Bank, 2017; WHO, 2023). Nelson et al. (2021) estimated the direct health care costs for patients hospitalised in the US with resistant bacteria in 2017 to about USD 4.6 billion (€ 4.1 billion). OECD (2023) estimated the annual direct health care cost of resistant infections until 2050 to USD 3 (€ 2.8) billion, and USD 1.6 (€ 1.5) billion for the US and the EU respectively.[1] In addition, it has been estimated that, world-wide, about 1.2 million persons die every year from infections caused by drug resistant bacteria (Antimicrobial Resistance Collaborators, 2022), and that more than 35 000 of these deaths occur in the EU (ECDC, 2022), and another 35 000 in the US (CDC, 2019).

The direct health care costs are only a part of the cost for society. The Value of a Statistical Life (VSL) estimates the value of shortened or lost lives via the utility function of the individuals. The VSL differs between countries depending on, *inter alia*, differences in incomes and age-structure (Lanoie et al, 1995; Ashenfelter, 2006; Viscusi, 2020; Sweis, 2022).[2] Using the estimates in Sweis (2022) the costs of the 35 000 deaths per year in the US would be about USD 252 billion annually (€ 225 billion), i.e. more than 50 times higher than the direct health care costs for 2017 reported by Nelson et al. (2021).

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[1] Direct health care costs only include the costs of resources used for treating the patient, that is, they do not include the costs of production losses caused by longer sickness periods or the costs of lives lost.

[2] Sweis (2022) estimated VSLs for 48 countries. Results indicated that the value of a VSL ranges from USD 9.4 million (Switzerland) to USD 0.06 million (Afghanistan). The VSL for the US was USD 7.2 million.

Agriculture is a major user of antibiotics

Largely the same antimicrobials are used in veterinary and human medicine. Moreover, larger quantities are used in livestock production than in human medicine[3]: It has been estimated that global consumption of antimicrobials in animal production was about 63 000 tonnes annually in 2010 (Van Boeckel et at, 2015), about 93 000 tonnes in 2017 (Tieso et al, 2020), and about 99 500 tonnes in 2020 (Mulchandani et al, 2023). All three studies project that, in a business as usual scenario, consumption will increase over time.and. The risk of bacteria acquiring resistance is regarded as larger in animals than in humans (Gildchrist et al, 2007; Van Boeckel et al, 2017; de Alcantara Rodrigues et al, 2020) because in many countries, substances are used in sub therapeutic doses for growth promotion and without veterinary prescription, Resistant bacteria from animals can transfer to humans (and vice versa). The risk of this is, however, difficult to quantify because of the complex ways in which transfer can occur (O'Neil et al, 2015b; FAO, 2016; Wu, 2018; Umar et al, 2020; Emes et al, 2022; Tiedje et al, 2023). As an example, studies estimate that between 70 and 90 percent of the active substance in antimicrobials administered to livestock is excreted without being fully metabolised. Bacteria in the environment can then be exposed to antimicrobials and transfer to humans. (Kim and Ahn, 2022; Tiedje et al, 2023).

The EU banned the use of antimicrobials for growth promotion in livestock production from 2006.[4] EU member states have also agreed on restrictions on the use of antimicrobials for *prophylaxis* (administration of antimicrobials to animals before clinical signs of disease) and for *metaphylaxis* (administration of antimicrobials to a group of animals after diagnosis of disease in some animals in the group) in livestock production which became effective in 2022.[5] Individual member states have gone further. For instance, in the Netherlands (2008) and Belgium (2016), agreements were reached between the government, veterinary organisations and other stakeholders to reduce antimicrobial use in farm animals by 50 percent (Speksnijder et al, 2015; Favv-afsca, 2018). In France, a similar agreement was reach in 2012 but with a more modest target, i.e. reduction of utilisation by 25 percent in 2016 (Agriculture.gov.fr, 2016). According to a study by Bergevoet et al (2019), the Dutch reduction target was achieved without negative effects on production and economic results in the livestock sector.

New substances are needed on a regular basis

In the "golden era" of antimicrobials from the 1940s to the 1970s, resistance to one drug was met with the introduction of a new one. However, few new antimicrobials have been introduced since the 1980s. Moreover, there are very few candidates for approval in the pipeline and large pharmaceutical companies appear to show little interest in antimicrobials (Kumar et al, 2020; Church and McKillip, 2021; Iskandar et al, 2022). Hence, to preserve the efficiency of existing drugs, several countries have implemented antimicrobial conservation and stewardship programmes and the World Health

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[3] For instance, in 2021 in the EU, more than 60 percent of total antimicrobial use was in animal medicine. EFSA Journal, 2024; 22: e8589. https://www.efsa.europa.eu/en/efsajournal/pub/8589

[4] See Regulation (EC) No 1831/2003 on additives for use in animal nutrition. https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003R1831. Accessed 2023-10-16.

[5] See Regulation (EU) 2019/6 on veterinary medical products, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0006, and Regulation (EU) 219/4 on medicated feed, https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32019R0004. Accessed 2023-10-16.

Organization (WHO) has adopted a global action plan on antimicrobial resistance targeting both human and veterinary medicine (WHO, 2015; Dyar et al. 2017; OIE, 2020). Key elements of these programmes and the WHO global action plan are to minimise the need for antimicrobials by reducing the incidence of infection through effective sanitation, hygiene, and infection preventing measures and, when antimicrobials are needed, use them as efficiently as possible. Along these lines, the WHO has developed a list of critically important antimicrobials for human medicine, and the World Organization for Animal Health (OIE) a similar list for veterinary medicine (WHO, 2018; OIE, 2021). The recommendation is that the use of these antimicrobials should be restricted to particular circumstances (WHO, 2022; OIE, 2021).

Ironically, the adoption of antimicrobial conservation and stewardship programmes could be one reason for pharmaceutical companies' declining interest in the field as restrictions on the prescription of new antimicrobials reduce economic incentives to engage in their development. It may also be that economic incentives for developing antimicrobials are inherently low in relation to those for other drugs. For instance, antimicrobials are usually prescribed for shorter periods while drugs that target chronic diseases are consumed during several years. Prices for new antimicrobials are also low in comparison as they often are benchmarked against prices of existing drugs, which, to a large extent include generic substances (O'Neil et al, 2016; Plackett, 2020; Morel et al, 2020; McKenna, 2020; Cama et al, 2021).

Public interventions may be required

The lack of new antimicrobials has resulted in calls for public sector intervention to increase incentives to engage in their development. This could be through subsidising research and development, by paying companies for bringing new drugs to the market (thereby partly separating remuneration from sales), or a combination (Årdal et al, 2018; Cama et al, 2021; Leonard et al, 2023). Regardless of the chosen strategy, the outlays of the public sector must be financed. As antimicrobial resistance is a negative externality (a cost caused by the use of antimicrobials that is not included in their prices), there is a role for government interventions since governments can force users to account for the cost of resistance by taxing antimicrobials.[6] Such a tax would be in accordance with the Polluter Pays Principle (Kahn, 2015). Apart from raising funds to finance strategies to increase incentives to develop and introduce new antimicrobials, the tax would also reduce the (over)use of antimicrobials by raising their prices. A tax on antimicrobials has been discussed by, for instance, Vågsholm and Höjgård (2010), O'Neil et al (2016), Van Boeckel et al (2017), Giubilini et al (2017), Lhermie et al (2017), Giubilini (2019), Anomaly (2020), and Morgan et al (2023).

However, there are several issues to consider regarding the size of such a tax. For an economically efficient solution, the tax should be equal to the marginal external cost of resistance caused by the use of a given antimicrobial, a so-called Pigouvian tax (Pigou, 1932). This is difficult given the present lack of knowledge on how marginal changes in

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[6] Some EU-countries have introduced taxes on veterinary antimicrobials. For instance, Denmark introduced a differentiated tax in 2013 ranging from 0.5 percent for narrow-spectrum penicillines to 10.8 percent for critically important antimicrobials (European Commission, 2016). Similarly, in 2014, Belgium introduced at differentiated tax ranging from € 1.75 per kilogram active substance for non-critically important to € 2.63 for critically important antimicrobials (European Commission, 2017).

the use of different types of antimicrobials contribute to selection for resistance in the bacterial population and how this in turn affects costs in human health care and livestock production.

Alternatively, the tax could be set so that the revenues from the sales of an antimicrobial cover the cost of developing a new one when resistance renders it ineffective. However, information on drug development costs are scarce and uncertain though some studies have attempted to estimate them (see list in Vågsholm and Höjgård, 2010). Results differ, partly because of different assumptions regarding the opportunity costs of capital and the rate of success, but costs appear to be increasing over time. This is further illustrated in DiMasi et al (2016). Moreover, only few studies report estimates of development costs for antimicrobials *per se*. Exceptions are Towse et al (2017) and Wouters et al (2020). According to Towse et al, the costs of bringing a new antimicrobial to the market were about USD 1.6 billion (€ 1.5 billion) in 2011 prices, while Wouters et al (2020) estimated them to about USD 1.3 billion (€ 1.2 billion) in 2018 prices. This suggests that the expected cost of a new antimicrobial could be about € 1.6 to 2 billion in 2023 prices (using the inflation calculator for the Eurozone).

There is also uncertainty regarding the expected time until resistance will make a new antimicrobial ineffective, and hence regarding the frequency with which the research investments referred to in the previous paragraph are required[7]. The results in in Dhingra et al (2020) suggest that onset of resistance can vary from zero (Penicillin G, Linezolid) to 40 years (Colistin). However, an antimicrobial could still be functional after onset of resistance, albeit in larger doses and for a selection of bacteria and health care settings. Information on how long it would take for resistance to become a serious problem for a newly introduced antimicrobial is difficult to find. In Vågsholm and Höjgård (2010), it was suggested that new antimicrobials to replace substances for which resistance had become a serious problem could be needed at 10-year intervals.

Our study complements previous studies of taxes on antimicrobials

Taxing antimicrobials in livestock production could affect productivity unless there is widespread overuse of antimicrobials. However, there are few empirical studies of the topic. Laxminarayan et al (2015) found the economic effects on livestock production of withdrawing antimicrobials used for growth promotion to be small in high-income countries but potentially large in low- and middle-income countries because of less developed hygiene and production practices. Results from the Dutch experiences of reducing antimicrobial use in livestock production (Bergevoet et al, 2019) also suggest that effects on production or economic performance may not be very large in a high-income country such as the Netherlands. Experiences from Belgium of reducing the use of antimicrobials in the pig sector point in the same direction (Rojo-Gimeno et al, 2016), as do results for the French poultry sector (Lhermie et al, 2022). Other results, however, suggest that effects differ according to production system and animal species also in high-income countries. For instance, Dejgård Jensen et al (2020) found that the marginal value of antibiotics to Danish pig-farmers was between 1.75 and 4.00 euro cent per standard unit dose in the short run. Similarly, Lhermie et al (2020) found that restricting

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[7] More precisely, with faster resistance formation, the shorter the expected depreciation time of the investments and hence the higher the annual cost for the research activities.

antimicrobial use to the treatment of sick animals only (that is, no use of antimicrobials for growth promotion, prophylaxis or metaphylaxis) would reduce net revenues by 6 to 9 percent in US feedlot cattle operations.

When simulating the effects of taxing antimicrobials, Van Boeckel et al (2017) used different assumptions on tax rates and the price elasticity of demand. They found that a global tax could reduce global antimicrobial use by between 9 and 46 percent and generate annual revenues of between USD 0.7 and 7.5 billion (€ 0.6 and 6.6 billion) depending on tax rate and price elasticity. However, the price elasticities used were quite substantial, ranging from – 0.5 to – 1.5, and the tax rates ranged from 10 to 100 percent. Morgan et al (2023) also investigated the effects on antimicrobial use and resistance of different tax policies (a flat rate tax over all antimicrobial classes, a tax targeted to single antimicrobial classes or a tax differentiated according to resistance to each antimicrobial class). In their analysis, resistance change over time according to a deterministic model depending on the amount of antimicrobials used, but they apply the same price elasticities as in Van Boeckel et al (2017). Results suggest that taxation could have similar effects on antibiotic use as a regulatory ban. In addition, taxation could generate revenues of about USD 1 billion annually (about € 0.9 billion).

The studies by van Boeckel et al (2017) and Morgan et al (2023) that have discussed taxation as a means to reduce antimicrobial use in livestock production have assumed that the tax is implemented globally. If not, countries or regions that do implement the tax could experience negative effects on competitiveness relative to countries/regions that do not. Other things equal, this would lead to increased imports and reduced exports of animal products for countries implementing the tax and vice versa for the countries that do not. In that case, the effects on global antimicrobial use is uncertain. One could regard this as a “leakage effect” of the tax strategy and the leakage could be substantial if countries/regions that increase exports and production also are countries/regions where the use of antimicrobials is large.

The aim of the present study is, therefore, to investigate the effects on production and economic performance in the livestock sector, as well as on producer prices, under different assumptions on the size of the tax, its geographical coverage, and the possible response of the intensity of antimicrobial use in agriculture. We do this by simulating different scenarios using the agricultural sector model CAPRI and data on present use of antimicrobials in the EU and other parts of the world.

Material and method

We use the CAPRI model (CAPRI network 2022), to estimate the impacts of introducing a tax on antimicrobials in the EU. CAPRI models production, consumption, and trade in agricultural products. The model covers the whole world, but it is more detailed both regarding the production technology and regarding the geographical resolution in the EU countries, whereas the global trade parts of the model focus on bilateral trade relations. CAPRI models supply, demand and trade for 70 food commodities among 80 countries or aggregates of countries. In most non-EU countries, agricultural production is modelled by (normalized quadratic profit) functions that relate production quantities to the prices of all outputs and inputs in the system. In particular, this means that the model does not simulate the number of animals or the explicit use of fodder or young animals. However, for the EU countries plus Norway, the UK, Turkey, and the Balkans, CAPRI models agricultural production in a technologically more explicit way based on agricultural production activities, such as animals of different species and age classes, linked by resource use and other technical constraints such as the availability of land, fodder and crop nutrients. Those supply models are also regionalized into 250 sub-regions corresponding approximately to the NUTS2 definition of Eurostat[8].

Antimicrobials are not included in the standard version of CAPRI, and hence the model had to be extended for our study. For most of the world, we need to estimate the use of antimicrobials per unit of output such as meat, eggs, or dairy products. For the EU countries and other regions where production is modelled in greater detail, we instead need to estimate the use of antimicrobials per animal of various species and age classes.

For the EU, Iceland, Norway, Switzerland, and the UK, we have data on the sales of antimicrobials to animals from the European Medicines Association (EMA). EMA collects the data through the European Surveillance of Veterinary Antimicrobials (ESVAC) project. Results are presented in annual reports and in the ESVAC interactive database.[9] The database contains information on the population of animals (cattle, pigs, poultry, sheep and goats, fish, rabbits, and horses) each year by country, and on the total annual sales of antimicrobials by country. It also includes information on the total annual sales by substance class (i.e. tertracyclines, penicillines, amphenicols, cephalosporines, sulphonamides, macrolides, fluoroquinolones, etc.), and percentages of sales according to pharmaceutical form (i.e. premixes, oral solutions, oral powder, injection, intramammary preparations and intrautetrine preparations) and country.[10]

Since the amounts of antimicrobials sold are linked to the number of animals of different species and, as this differs between countries, the sales data are normalised by the so-called Population Correction Unit (PCU). This means that data on the number of animals according to species is given in PCU, where one PCU is one kilogramme of bodyweight, and data on the sales of antimicrobials in milligrams of active substance per PCU (mg/PCU). For poultry, only the number of slaughtered broilers and turkeys are included when calculating the PCU. Similarly, for goats, rabbits and fish, only the number of slaughtered animals are included in the PCU calculations. For all other species, the data also includes live animals.[11]

A drawback is that the ESVAC database does not contain information on the amounts of antimicrobials sold disaggregated by animal species. However, some of the participating countries do report such data, at least for some years and some species. A full list of data sources are given in Table A1 in the supplementary material.

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[8] https://ec.europa.eu/eurostat/web/nuts

[9] See ESVAC home page: https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac. Accessed 2023-10-03.

[10] Sources for the sales data differ between countries. For details, see the latest ESVAC-report (ESVAC 2022. https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2021-trends-2010-2021-twelfth-esvac_en.pdf). Accessed 2023-10-03.

[11] For details on how the PCU is calculated, see appendix two in ESVAC (2011). https://www.ema.europa.eu/en/documents/report/trends-sales-veterinary-antimicrobial-agents-nine-european-countries_en.pdf. Accessed 2023-10-03.

To obtain species specific use of antimicrobials in all ESVAC countries we adopt a regression based approach. In the first step, we regress available reported mg/PCU of antimicrobials for each animal species on a number of country specific and time varying variables. The estimated regression coefficients are then used in a second step to predict antimicrobial use by animal species for all ESVAC countries and years (2010-2021). Finally, the predictions are calibrated to be consistent with national sales data from ESVAC. The estimation approach is described in more detail in the supplementary material.

For countries outside the ESVAC project, data on the amount of antimicrobials used in food animals are generally scarce. Laxminarayan et al (2015), Van Boeckel et al (2015, 2017 and 2019), Tieso et al (2020) and Mulchandani et al (2023) have attempted to estimate the global consumption of antimicrobials. In particular, Mulchandani et al covers 226 countries of the world and accounts for antimicrobial use in the three broad animal sectors cattle, pigs and poultry. They base their estimates on representative production systems for geographical areas and each animal sector, and compute antimicrobial use per PCU in each such production system. Those data were then mapped to the countries using GIS, and, where data was available, scaled to fit estimates of total use in the country.

For the global trade model, we estimate the use of antimicrobials in the production of each internationally tradable animal output, except fish[12], that is represented in the CAPRI model, i.e. beef meat, dairy products, pork, poultry meat, eggs, and sheep and goat meat.

It is important to get total global antimicrobial use right, since we argue that – *ceteris paribus* – total antimicrobial use drives resistance. The totals that we aim to reproduce come from various sources depending on the region. For European countries, we prefer the ESVAC data. For other countries, we use the total use per country computed by Mulchandani et al (2023)[13].

We then distribute the total antimicrobial use to commodities in several steps:

Step 1: Collect estimates (see above) on total veterinary antimicrobial use per region *r*, and where available, use per type of animal $s = \{\text{cattle, pigs, poultry, caprines}\}$

Step 2: Augment the data with estimates on how total veterinary antimicrobial use Q in region r is distributed across use q per type of animal s. We do this by first approximating q_{rs} by mg/PCU times PCU and then adjusting a scaling factor α to obtain a perfect fit to total use.

$$Q_r = \alpha_r \sum_s q_{rs} \tag{1}$$

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[12] The production of farmed fish uses large quantities of antimicrobials worldwide. We ignore this in our computations because data on antimicrobial use for fish is more scarce than for terrestrial animals in many countries, and aquaculture is not represented in the CAPRI supply models.

[13] Except or Kosovo and Albania, for which we found a country-specific study in Topi and Spahiu (2020), and New Zealand, where we use official reports (MPI, 2023).

This step requires us to know the number of PCU in each model region. For regions where this is not known, we estimate it from the sample of European countries r, where we have data on both number of PCU of each animal type s and agricultural production x_{rj} of various products j. Let the indicator function $I_{sj} = 1$ whenever the product j is produced by animal s. We then estimate a coefficient β_{sj} using equation (2), with OLS.

$$PCU_{rs} = \sum_{j} I_{sj}\beta_{sj}x_{rj} + u_{rs} \tag{2}$$

We use the coefficients to compute (predict) PCU in countries where we only have data on production x_{rj}. Indirectly, with the scaling in (1), this means that in regions where we don't have ESVAC data, we assume that the productivity of each animal type relative to other animal types in the same region is the same as the average of the ESVAC regions. That assumption thus affects the distribution of total antimicrobial use across animal types within each non-European region.

Step 3: Allocate total use per animal type to the commodities produced in proportion to total revenue per commodity. Denoting antimicrobial use per kg of commodity j in region r by a_{rj}, the quantity of commodity j produced in region r by x_{rj}, and the average price of the commodity in region r by p_{rj}. Moreover, let I_{sj} take the value of "1" if commodity j or k is produced by animal type s. Then we assume that the share λ_{rsj} of q_{rs} that goes to product j equals the share of that product's output value.

$$a_{rj} = \lambda_{rsj}q_{rs} = \frac{x_{rj}p_{rj}}{\sum_k I_{sk}x_{rk}p_{rk}}q_{rs} \quad \forall(s,j){:}\, I_{sj} = 1 \tag{3}$$

It would be desirable to obtain estimates not only on how much antimicrobials are used per unit of product or per animal (the intensity), but also on how that intensity changes when prices of antimicrobials, substitutes to antimicrobials, or products change. Given the paucity of data on quantities and prices of antimicrobials, it is not straightforward to estimate the price elasticity of demand for antimicrobials. In Vågsholm and Höjgård (2010), it was assumed to be close to zero, implying that increasing the price of antimicrobials would have very small effects on consumption.[14] Van Boeckel et al (2017), on the other hand, estimated price elasticities of demand for antimicrobials for, respectively, high-income countries, low- and middle-income countries, and China using information on quantities and prices of imports of antimicrobials in the UN COMTRADE database. They found price elasticities of – 1.75 for the group of low- and middle-income countries, – 1.43 for the group of high-income countries, and – 0.68 for China. Apart from perhaps for China, these seem unexpectedly large in absolute value, and suggest that use

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[14] Given that alternatives to antimicrobials to keep animals healthy (investments in infection prevention measures such as improved sanitation and hygiene, all in – all out systems, facilities with separated water and ventilation systems, etc.) often are more costly than antimicrobials it may be conjectured that the effect of an increase in the price of antimicrobials would not affect consumption very much.

of antimicrobials is highly sensitive to price changes.[15] One reason could be that the import data used only covers one class of antimicrobials.[16] In that case, it is relatively easy for livestock producers to adapt to an increase in the price of that class by changing to another class, maintaining the total use of antimicrobials.

Scenarios

We simulated two sets of scenarios. All scenarios were computed as counterfactuals for the year 2020, with the actual EU agricultural and trade policies in place. In the first set of scenarios, we implemented a tax on veterinary antimicrobials in the EU. Given the difficulties to find the optimal (Pigouvian) tax rate, we set the rate with the aim of raising sufficient tax revenues within the EU to fund the research into new active substances. To cover the range of uncertainty regarding the annual investment costs needed, we chose two different tax levels per gram of antimicrobials: 10 cent/g and 1 euro/g respectively.

The use of antimicrobials per animal was kept constant in this first set of scenarios. That implies that the effect on antimicrobial use is caused by the effect the tax has on the overall cost of livestock production. This is obtained by adding, for each type of animal product in each member state, the tax per gram of antimicrobial times the quantity of antimicrobials used in that member state to the variable costs of production.

The second set of scenarios was similar to the first set in terms of tax levels, but here we also assumed that farmers in all EU countries would reduce the use of antimicrobials to the same level as in the Netherlands if their use per animal were higher. This could be the result of either new regulations put in place, as in the Netherlands, or it could indicate what would happen if (in contrast to the first set of scenarios) farmers would react to higher antimicrobials prices by changing their production technology. The Dutch benchmark was chosen because of the indication that the country has achieved a substantial reduction in antimicrobial use without negative impacts on profitability[17]. Therefore, this reduction was assumed to be achieved without any impact on the cost of production except for the effect that the cost of the antimicrobial tax per animal became correspondingly lower.

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[15] A price elasticity of, for example, – 1.43 implies that a one percent increase in the price reduces consumption by 1.43 percent.

[16] The authors state that they used data for the commodity code 294130 in the UN COMTRADE database, which refers to tetracyclines and their derivatives.

[17] This is somewhat in contrast to e.g. Denmark, where there has also been a reduction in antimicrobial drug use, but where at least for pigs there is an indication that antimicrobials have a statistically significant positive impact on revenues.

Table 1. Scenario overview

SCENARIO	ANTIMICROBIAL TAX	ANTIMICROBIAL USE COEFFICIENT PER ANIMAL
REF	None	Estimated
TAX_10_C	10 euro cent per gram	Estimated
TAX_1_E	1 euro per gram	Estimated
CONV_NL	None	MIN("Estimated","Netherlands")
TAX_10_C_CONV_NL	10 euro cent per gram	MIN("Estimated","Netherlands")
TAX_1_E_CONV_NL	1 euro per gram	MIN("Estimated","Netherlands")

Antimicrobials taxes have been used in practice in at least Denmark and Belgium, with rates differentiated by the type of antimicrobial. Compared to those cases, the taxes on antimicrobials applied in our scenarios are quite substantial, especially in the 1 euro case. I addition, a tax that is constant in euros for all substance classes implies different tax rates for different substance classes as their prices differ. For instance, using Swedish prices from 2020, a tax of 10 euro cents corresponds to a tax rate of about 62 percent of the price of benzyl penicillin, but only about 6 percent of the price of aminoglycoside. Differences in tax rates could lead to substitutions between substance classes that are close substitutes. However, as our data is insufficient to estimate the cross elasticities of demand for the respective substances, that is, how sensitive the demand for drug A is to an increase in the price of drug B, we are unable account for such effects. Notwithstanding, since the tax raises the prices of all substance classes, it is expected to reduce overall antimicrobial use in the EU.

Results

Estimates of antimicrobial use per commodity before applying the tax

Before analysing the effects of taxes on antimicrobial use, we do a quality check to see if the CAPRI baseline scenario is consistent with estimates of antimicrobial use from other sources in the literature. As shown in Figure 1, our estimates of the use of antimicrobials is much lower for beef meat (BEEF) and pig meat (PORK) in the EU than in the rest of the world. For poultry meat (POUM) and eggs, while use is still lower in the EU, the differences between EU and non-EU countries are smaller.

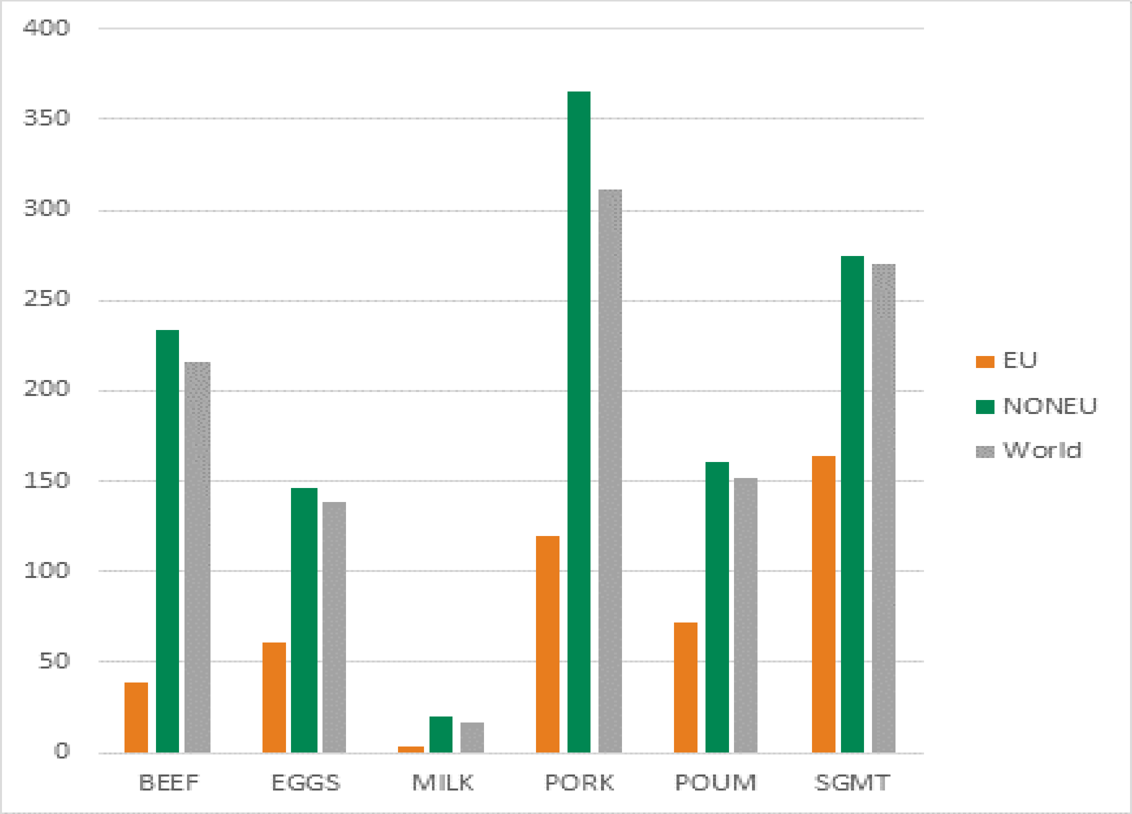

Figure 1. Use of antimicrobials per unit of commodity produced (mg/kg).

In Table 2, we compare the total antimicrobial use according to our estimates with the amounts reported to the World Organization for Animal Health (WOAH 2023) for the year 2019. WHOA provides a mapping from countries to broad regions, and the reported amount of antimicrobial use per region if the number of reporters is sufficiently large. In the latest (seventh) report, no regional figures were provided for the Middle East. In total, 110 countries of the world reported quantities of antimicrobial use. Since WOAH provides a mapping from countries to regions, we could aggregate our estimates and those of Mulchandani et al (2023) to the same regions and compare our results.

Since not all countries in each region reports to the WOAH, we would expect our estimates, that cover all countries, to be systematically larger. This is also the case for all regions except for the Americas. The table shows that for Africa, the quantities reported by WOAH (based on 28 reporting countries) are lower than the aggregated numbers computed by Mulchandani et al., and ours are identical to the latter. For the Americas, the numbers of WOAH (based on are instead somewhat higher. For Asia, the Far East and Oceania, we find the largest (relative) mismatch in quantity, with our estimates implying that antimicrobial use is almost twice as big or about 12 000 tons larger than in the WOAH estimate. However, the WOAH estimate is based on only 22 out of 32 reporting countries that belong to that region. In relative terms, the deviation is larger for Europe, where our estimate is 73 percent higher than that of WOAH. However, we should then recall that our estimates includes data for 32 European countries reporting to ESVAC, which are presumably also included in 42 reporting countries of the WOAH data, and that those ESVAC countries together use close to 5 000 tons of antimicrobials annually. Therefore, one may assume that some of the 11 countries that belong to Europe in the WOAH mapping, but are covered by Mulchandani et al., use substantial amounts of antimicrobials. The WOAH does not disclose which countries did not respond to the survey. In our estimates, e.g. Russia and Turkey alone use about 3 500 tons of antimicrobials annually.

Table 2. Comparison of total AMD use per WOAH region (metric tons).

WOAH region	Nr. of reporting countries (possible)	WOAH 2019	Mulchandani et al. 2023, for 2020	Our estimates for 2020
Africa	28 (54)	2 441	3 044	3 044
Americas	15 (31)	31 216	25 656	25 656
Middle East	0 (12)	0	2 912	2 911
Asia, Far East and Oceania	22 (32)	44 228	56 162	56 158
Europe	42 (53)	6 501	11 763	11 265
Missing*	Kosovo	0	0	15

* Countries in the CAPRI model that are not present in neither Mulchandani et al (2023) nor in WOAH. Presently only Kosovo, which is not globally recognized as a state.

Scenario outcomes

The first three columns of Table show the total veterinary antimicrobial consumption for the covered animal types in the scenarios. The consumption has been aggregated to the EU, Non-EU, and World, where the latter is the sum of the other two. The first row of the table shows the total consumption in the reference scenario, and the remaining rows show the difference in total consumption to the reference scenario.[18]

Looking at the first two scenarios with only a tax, we see that antimicrobial use in the EU responds proportionally to the tax, and that the reduction in antimicrobial use is small in relation to overall use; 22 and 221 tons per year for the 10 euro cent and 1 euro taxes respectively. The explanation for the relatively small impact is that we, in the absence of sufficient data, cannot account for the price elasticity of demand for *antimicrobials per se*. Therefore, the effect on antimicrobial use results from only changes in animal production as the tax increases overall costs of livestock production in the EU, but does not include any response in the amount of antimicrobials used per animal. However, as the antimicrobial tax is small in relation to the overall costs in livestock production, the effect on production, and hence antimicrobial use, is limited. The consumption in the rest of the world (Non-EU) increases by quantities similar to the reduction in the EU, so that the net effect on global antimicrobial consumption becomes zero in the 10 euro cent scenario and a reduction of 6 tons per year in the 1 euro scenario. This effect is called "leakage" in the literature on e.g. climate change mitigation, and results from adjustments

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[18] The reason why the quantity of antimicrobial use for the EU in the reference scenario in Table 3 does not correspond to the quantity for Europe in Table 2 above is that many countries that belong to "Europe" in the WOAH regional mapping, e.g. Russia, Turkey, Ukraine, Belarus, Kazakhstan, Norway, Switzerland, Iceland, and the UK, are not EU members.

of global food production. The tax somewhat reduces production of animal products in the EU, which leads to less exports and more imports, which stimulates production abroad. Since the use of antimicrobials per kg of animal product is generally higher outside the EU, a small production increase there can suffice to offset (in terms of antimicrobials use) a larger production reduction in the EU. This effect becomes even more evident in the tax scenarios with reduced antimicrobials use per animal in the EU (i.e. TAX_10_C_CONV_NL and TAX_1_E_CONV_NL).

The scenario CONV_NL, where there is no tax but a convergence in antimicrobial use per animal to at most the level in the Netherlands, gives a very substantial reduction (3 286 tons per year) in antimicrobial use in the EU. There is no effect at all on antimicrobial use abroad in this scenario, which is explained by our assumption that the reduction can be achieved without any impact on the marginal cost of production as was reportedly the case in the Netherlands.

The two bottom rows show the changes in antimicrobial use when a tax is introduced in addition to the convergence to Dutch antimicrobial use intensity levels. Numbers in brackets show the difference to the CONV_NL scenario. The change in total antimicrobial use in the EU is very similar to that in CONV_NL, i.e. the additional impact of the tax is small (1 and 9 tons respectively). The tax results in increased antimicrobial use in Non-EU of 6 and 57 tons per year, respectively. That leakage causes the tax to have a slightly adverse impact on total world antimicrobial consumption compared to the CONV_NL scenario; the global reduction becomes 5 and 47 tons larger than in the CONV_NL scenario when a tax of 10 euro cents or 1 euro per gram is added.

Table 3. Change in antimicrobial use in the scenarios compared to REF (metric tons per year) and total revenues from the tax on antimicrobials (million euro per year)

	EU	**Non-EU**	**World**	**Tax revenues**
REF	4 988	90 610	95 597	0
TAX_10_C	-22	22	0	496
TAX_1_E	-221	215	-6	4 736
CONV_NL	-3 286	0	-3 286	0
TAX_10_C_CONV_NL	-3 287 (-1)	6 (6)	-3 281 (5)	170
TAX_1_E_CONV_NL	-3 295 (-9)	57 (57)	-3 239 (47)	1 688

Note: numbers in brackets show difference to scenario CONV_NL

If the leakage (the increased antimicrobial use in Non-EU) associated with the introduction of the tax is put in relation to the reduction in the EU, we obtain what we call the leakage rate. For instance, in the convergence scenario with 10 cents tax, a reduction of 1 metric ton in the EU is matched by an increase of 6 metric tons in Non-EU. Thus, the leakage rate computed this way is larger in the convergence scenarios. The increased rate of leakage is explained by the increased difference in antimicrobial use intensity between the EU and Non-EU in these scenarios. Each unit of commodity that is produced abroad instead of in the EU in these scenarios causes the same increase in non-EU use as in the scenarios without convergence (since the antimicrobial intensity of Non-EU is unchanged), but the reduction of antimicrobial use in the EU is smaller (because agriculture now uses less antimicrobials per unit of produce). However, if the convergence of antimicrobials use in the EU to Dutch levels is interpreted as being brought about by the tax, then the leakage should be put in relation to the total reduction in the EU (i.e. -3287 metric tons in the 10 cent convergence scenario). Then the leakage rate becomes only 0.2% in that scenario. This illustrates the sensitivity of the leakage to the flexibility of farmers in their response to changes in the price of antimicrobials, i.e. the price elasticity of demand for antimicrobials.

The rightmost column of *Table* shows total tax revenues in the scenarios. Without convergence of antimicrobial use intensity to Dutch levels, the revenues become 496 million euro per year with the 10 euro cent tax and 4 736 million euro per year with the 1 euro tax. With convergence, the tax revenues become lower, reflecting the lower total use of antimicrobials, amounting to 170 million euro and 1 688 million euro per year respectively.

Table 4. Impact on the production of animal products in parts of the world in the scenarios (thousand tons and percent difference to REF)

Scenario	**Region**	**Beef**	**Pork meat**	**Sheep and goat meat**	**Poultry meat**	**Raw milk**	**Eggs**
REF	EU	6 254	23 034	629	13 094	143 045	7 096
REF	Non-EU	62 640	81 064	14 031	113 534	645 030	78 481
REF	World	68 893	104 099	14 660	126 628	788 075	85 577
TAX_10_C	EU	-0.03%	-0.33%	-0.03%	-0.39%	0.00%	-0.01%
TAX_10_C	Non-EU	0.00%	0.06%	0.00%	0.03%	0.00%	0.00%
TAX_10_C	World	0.00%	-0.02%	0.00%	-0.02%	0.00%	0.00%
TAX_1_E	EU	-0.31%	-3.22%	-0.33%	-3.81%	0.00%	-0.10%
TAX_1_E	Non-EU	0.02%	0.63%	-0.02%	0.28%	0.01%	-0.02%
TAX_1_E	World	-0.01%	-0.22%	-0.03%	-0.14%	0.00%	-0.03%
CONV_NL	EU	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
CONV_NL	Non-EU	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
CONV_NL	World	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%
TAX_10_C_CONV_NL	EU	-0.05%	-0.09%	-0.03%	-0.04%	0.00%	0.00%
TAX_10_C_CONV_NL	Non-EU	0.00%	0.02%	0.00%	0.00%	0.00%	0.00%
TAX_10_C_CONV_NL	World	0.00%	-0.01%	0.00%	0.00%	0.00%	0.00%
TAX_1_E_CONV_NL	EU	-0.50%	-0.87%	-0.29%	-0.44%	-0.05%	0.00%
TAX_1_E_CONV_NL	Non-EU	0.02%	0.18%	0.00%	0.04%	0.00%	-0.01%
TAX_1_E_CONV_NL	World	-0.03%	-0.06%	-0.01%	-0.01%	-0.01%	-0.01%

Table 4 shows the impact on the production of animal outputs in the EU, Non-EU and in the World. For the reference scenario, the values are in thousands of metric tons, and for the other scenarios, the values are percentage difference to the reference scenario. The biggest impacts, in relative terms, are found for the commodities pork and poultry meat in the EU at the highest tax rate (1 euro per gram). In that scenario, we find a decrease of 3.2 and 3.8 percent respectively for pork and poultry. The production response of the model is explained by the combination of (1) how much antimicrobials is used per animal and hence how large the tax per animal becomes, and (2) how strongly the production reacts to a given change in costs, indirectly determined by parameters such as the amount of meat per animal, prices, and restrictions of the model. In the corresponding convergence scenario (TAX_1_E_CONV_NL), the use of antimicrobials is lower and hence also the impact of the tax on pork and poultry production in the EU is smaller, at 0.87 and 0.44 percent respectively.

Pork production is of particular importance since the sector uses much antimicrobials and is economically important in many countries. Table 5 shows the impacts on income, as computed by revenues plus subsidies minus variable costs, of the production activity “pig fattening” in the EU. The top row is the situation in the reference scenario (euro per head), the remaining rows show difference to the reference situation. The column “Revenues” shows how the value of the pork per pig changes. In all taxation scenarios, the revenues rise because the price of pork in the EU rises when production is reduced. The column “Variable costs” shows the sum of all variable costs, including the tax. Comparing the change in costs with the change in revenues, we see that the farmers can shift about half the cost increase to consumers in the form of higher output prices. The column “Premiums” shows the average value of various subsidies that some countries pay to pig farmers. The values are small and only change minimally as pork production shifts somewhat between EU countries in the scenarios. The column “Income” shows the net effect on income per pig, defined as the gross value added, i.e. not taking labour and capital costs into account. The tax reduces income for the average EU pig farmer by 5 euro per pig in the scenario with the 1 euro tax and no conversion of antimicrobial intensity.

Table 5. Profitability of pig fattening in the EU (euro per head)

	Revenues	Variable costs	Subsidies	Income[a]
REF	160.67	119.02	1.68	43.33
TAX_10_C	0.52	1.06	0	-0.54
TAX_1_E	5.34	10.39	0.03	-5.02
CONV_NL	0	0	0	0
TAX_10_C_CONV_NL	0.15	0.29	0	-0.13
TAX_1_E_CONV_NL	1.54	2.88	0.01	-1.33

a) Revenues minus variable costs plus subsidies.

Table 6 shows how pork production develops in the separate EU countries in the respective scenarios. The first column shows production in the reference scenario and the rest of the columns show the relative change (percent) in relation to the reference. As can be seen, application of the tax causes pork production to decrease in most countries (columns two and three). This is as expected since the tax increases production costs, thereby reducing competitiveness relative to the rest of the world. However, in some countries – the Nordic, the Baltic, the Netherlands and Slovenia – production actually increases in both tax scenarios. This is because these countries use comparatively small amounts of antimicrobials (measured as mg/PCU). Therefore, the increase in their overall costs of production caused by the tax is also small and smaller than the increase in the price of pork products caused by the tax, implying that these countries become more competitive after the application of the tax.

Table 6. Impacts on pork production in the different EU countries (1000 heads per year in REF and percent difference to REF in other scenarios)

	REF	TAX_10_C	TAX_1_E	CONV_NL	TAX_10_C_CONV_NL	TAX_1_E_CONV_NL
Austria	482	-0.1%	-0.9%	0.0%	-0.1%	-0.7%
Belgium and Luxembourg	1 085	-0.3%	-2.9%	0.0%	-0.1%	-0.9%
Bulgaria	77	-1.3%	-12.7%	0.0%	-0.1%	-0.9%
Croatia	112	-0.2%	-1.8%	0.0%	-0.2%	-1.6%
Cyprus	50	-3.7%	-37.0%	0.0%	-0.1%	-0.7%
Czech Republic	226	-0.1%	-1.3%	0.0%	-0.1%	-0.9%
Denmark	1 805	0.1%	1.1%	0.0%	-0.1%	-0.9%
Estonia	53	0.0%	0.4%	0.0%	-0.1%	-1.2%
Finland	179	0.1%	1.4%	0.0%	0.0%	-0.5%
France	2 258	-0.1%	-0.5%	0.0%	-0.1%	-1.0%
Germany	5 143	-0,2%	-1.7%	0.0%	-0.1%	-0.8%
Greece	87	-1.3%	-12.9%	0.0%	-0.1%	-1.3%
Hungary	397	-0.5%	-4.7%	0.0%	0.0%	-0.3%
Ireland	301	-0.6%	-5.5%	0.0%	-0.1%	-1.0%
Italy	1 501	-0.4%	-3.5%	0.0%	0.0%	0.0%
Latvia	42	0.1%	1.4%	0.0%	-0.1%	-1.6%
Lithuania	93	0.0%	0.6%	0.0%	-0.2%	-2.2%
Malta	5	-0.4%	-3.1%	0.0%	0.0%	-0.2%
Netherlands	1 631	0.0%	0.5%	0.0%	-0.2%	-1.8%
Poland	2 019	-0.7%	-6.9%	0.0%	-0.1%	-1.1%
Portugal	379	-1.1%	-11.1%	0.0%	-0.1%	-1.3%
Romania	412	-0.6%	-5.7%	0.0%	-0.1%	-0.7%
Slovak Republic	56	-0.1%	-0.8%	0.0%	-0.1%	-0.6%
Slovenia	27	0.0%	0.5%	0.0%	-0.1%	-0.7%
Spain	4 365	-0.7%	-7.0%	0.0%	-0.1%	-0.8%
Sweden	248	0.2%	2.4%	0.0%	0.0%	0.2%

If all countries reduce antimicrobial use to that of the Netherlands in 2020, the competitive advantage provided by the tax to countries that already use relatively little antimicrobials is eroded. This is seen in the last two columns, showing the combined effects on pork production of a tax and convergence to Dutch antimicrobial use. For instance, the 1 euro tax causes pork production in Denmark to decrease by 0.9% if farmers in all countries reduce the antimicrobial use to Dutch levels, compared to an increase by 1.1% if there is no such convergence in antimicrobial intensity. Similar effects are seen in Sweden and in the Baltic countries – these countries then face the same tax per animal as in the scenarios without convergence, but benefit (as all countries) from a smaller price increase.

Discussion and limitations

The lack of empirical data on antimicrobial use per species and on the prices of antimicrobials in different countries cause limitations to the interpretation of the results of our study. First, our method of allocating antimicrobial use according to species in the EU relies on information from a limited number of national studies and a regression on a limited number of variables for countries where there are no national studies (see supplementary material). There are likely other factors that could cause differences in the use of antimicrobials per species between countries on which we have no information.[19] Thus, the regression results may deviate from actual antimicrobial use per species, implying that the results on how the tax would affect the different animal products in Table 4 above should be interpreted with care. For instance, the reduction in the production of sheep and goat meat in the EU may be too large since, according to personal information from the Swedish Veterinary Agency, antimicrobial use is low for these species.

Second, the available data does not enable us to estimate price elasticities of demand for antimicrobials. Antimicrobial use per animal unit was therefore assumed to be static in our computations. If that would instead be sensitive to the price of antimicrobials, then the reduction in antimicrobial use caused by the tax would be larger than in our results, and the rate of leakage to the rest of the world would be lower. Corresponding to this, the tax revenues would be smaller. The size of this potential effect on intensity of use is not known. In some respect, this case is covered in the “convergence scenarios” where European countries that use more antimicrobial per animal unit than the Netherlands converge to the level of the Netherlands.

Third, the information on intensity of use per species in the rest of the world is uncertain. If we have underestimated the quantities used in countries outside the EU, then the leakage caused by the tax will be larger than in our simulations and the other way around if we have overestimated quantities used outside the EU.

Fourth, as largely the same substance classes are used in both human and veterinary medicine, resistance developing from human antimicrobial is also a problem for both human- and veterinary medicine. Also. applying a tax on antimicrobials used in veterinary medicine only could result in “black market problems”. One might, therefore consider applying the same tax to all antimicrobials regardless of their intended use. Assuming that

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[19] For instance, differences in production systems such as in stocking density, in the movement of animals between farms, in the use of infective prevention measures, etc.

the price elasticity of demand for antimicrobials in human medicine is also close to zero, and using the data in JIACRA IV,[20] a tax of 10 euro cents per gram of active substance on antimicrobials in human medicine would raise another 300 million euro in tax revenues annually.

Despite these limitations, the simulation results do suggest that levying a tax on antimicrobials in the EU only would not affect global use substantially. Therefore, it would also not be an efficient tool for reducing the development of antimicrobial resistance. On the other hand, the annual revenues from the tax could be substantial enough to cover the expected cost of developing and introducing new antimicrobial at ten-year intervals.

Conclusions

The simulations suggest that a tax on antimicrobials in Europe would not be an effective way to reduce antimicrobial resistance globally unless the use per animal is also reduced. If the tax is sufficiently high to become a significant cost in animal husbandry, exports from the EU would decrease and imports increase, stimulating production in the rest of the world and thereby increasing antimicrobial use there. This effect, known as “leakage”, would be sufficiently large to entirely offset the reduced use of antimicrobials in the EU. This result hinges on the assumption that the tax alone is not sufficient to incentivize a significant switch from antimicrobials to other means of protecting animal health.

In contrast, the tax can be an effective way of raising funds for research into new types of antimicrobials, vaccines or other ways to treat bacterial infections. At the antimicrobial use rates of 2020, a tax of 10 euro cents per gram of active antimicrobial substance sold for veterinary purposes in the EU would raise about 500 million euro per year. If the development of a new drug costs 2 billion euro, as suggested in the introduction, 500 million euro could be sufficient to cover the costs for developing new types of antimicrobials every 2.5 year, ignoring discounting and disregarding tax revenues from human medicine use.

Our research suggests that administrative measures on the national level can reduce antimicrobial use much more than the tax, at the tax levels considered in this study. Using a combination of administrative measures similar to those used in the Netherlands, Denmark and Sweden (for instance, adopting quantitative targets for reducing antimicrobial usage, benchmarking of antimicrobial use per herd and veterinarian, implementation of mandatory animal health plans), and a tax on antimicrobials can reach two objectives at the same time: strongly reduce the use of antimicrobials in the EU with minimal leakage, and raising funds for developing new active substances. However, at the lower antimicrobial sales associated with a successful such administrative program, the tax revenues would be lower. Revenues at the 10 cent tax level could amount to 170 million euro per year from veterinary sales. With a total development cost for a new drug of 2 billion euro, the revenues could cover the cost of a new drug every 2000/170 = 11.8 years, again ignoring discounting and revenues from human medicine.

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[20] JIACRA IV. Antimicrobial consumption and resistance in bacteria from humans and food producing animals. *EFSA Journal*, 2024; 22: e8589. https://www.efsa.europa.eu/en/efsajournal/pub/8589

The impacts of a tax on the agricultural sector depend critically on the extent to which farmers are able to substitute from antimicrobials to other sanitary measures to maintain animal health. If such substitutes are cheap and accessible, the impacts on production are small. If, in contrast, substitutes are costly or otherwise difficult to achieve, then the cost increase associated with the tax can be significant in sectors and countries with high use of antimicrobials.

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Supplementary material: Antimicrobial use by animal species in ESVAC countries

We use a three-step procedure to extrapolate antimicrobial use from countries reporting sales by animal species to all ESVAC countries. The objective of this procedure is to obtain estimates of antimicrobial usage for the four major food-producing animals (cattle, pig, poultry and caprine), which are subsequently used in the CAPRI model. We ignore possible storage of antimicrobials and simply assume that sales volumes represent usage. Total sales of antimicrobials are normalised by the Population Correction Unit (PCU) reported by ESVAC to produce antimicrobial intensity (sales in milligrams of active substance per PCU). The data sources for reported animal specific sales of antimicrobials are given in Table A1 below.

The three-step approach proceeds as follows:

Step 1: Let y_{sit} denote antimicrobial intensity (mg/PCU) for animal s in country i in year t, where s = *(cattle, pig, poultry, caprine)*. For each animal group, we seek an appropriate regression model that can be used to predict antimicrobial intensity for non-reporting countries. The dependent variable y_{sit} is non-negative and turns out to be positively skewed. To account for this, we opted for a Poisson regression approach, i.e. a generalized linear model (GLM) with a logarithmic link function. We gathered data on a number of variables that may explain variation in antimicrobial intensity across countries over time. The following variables were included in the final regressions (separate regressions for each animal):

- Cattle: 1) average number of cattle per farm[21], 2) share of total cattle production originating from fattened calves[22], and 3) aggregated antimicrobial intensity measured as mg/PCU at the national level.[23]
- Pigs: 1) share of antimicrobials sales aimed for group treatment[24], and 2) aggregated antimicrobial intensity measured as mg/PCU at the national level.
- Poultry: 1) share of antimicrobials sales aimed for group treatment, and 2) aggregated antimicrobial intensity measured as mg/PCU at the national level.
- Caprine: 1) average number of sheep and goats per farm.[25]

All variables are measured annually (2010-2021) on a country basis. In case there are gaps in the time series, linear interpolation is used to obtain complete time series.

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[21] Source Eurostat: https://ec.europa.eu/eurostat/data/database.

[22] Source: CAPRI baseline for 2030, created with model revision 10994 in repository https://svn1.agp.uni-bonn.de/svn/capri/branches/slu-2024

[23] Source ESVAC: https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac. ESVAC data on aggregate antibiotic intensity include all food-producing animals (cattle, pig, poultry, caprine, horse, fish, rabbit).

[24] Source ESVAC: https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac. Classification of group vs. individual treatment is based on distributional form as follows. Group treatment: Premixes, oral powders, and oral solutions. Individual treatment: Oral pastes, Boluses, Intramammary, Injectable and intrauterine products.

[25] Source Eurostat: https://ec.europa.eu/eurostat/data/database

Step 2: The estimated coefficients from step 1 are used to predict antimicrobial intensity ($\hat{y}_{sit}$) for all ESVAC countries in the period 2010-2021. For countries reporting animal-specific data (Table A1), reported data are maintained instead of predictions. However, the predictions $\hat{y}_{sit}$ are used to extrapolate data across missing time periods for reporting countries as follows: 1) Define the quota: $q_{sit} = y_{sit}/\hat{y}_{sit}$. 2) Calculate $\bar{q}_{si} = \sum_t q_{sit}/T_{si}$ to obtain a measure of average overestimation/underestimation for animal *s* in reporting country i, where T_{si} is the number of reported observations for animal *s* in country i. 3) In cases y_{sit} is missing for some *t* and *s* in a reporting country, we use the estimate $\hat{y}_{sit} \times \bar{q}_{si}$ as a measure of antimicrobial intensity. To sum up, the estimated antimicrobial intensity (y_{sit}^{p}) is given by:

- $y_{sit}^{p} = \hat{y}_{sit}$ (predictions from regression model for non-reporting countries).
- $y_{sit}^{p} = y_{sit}$ (for reporting countries according to Table A1).
- $y_{sit}^{p} = \hat{y}_{sit} \times \bar{q}_{si}$ (for reporting countries with missing data in some time periods).

In order to calibrate estimates to be consistent with ESVAC national sales data (step 3), we need y_{sit}^{p} for all food producing animals (cattle, pig, poultry, caprine, horse, fish and rabbit). Given the scarcity of data for horse, fish and rabbit, we avoid specifying regression models for these animals. Instead, we simply let y_{sit}^{p} be the average antimicrobial intensity from reporting countries in Table A1: $y_{s}^{p} = \sum_i \sum_t y_{it}/NT$.

Step 3: In the final step, the predictions from step 2 are calibrated to be consistent with national sales data from ESVAC. Let z_{it} denote aggregated antimicrobial intensity (mg/PCU) for all food-producing animals as reported by ESVAC. By definition, we have that:

$$z_{it} = \sum\nolimits_{s} y_{sit} \times \text{sh\_pcu}_{sit},$$

where sh_pcu_{sit} is ESVAC reported PCU for animal *s* divided by total PCU in country *i* in year *t*, and *s* includes all food-producing animals: *s = (cattle, pig, poultry, caprine, horse, fish, rabbit*). Note that z_{it} and share_{sit} are known but y_{sit} is unknown for most countries. We may calculate predicted aggregated antimicrobial intensity for all countries as follows:

$$\hat{z}_{it} = \sum\nolimits_{s} y_{sit}^{p} \times \text{sh\_pcu}_{sit},$$

where y_{sit}^{p} is predicted antimicrobial intensity from step 2. We calculate $k_{it} = z_{it}/\hat{z}_{it}$ and subsequently obtain our final estimates for antimicrobial intensity as:

$$y_{sit}^{e} = k_{it} \times y_{sit}^{p},$$

which implies that $z_{it}^{e} = z_{it}$ necessarily holds for $z_{it}^{e} = \sum_s y_{sit}^{e} \times sh\_pcu_{sit}$.

Table A1. Sources for reported animal specific sales of antimicrobials

Country	Report	Animals	Year	Link
Austria	AGES	Pig, Cattle, Poultry	2017-2021	https://bit.ly/3cX07Mc
Belgium	BelVet	Pig, Cattle	2018-2021	https://belvetsac.ugent.be/belvetsac_SaniMed_rapport_2020.pdf
Czech Republic	ÚSKVBL	Pig, Cattle, Poultry, Caprine, Horses, Fish, Rabbits	2016	https://www.uskvbl.cz/attachments/1308_Spot%C5%99eba%20antibiotik%20%C4%8CR%20obdob%C3%AD%202010-2017.pdf
Denmark	DANMAP	Pig, Cattle, Poultry, Caprine, Horses, Fish	2010-2021	https://www.danmap.org/reports/2021; https://vetstat.fvst.dk/ Horses: https://backend.orbit.dtu.dk/ws/files/266092399/DANMAP_2020_18102021_version_4_low_12_.pdf
France	ANSES	Pig, Cattle, Poultry, Caprine, Horses, Fish, Rabbits	2010-2021	https://www.anses.fr/en/system/files/ANMV-Ra-Antibiotiques2020EN.pdf
Iceland	Ministry of Food, Agriculture and Fisheries	Fish	2021	https://www.stjornarradid.is/raduneyti/matvaelaraduneytid/
Ireland	European Public Health Alliance (EPHA)	Pig	2016	https://www.saveourantibiotics.org/media/2019/report_ending-routine-farm-antibiotic-use-in-europe_final_january2022-1.pdf
Netherlands	SDa	Pig, Cattle, Poultry, Rabbits	2013-2021	https://www.autoriteitdiergeneesmiddelen.nl/en/publications/general-reports
Norway	NORMVET	Fish	2011-2021	https://www.fhi.no/en/publ/2022/norm-og-norm-vet-usage-of-antimicrobial-agents-and-occurrence-of-antimicrob/
Sweden	Swedres-Svarm	Pig, Poultry, Fish	2011-2021	www.sva.se/en/our-topics/antibiotics/svarm-resistance-monitoring/swedres-svarm-reports/
Switzerland	FSVO	Cattle, Pig, Poultry, Caprine, Horses, Rabbits	2020	https://www.blv.admin.ch/blv/en/home/tiere/publikationen/statistiken-berichte-tiere.html#accordion_3420713181694542036105
UK	VMD	Pig, Poultry	2015-2021	https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/1072796/03.05.22_VARSS_Main_Report__Final_Accessible_version__3_.pdf

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