

Please cite this paper as:

Ryan, M. (2019-07-10), "Evaluating the economic benefits and costs of antimicrobial use in food-producing animals", *OECD Food, Agriculture and Fisheries Papers*, No. 132, OECD Publishing, Paris. <u>http://dx.doi.org/10.1787/f859f644-en</u>



OECD Food, Agriculture and Fisheries Papers No. 132

Evaluating the economic benefits and costs of antimicrobial use in foodproducing animals

Michael Ryan



OECD FOOD, AGRICULTURE AND FISHERIES PAPERS

This paper is published under the responsibility of the Secretary General of the OECD. The opinions expressed and the arguments employed herein do not necessarily reflect the official views of OECD countries.

The statistical data for Israel are supplied by and under the responsibility of the relevant Israeli authorities. The use of such data by the OECD is without prejudice to the status of the Golan Heights, East Jerusalem and Israeli settlements in the West Bank under the terms of international law.

This document has been declassified on the responsibility of the Working Party on Agricultural Policies and Markets under the OECD reference number TAD/CA/APM/WP(2018)17/FINAL.

The publication of this document has been authorised by Ken Ash, Director of the Trade and Agriculture Directorate.

Comments are welcome and can be sent to tad.contact@oecd.org.

© OECD (2019)

You can copy, download or print OECD content for your own use, and you can include excerpts from OECD publications, databases and multimedia products in your own documents, presentations, blogs, websites and teaching materials, provided that suitable acknowledgment of OECD as source and copyright owner is given. All requests for commercial use and translation rights should be submitted to *rights* @oecd.org.

EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD-PRODUCING ANIMALS

Michael Ryan (OECD)

Antimicrobial drugs are used in food animal production for several purposes: to treat a disease outbreak, to prevent disease, and to enhance feed efficiency and animal growth. While the technical benefits of antimicrobial use in animal production are well documented, there is a major lack of information on the economic impact on farmers' incomes. This report reviews evidence on the economic benefits and costs of antimicrobials for the major animal producing species across several OECD countries as well as in Brazil and China. The findings indicate that the economic benefits are modest in modern farming systems where good production facilities, biosecurity measures, and management practices are in place. In large food animal producing countries such as Brazil, the use of antimicrobials is an important input to enhance the competitiveness of the industry. In China, the largest producer and user of antibiotics in animal production, antibiotics are often used as a substitute for less sanitary animal production facilities and the lack of appropriate biosecurity on the farm. This report concludes with several key policy options and practices, in particular those that induce farmers to place a greater emphasis on the economic benefits and costs of antimicrobials and alternative interventions in production in order to stem the rise in antimicrobial resistance.

Key words: Antibiotics, farm animals

JEL Codes: Q1

Table of contents

Abbreviations	4
Definitions	5
Executive Summary	6
1. Introduction	9
2. Background and scope of the work	10
3. Factors that drive the use of antimicrobials in animal production	13
4. Framework to evaluate the economic costs and benefits of antibiotics in livestock production	16
5. Main findings of case studies from selected OECD countries, Brazil and China	18
Annex A. Expert Steering Group (ESG) on AMR in Food Producing Animals	35

Tables

Table 1.	Reduction in antibiotic use per sector 2009-2014	21
Table 2.	Medicinal costs on pig and broiler farms in China (CNY)	28

Figures

Figure 1. Sales of antibiotics for animals expressed as mg per population correction unit (PCU) 23

4 | EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

Abbreviations

ABC	Antibiotic consumption
AMU	Antimicrobial use
AMR	Antimicrobial resistance
СВА	Cost-benefit analysis
CIAs	Critically important antimicrobials
BRIICS	Brazil, Russian Federation, India, Indonesia, China, and South Africa
ECDC	European Centre for Disease Prevention and Control
EFSA	European Food Safety Authority
ELS	Education, Labour and Social Affairs Directorate
EMA	European Medicines Agency
ESG	Expert Steering Group
EU	European Union
FAO	Food and Agriculture Organisation of the United Nations
HPCIA	Highest Priority Critically Important Antimicrobials
lOs	International Organisations
JIACRA	Joint Interagency Antimicrobial Consumption and Resistance Analysis
LIC	Low income countries
MIC	Middle income countries
MRSA	Methicillin-resistant Staphylococcus aureus
Mt	Million tonnes
NGO	Non-governmental organisation
OECD	Organisation for Economic Cooperation and Development
OIE	World Organisation for Animal Health
PCU	Population Correction Unit
R&D	Research and Development
SDGs	Sustainable Development Goals
SVARM	Swedish antibiotic resistance monitoring
SVA	Swedish National Veterinary Institute
SWEDRES	Swedish utilisation and resistance in human medicine
TAD	Trade and Agriculture Directorate
USDA	United States Department of Agriculture
WB	World Bank
WHO	World Health Organisation
WTO	World Trade Organization

Definitions

Antibiotic	An antimicrobial agent that kills or slows the growth of pathogenic bacteria
Antimicrobials	Medicines that are used to treat infections
Acquired resistance	Occurs through mutation in bacterial DNA or by getting the resistance genes through horizontal gene transfer when DNA moves from one bacterium to another
Companion animals	Domestic pets, such as cats and dogs and sport animals
Epidemiology	The study of the spread of disease
Infection	The entry and multiplication of an infectious agent in animals or humans
lonophores	Compounds that facilitate the transmission of an ion across a lipid barrier by combining with the ion or by increasing the permeability of the barrier
Metaphylaxis	Control of disease in a group of animals
Multidrug resistant	A bacterial pathogen that is resistant to two or more antimicrobial agents
One Health approach	A framework for collaboration on areas of common interest such as AMR, and which attempts to deal with risks at the interface of animal-human- environment
Pathogens	Bacteria, viruses, parasites and fungi that can cause disease
Prophylaxis	Preventative treatment of a group of animals against the outbreak of a disease
Therapeutic	Treatment of animals against a specific disease

Executive Summary

The use of antimicrobials in animal production has become an important and controversial issue due to the emergence and spread of resistant organisms and "super bugs". With growing scientific evidence of the spread of resistant bacteria between animals, humans and the environment, policy makers are particularly concerned about the potential impact on human and animal health, animal welfare, and food security.

Antimicrobials are used for a range of purposes in animal production including treatment of disease, prevention and control of a disease outbreak, and to promote animal growth. The main policy issue derives from the fact that the long-term social costs of antimicrobial resistance may not be fully reflected in the business calculations of livestock producers, as they weigh the benefits and costs of anti-microbial use.

This paper attempts to bridge the information gap by contributing to a better understanding of the economic dimension of antimicrobial use in animal production, with a view to identifying policies that can better align producers' incentives with a responsible and prudent (and socially beneficial) use of antimicrobials. The starting point for this assessment is an examination of the costs and benefits of antimicrobial use at the farm level in several countries. The focus on the economic dimension of the problem seeks to complement the technical work and guidelines of the World Organisation for Animal Health (OIE) and the United Nation's Food and Agriculture Organisation (FAO) on antimicrobial use in animal production. This work also complements the ongoing work on antimicrobial resistance (AMR) in the OECD Health Committee.

This paper analyses the findings of existing case studies for several European countries on their use of antibiotics in animal production. Assessing the impacts of antibiotic use in animal production is complex and challenging due to many factors including data limitations, purpose of use, as well as the regulatory system and policy environment. It should be noted that the starting point for European countries is different to many other countries around the world, as the level of use of antimicrobials is generally lower, as antimicrobial growth promoters have been banned in the European Union since 2006. Moreover, the issue of animal welfare standards has also been a policy priority and this has had an important impact on production practices. Most of the farms that participated in these surveys from Northern Europe tended to have industries that were more advanced in terms of their management and adherence to high standards of disease biosecurity. A number of case studies for pigs and poultry are analysed and some pertinent lessons and best practices are identified. Many of these practices may be applicable to similar production systems in other countries and other regions of the world.

For these countries, the case studies show that optimising the use of antibiotics on animal farms has little or no adverse impact on the economic or technical performance of the farms. On some pig farms, the studies showed a small net increase in profit margins. On other farms, the economic impact was neutral, due to the need to invest in other disease preventative measures such as selective vaccinations and biosecurity measures. A key aspect was the critical role of veterinarians working closely with farmers in developing and implementing husbandry and biosecurity measures which are specific to the particular farm. Another finding was that more educated farmers (usually the younger farmers), tend to have a better understanding of the short term benefits and potential longer term risks to animal production, and to human health, associated with the unnecessary use of antibiotics in food animal production. In practical terms, these case studies show that relatively modest changes in current production systems can lead to high animal health and welfare standards, high animal productivity, less need for antimicrobial drugs and consequently less pressure on microbes to mutate and develop resistance.

The work on Brazil and the People's Republic of China (hereafter "China") involved taking a more aggregate approach due to the lack of farm level case studies in these countries. The findings on the use of antimicrobials in China and Brazil give quite a different picture to the evidence from the European countries. In both countries, antimicrobials are seen as a critical input to enhance animal growth and production efficiency and, in the case of China, to support food security. In China the high usage of antibiotics, more than five times higher than in animal production in Europe, is often associated with poor

hygiene conditions on many farms, and antibiotics provide a low cost alternative to investing in better management and biosecurity measures on animal farms. In Brazil, however, antibiotics are often seen as key to enhancing competitive production in an industry where profit margins are very tight. China has recently introduced regulations to restrict the use of antibiotics in animal production due to the growing concerns over the transmission of resistant pathogens between animals and humans, e.g. colistin. Since 1998, Brazil has restricted the use of various growth-enhancing antimicrobials such as avoparcin, amphenicols, tetracyclines and others that have been used in animal production.

These two studies indicate that antimicrobials play a much more significant economic role in animal production, especially as an additive to enhance animal growth. In practice, antibiotics are perceived to be an important input to increase competitiveness, and, in the case of China, to compensate for lower sanitary and management standards. At this juncture, the evidence on Brazil and China indicates that the use of antimicrobials in animal production has a slightly positive impact on both the economic and technical performance at the farm level.

Insights from the case studies have been complemented by views from an Expert Steering Group, to identify practical ways in which a more responsible and prudent use of antibiotics can be encouraged at the farm level. Given that countries and regions are at quite different stages in terms of progress towards more prudent use of antimicrobials, a country specific approach is likely to be more pragmatic in terms of encouraging better husbandry practices and policies. For example, farmers in China and Brazil are primarily concerned about the economic benefits arising from the use of antimicrobials as an additive in the feed or water, whereas farmers in many European countries are increasingly concerned about the potential longer term risks associated with AMR. While the policy recommendations need to be country and context specific, the analysis and associated expert input suggest some common areas for policies to ensure that the use of antimicrobials deliver private benefits in terms of improved animal health and limiting the development of AMR.

In summary, the demand for antimicrobials in animal production is driven by a combination of demand and supply factors. The evidence shows that there is no "one solution" that fits all animal production systems, species or country. In effect, a package or combination of measures are needed, including modest improvements in current animal biosecurity on farms, as well as some changes in management practices that work towards finding a better balance between the short term private benefits/costs and the potential large long term social costs associated with the spread of AMR between animals and humans. A further important development in many developed countries is the growing concern about the potential health effects of AMR, which has resulted in changing consumer preferences and a rise in demand for animal products with low or no antimicrobials in their production.

This trend is likely to continue in many countries and contribute to the drive for alternative interventions in livestock production. This study also noted the need for further improvements in co-operation and better coherence amongst stakeholders along the food chain, as well as the responsible Ministries and Regulators. The limited availability of information on antimicrobials in production and the cost effectiveness of alternative interventions continue to be a challenge in many countries, especially the large livestock producing developing countries.

8 EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

Main recommendations

1. Enhance the availability of information on the economic benefits and costs of antibiotics in food-producing animals. This could be done through:

- Specific training and providing better information on the economic impact of antimicrobials to key stakeholders, especially farmers and veterinarians.
- Providing examples of "best practice" in terms of the optimal level of antimicrobial use on animal farms based on research in other countries and other animal enterprises.
- Improving the diagnostic tests of animal diseases in order to optimise the use of preventive and affordable veterinary medication, as well as information on the antimicrobial classes best suited to treat and control the disease.

2. Improve the availability of information and knowledge on alternative interventions, and the relative costs and benefits of these interventions. A range of practical alternatives to antimicrobials has been proposed by the OIE, and which are analysed in this report.

• Access to alternative interventions at affordable prices.

3. Provide flexible regulations and a step-by-step approach to facilitate adjustment at farm level. A regulatory approach that nudges producers to more sustainable levels of antimicrobial use may involve several elements, including:

- The existence of quality veterinary services and clear legislation on the use of antimicrobials in animal production.
- Good co-operation and understanding of the regulations by all stakeholders supported by appropriate enforcement, adequate expertise, and a well-functioning surveillance system.
- High priority should be given to abolishing molecules used as growth promoters in animal production but which are important to human health.

4. Optimise the mix of management and biosecurity measures on the farm. While the package of disease preventive measures can vary between countries, several basic elements are critical in all animal farming situations:

- o Good internal and external biosecurity on the farm.
- Increase the natural immunity of the animals by improving breeding, housing, nutrition, and stocking density on the farm.
- Improve overall management on the farm.

5. Take an inter-sectoral or "One Health" approach to combat the negative externalities arising from AMR. The transmission of resistant bacteria to food-producing animals can result in economic losses on livestock farms and raise concerns on disease management strategies on farms. There has been considerable work undertaken to estimate the economic burden to human healthcare due to a rise in antimicrobial resistance, and many of the lessons learned can be applied to antibiotic use in animal agriculture.

1. Introduction

The World Health Organisation (WHO) published in 2015 the Global Action Plan (GAP) on AMR in collaboration with the FAO and OIE. The GAP set out the overarching framework and actions needed to contain the emergence and spread of antimicrobial resistance in humans and in animals. It identified five strategic focus areas to achieve this goal:

- Improve awareness and understanding of antimicrobial resistance though effective communication, education and training
- Strengthen the knowledge and evidence base through surveillance and research
- Reduce the incidence of infection through effective sanitation, hygiene and infection prevention measures
- Optimize the use of antimicrobial medicines in human and in animal health
- Develop the economic case for sustainable investment that takes account of the needs of all countries, and increase investment in new medicines, diagnostic tools, vaccines and other interventions.

The OIE has developed intergovernmental standards and guidelines on the responsible and prudent use of antimicrobials, in line with the WTO/GAP. The FAO Action Plan on Antimicrobial Resistance 2016-20, identifies several implementation areas to support the GAP in the food and agriculture sectors. In essence, the FAO plan focusses on four key pillar: awareness, surveillance and monitoring, governance, and the promotion of good practices. Member countries of the WHO have recognised the benefits of containing the growth in AMR and have started to implement their national strategies and plans with specific measures to deal with the rise in antimicrobial resistance. A 2016 World Bank report estimated the aggregate benefits and costs of antimicrobial resistance, and noted that the potential benefits of containing AMR will vary between high and middle-income countries, with the monetary benefits ranging from USD 7 to USD 22 trillion if measures are implemented to reduce AMR by 50%. Notwithstanding these broad estimates at the global level, there has been little work on defining the short-term private benefits (and costs) of antimicrobial use in animal production and the longer-term social costs associated with the rise in AMR.

The lack of information on the economic impact of antimicrobial usage at the farm level is a key factor that may have slowed the adjustment in animal production. This study aims to help fill this information gap and to complement the technical activities of the WHO, OIE and FAO to combat the rise in AMR. A further aim is to complement the extensive economic work on AMR in human health and health care systems that is ongoing in the Directorate for Employment, Labour and Social Affairs (ELS) at the OECD. This work focuses on several areas related to the rise in AMR. Firstly, the modelling of the trends in the AMR rates which are used to gauge the health and economic burden of AMR and to evaluate the efficiency and cost-effectiveness of current and innovative policy options. Second, the work reviews the implementation level of national action plans to reduce AMR and antimicrobial consumption, as well as policies currently in place in some OECD countries. This work also aims to identify best practices to promote the prudent use of antimicrobials and to help countries implement these actions. Third, the work undertaken by ELS also aims to incentivise the various phases of the R&D pipeline.

This paper focuses on the economic aspects of antibiotic usage in food-producing animals and assesses the direct costs and benefits of including antibiotics in the production system. The data examined relates to antibiotic usage (largely based on sales data) and does not differentiate between antibiotics or use by different food animal species. Further challenges relate to country-specific administration and regulatory systems, and the specific definition of antibiotics in the regulations, which can vary from country to country and region to region. For example, ionophores are not normally classified as antibiotics in Europe, but are included in the list of antibiotics in the United States and may account for up to 30% of antibiotics used in veterinary medicine. Despite these limitations, useful insights and guidance can be gleaned from the analysis and, in particular, from the case studies for pigs, poultry and cattle.

10 EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

This report reviews the evidence from a number of existing case studies on the economic costs and benefits of antimicrobial use in European OECD countries, and provides additional information on the extent of the challenge of optimising antimicrobial use in China and Brazil. While the benefits/costs approach is a useful guide in this context, it has several limitations, not least of which is that it takes a short-term static approach to the issue and does not fully account for all the costs and benefits incurred in the production process. Moreover, the reliable availability of data on the BRIICS is limited, even though these countries account for an increasing share of the global production of livestock and livestock products, as well as a rising share of global antibiotics sales. A number of case studies for pigs and poultry are analysed and some pertinent lessons and best practices are identified. Notwithstanding, many of the best production practices identified can be applied to other countries depending on specific factors such as the type of production system, degree of modernisation, climate, husbandry standards, nutrition, and the biosecurity measures that are already in place.

This report attempts to quantify the costs and benefits associated with the use of antimicrobials in animal production and to identify the optimal economic level of use in animal production in the context of a broader social perspective. Assessing the impact of antibiotic use in animal production is complex due to many factors, not least that antibiotics in practice are used for a range of purposes, including treating an outbreak of disease, preventing and controlling a disease outbreak, and to promote growth. This report also explores the economic impact of the regular and systematic use of antimicrobials in pig, cattle and poultry production, which together account for more than three-quarters of global meat production. This work assesses the short-term benefits and costs of using antimicrobials in production, as well as the possible economic and policy implications of the emergence of AMR, the impact on animal health and animal welfare, production, food safety and food security.

The report is organised as follows. Section 2 provides some background to this work and outlines the scope of the study. Section 3 gives a brief summary of the use of antimicrobials in food animal production and discusses some of the key factors that drive the emergence and spread of antimicrobial resistance. Section 4 discusses the use of the benefits/costs methodology to analyse this issue and identifies some of the deficiencies when using such an approach. Section 5 draws together the findings of selected case studies on poultry, pigs and cattle from several European countries as well as an analysis of the situation in China and Brazil. Section 6 discusses some policy options and suggests farm and national level practices that would curb the rise in antimicrobial use and contain the emergence and spread of resistant pathogens in different environments.

2. Background and scope of the work

The growing resistance of microbes to the commonly used antimicrobial drugs pose a serious challenge to policy makers in human and animal health, the environment as well as the food sector in all countries. The emergence of AMR is a natural phenomenon with bacteria mutating and developing new traits that are resistant to the standard antimicrobial drugs. In essence, resistance to antimicrobials can be intrinsic (natural mutation) or acquired, and can lead to the failure of existing treatments for humans and animals (2017 UNEP Report). Globally, there has been substantial progress in raising awareness on the impact of AMR and the potential social and economic implications for human and animal health (OECD, 2016). Several studies have estimated that by 2050 the global consequences could result in up to ten million deaths and a decrease in global GDP of 2%-3.8% (WHO, 2015; WB, 2016). Moreover, the economic impact of the development and spread of AMR impedes countries from attaining the Sustainable Development Goals (SDG) by 2030, especially the goal of realising food security (WB, 2016).

Antimicrobials are drugs that kill or inhibit the growth of micro-organisms and include antibiotics, antimycobacterial drugs (antibiotics specifically designed to treat mycobacterial infections such as TB), antivirals, antifungals, and antiparasitals (Morel, 2017). As antibiotics receive the most attention in this group, the term antimicrobial resistance (AMR) is used interchangeably with the term antibiotic resistance in this report. Despite the use of both terms, the data and information mainly refer to antibiotic use and antibiotic resistance. In practice, resistance reduces the effectiveness of the antibiotic in preventing or treating infections caused by the pathogens, resulting in greater morbidity, mortality and treatment costs.

At the core of this issue is the fact that all use of antimicrobials, including frequent and inappropriate use in animals and humans, accelerates the emergence and spread of resistant bacteria. Research has shown that the over-use and incorrect use of antibiotics in human medicine has a critical impact on the emergence of antimicrobial resistance infections in humans. Moreover, the high usage or inappropriate use of antibiotics in animals can contribute to antimicrobial resistance, as well as raise important questions on the possible routes of transmission between animals, humans, and the environment.

The emergence and spread of resistant bacteria raises important concerns for livestock producers with potentially serious implications for animal health and welfare, food production, food safety, food security, trade, and market access for food and animal products. The production and trade in livestock and livestock products can be particularly sensitive to the impact of AMR, due not only to reduced productivity (animal mortality and morbidity) and output, but also because of potential disruptions between individual farms arising from disease outbreaks (Rushton, 2015). A 2016 report by the World Bank estimated that by 2050, the potential impact of AMR on animal health could reduce global animal production by between 2.6% and 7.5%.

In modern animal production managing production costs is critical to efficient and profitable production. In animal production, an important and increasing share of production costs are those incurred in preventing and controlling the outbreak of disease. The cost/benefit economic framework has been widely used in animal disease analyses to assess the benefits and costs of alternative methods to prevent a disease outbreak. While it is difficult to determine the optimal input level of animal medicines in production, including antibiotics, to a large extent this becomes an economic decision on the part of the farmer. In economic terms, farmers will use preventative medicines such as antibiotics up to the point where the marginal cost of the input is equal to the marginal benefit from the use of this input in their production system. The literature on animal health economics refers to this as the "equimarginal principle". It should be noted that there are major differences between the net private benefits and costs to animal producers in the short term. At a later stage, the longer-term impact of AMR on animal production can be evaluated.

The use of antibiotics in animal production is complex and difficult to estimate at the industry and species levels. In food animal production, antibiotics have been widely used due to their availability, relatively low cost and high effectiveness in preventing a wide range of infectious animal diseases compared to alternatives such as vaccines. In animal production, antibiotics are used to treat infectious diseases and improve animal health and animal welfare. To prevent and control the outbreak of a disease, antimicrobials are often given as an additive in feed or in drinking water. In some countries, they are also used at low dosage levels to enhance feed efficiency and promote growth and, in some cases, this has given rise to the overuse and misuse of antibiotics which has further contributed to the global rise in AMR. Over the last three decades, the global demand for antimicrobials has risen sharply, with the largest increase attributed to the growth in demand from livestock producers (Laxminarayan et al., 2015). This trend is perceived to be closely linked to the development of large intensive animal production operations, driven by strong growth in demand for animal products. Over the last decades the highest growth rates have been in the emerging economies, while antibiotics used in animal production, with a substantial volume of falsified and substandard products currently used in certain countries and regions.

The use of antibiotics is a feature of modern high density production systems, most notably for poultry, pigs and cattle. These drugs have played an important role in preventing and managing the outbreak of disease, especially under sub-optimal sanitary conditions and weak biosecurity measures. The rise in antibiotic use in animal production is one of the drivers of the emergence and spread of antibiotic resistant microbes in the food chain. At this juncture, it should be noted there is no standardized and globally accepted approach to measuring resistance, but the OIE is making good progress in finding a solution to this issue. In the short term, high density animal production systems may "benefit" from the regular and systematic use of antibiotics, but in the long term with the emergence and spread of resistant pathogens, in particular multi-drug resistant pathogens, the private and social costs are likely to be substantial for animal health, animal production, and human health.

While work on the technical productivity aspects of antimicrobial use in animal production has made good progress, there have been few attempts to quantify the economic benefits and costs associated with the

12 | EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

optimization of antimicrobial use in animal production. The lack of economic knowledge at the farm level is a serious impediment to building awareness and understanding of the impacts on human and animal health of the emergence and spread of resistant pathogens. This attempts to fill the information gap by focusing on the economic aspects, in particular the costs and benefits of antibiotic usage in food animal production. The complexity of the issue and data requirements can be gleaned from Figure 1, which shows the epidemiology associated with the development and spread of antimicrobial resistance.

This report draws on the outcome of case studies in several OECD countries and provides a snapshot of the estimated economic impact on farmers' income and farm viability resulting from optimizing the use of antibiotics in production. While these results give useful insights into the impact on production and profitability, in order to better understand the long-term impact similar harmonised studies would need to be undertaken over several years and over different production systems. The findings from available case studies have been synthesised and are presented in Section 5. However, globally, it is the use of antimicrobials in large emerging economies that is most significant, and the economic benefits of antimicrobial use in these countries may differ fundamentally from that in more developed economies. Based on the outcome of these case studies some best practices and policy options are identified and discussed. These best practices can be extended to similar production systems in other countries and other regions with similar environmental specificities.

As publicly available information on AMU and AMR in China and Brazil is sparse, OECD commissioned two background papers from experts in these countries (see OECD Food, Agriculture and Fisheries Papers N°132 and N°133). The key findings of these two papers are included in this report. Key elements of an additional paper synthesising the current state of knowledge on the transmission of resistance between species (OECD, 2019) are also highlighted here. The Expert Steering Group (ESG) on AMR, established in 2017, provided valuable oversight and guidance during the preparation of this report.

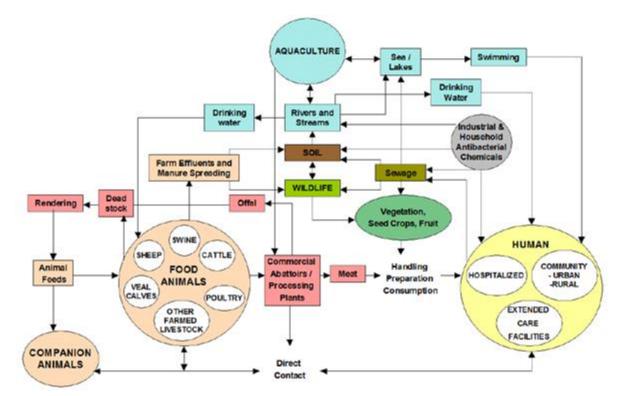


Figure 1. An outline of the epidemiology on the emergence and potential spread of antimicrobial resistance

Source: Adapted from a presentation by Dr. Hilde Kruse, FAO, to the OECD Health Committee (2016).

3. Factors that drive the use of antimicrobials in animal production

This section summarises the current understanding of the key factors that may drive the increasing use of antibiotics in food producing animals and the emergence of resistant pathogens. The epidemiology literature on antimicrobial resistance identifies several factors that influence the rise in resistant pathogens in food animals, including the volume of antimicrobial use, the type of production system, the risk behaviour of producers, the extent of transmission of resistant pathogens between species, and the interface with the environment.

Influencing factors on antimicrobial use

The world population is projected to exceed 8 billion by 2025, creating greater pressure on agricultural resources to feed this rising population. In addition to population growth, incomes are steadily rising and result in an increase in demand for food, in particular for animal proteins. To meet this increased demand, food animal operations are larger and more intensive, with higher animal densities related to the development of modern technologies and know-how. Globally, meat production is estimated to have risen by 2% per year over the last decade; this trend is expected to continue, but at a slightly lower rate of 1.6% per year between 2018 and 2027 (*OECD/FAO Agricultural Outlook 2018-2027*).

Together, OECD countries and the BRIICS account for almost 80% of global meat production. More specifically, poultry meat, pig meat and beef account for over three-quarters of global meat production, with the production of poultry meat continuing to grow more rapidly than that for red meats. This growth has led to significant changes in the structure of animal production systems with more emphasis on production efficiency, including greater attention to on-farm disease control measures. The more intensive and high-density systems have increased as a share of total production and these developments have been accompanied by a rise in demand for antibiotics.

Antibiotics are an important variable input in animal production as they bring both health and productivity benefits, which can contribute to an increase in farm output and a rise in farm revenue. In animal production, the rise in antimicrobial resistance may increase the risk of animal mortality and reduce animal performance, thereby reducing the economic returns from livestock production and generate possibly higher food prices for consumers in the long run. The productivity effects on food animal production in the BRIICS and in low- and middle-income countries are perceived to be higher than in high income countries due to differences in animal production systems, biosecurity measures, climatic factors, and management practices (WB 2016).

There are several major differences that influence the consumption of antimicrobials in animals and humans. A major difference relates to the purpose for which antimicrobials are used. For example, the main source of AMR in humans is the use, overuse, and inappropriate use of antimicrobials in treating, preventing and controlling bacterial diseases. However, antimicrobials in animal production are used for growth promotion, in addition to the treatment, prevention and control of disease. Reliable empirical data on antimicrobial use in different livestock systems is generally limited to a number of high-income countries, mainly in Europe. Therefore, estimating the global use of antimicrobials in animal agriculture is challenging and involves assumptions and some degree of extrapolation. This is particularly the case for food animal production in the BRIICS, as well as in low- and middle-income countries.

The volume of antibiotics used is closely related to the size of the livestock population, the intensity of the production system, the biosecurity measures on the farm, and management practices. A study by Landers et al. (2012) for the United States noted that over two-fifths of all feedlot cattle and over four-fifths of hogs were given antibiotics in their feed. Van Boeckel et al. (2017) recently revised upwards their earlier estimates of global consumption of antimicrobials in livestock production; estimated at 131k tonnes in 2013, global consumption is projected increase to 200k tonnes by 2030. The consumption levels varied significantly between countries, with the estimates ranging from 8 mg/PCU in Norway to 318 mg/PCU in China. However, several countries have introduced policies to limit antimicrobial consumption for humans and animals. For example, in 2017, the Chinese government introduced several nutritional guidelines on

14 EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

human consumption of meat (set at 50% of the current level), which should result in a slight decline in demand for animal products.

A USDA study (Sneeringer et al., 2015) examined the use of antibiotics in the production of hogs, broilers and feedlot cattle. This study concluded that while antibiotics are still widely used in animal production, there is evidence of a decline in the mass routine use of antibiotics in feed as the productivity effects are estimated to be low at only 1%-2%. The study also examined the economic effects of restricting antibiotics in animal production systems at the animal, farm and market levels. The results indicated a relatively small economic effect in hog and poultry production, with estimates indicating a 1% fall in both production and prices and a similar increase in gross margins. Moreover, the study noted that while some producers would gain in terms of gross revenue, others would lose, depending to a large extent on factors such as management practices and biosecurity measures prevailing on the farm.

A World Bank report (2016) estimated the costs and benefits of antimicrobial use in livestock production in low- and middle-income countries. It identified many serious challenges in estimating the financial effects of antimicrobial use at the farm level due to the lack of reliable data and information on the volume of antibiotics consumed, class of antimicrobial, and the food animal species. The report concluded that by 2050 the emergence of AMR could reduce animal production in low-income countries by up to 11%.

Preliminary work was undertaken by the OECD (2015) to estimate the production, price and trade effects of lowering the use of antimicrobials in the production system for a number of countries. The four large livestock-producing countries of Brazil, China, India and the United States were analysed using the Aglink Cosimo model. These changes in productivity were estimated assuming *ceteris paribus* that there were no changes in any aspects of the production systems. While the results varied by country, a number of interesting observations emerged. More specifically, reducing the use of antibiotics in production resulted in a decline in meat production accompanied by some substitution to lower-priced meat such as poultry, a small increase in farm gate prices, and some rise in exports of animal products from countries that had low antibiotic usage. In terms of the distribution of costs, adjustment costs fell more heavily on producers in emerging economies due to their less than optimum production systems.

In 2017, the OIE made a first global calculation of animal biomass based on an analysis of the antimicrobial quantities reported (adjusted by a denominator). Member countries were also asked about barriers to reporting the amount of antimicrobials to OIE. For the countries unable to report antimicrobial quantities, the main barrier reported was the structure or enforcement of their regulatory framework for veterinary products. It was noted that in some countries, national authorities (generally from the Ministry of Health), outside the veterinary services manage veterinary antimicrobials in the country. The report also summarised the processes that countries have undertaken to facilitate the future collection of antimicrobial use data in animal production.

Hennessy et al. (2005) concluded that disease prevention and control on livestock farms is closely related to farm size, resource availability, and production technology. In the farmers' production decision these factors are usually jointly determined. Over the last 30 years, livestock production has undergone major changes in terms of the type of production system, advances in breeding and nutrition, and production technologies. As large-scale commercial producers become more specialised, this has resulted in greater efficiency, lower costs and higher investment in biosecurity measures due to the potential financial risks associated with a disease outbreak. While the structure of livestock and poultry production is diverse across countries and regions, high density animal production has grown, especially for pigs and poultry. While part-time and hobby farmers continue to play a role in animal production in many countries, most do not have the necessary resources to invest in improving biosecurity measures as compared to commercial producers.

For livestock producers, disease management is a critical part of their production system. Many adopt a common disease management strategy to control infectious diseases with a view to minimizing losses from a potential disease outbreak, which can cause substantial economic losses to animal producers and have important implications for their livelihood and the overall viability of the farm. A recent OECD (2017) study examined the different incentives to manage animal disease on livestock farms. It concluded that uncertainty and risk increase the complexity of farmers' decision-making process and that while the economic aspects are important, they do not fully explain farmer behaviour. For example, non- economic

aspects, such as the level of education, social concerns and farmers' habits, are also important factors in how animal disease is managed.

Commercial livestock producers usually focus on maximising profits and employ the most effective husbandry and biosecurity practices to prevent a disease outbreak, up to the point where the marginal benefit equals the marginal cost of the control. At the farm level, the risk of a disease outbreak is seen as a production risk, and producers adopt better management practices to limit the potential negative effects. In practice, producers evaluate the costs arising from potential losses due to animal and poultry diseases, as well as the costs of prevention and control in the event of an outbreak. However, managing disease risk usually does not include the public goods dimension or the externalities (positive and negative) that may arise in the broader environment. The evidence suggests that there are positive spill over effects of adopting stringent biosecurity measures to prevent disease and reduce the need for antimicrobials in production. Moreover, good management practices such as improving nutrition, housing and sanitation measures will have a positive impact on reducing the outbreak of disease on the farm. The selective use of vaccinations can also make a significant contribution to reducing disease in animals and in lowering the need for antimicrobials.

The epidemiology on the transmission of resistant pathogens between animals, the environment and humans, and vice versa, is very complex. Several reports have attempted to shed more light on this complex issue including the FAO (2016) report "Drivers, Dynamics and Epidemiology of Antimicrobial Resistance in Animal Production". An OECD report (Morel, 2019) summarises the current state of knowledge on the linkages and modes of transmission of AMR between animal species and humans and between humans and animals, as well as the role of the environment in the transmission process.

Hoelzer et al. (July 2017) assessed the scientific evidence on the use of antimicrobial drugs in foodproducing animals and risks to human health. The main objective of this study was to provide an objective methodical summary of the available scientific evidence for or against an association between antibiotic use on farms and antibiotic resistant human infections. This study systematically evaluated the available evidence on the pathway of transmission of resistant pathogens from animals to humans. The authors also attempted to evaluate the strength of the evidence within the Grades of Recommendations, Assessment, Development and Evaluation (GRADE) framework. The study stresses the complexity of any analysis of the link between the use of antibiotics on animal producing farms and the risks to human health. It also noted that the dynamics of antibiotic resistance may be further complicated by the potential for crossresistance and co-resistance.

The study concluded that there is compelling scientific evidence available that supports the causal pathway from antimicrobial use on the farm to a public health burden caused by infections from resistant pathogens. The authors noted that the speed at which resistance emerges and spreads, and the persistence of the resistance in the environment depends on many factors including the type of pathogen, the class of antibiotic used, the treatment approach, and the general environmental conditions for livestock production. They also noted that a precise quantification of the extent of the transmission of resistance between animals and human health is not possible at this juncture, but that some transmission does occur.

Tang et al. (2017) also reported the results of a study that involved a systematic analysis of the evidence on the use of antibiotics in food producing animals and its association with antibiotic resistance in food producing animals and humans. This study compared organic and conventionally produced animal products and examined the level of resistance from samples taken at the retail level. The study found that reducing the use of antibiotics in animal production lowered the prevalence of antibiotic-resistant bacteria in animals by about 15%. However, the evidence of the effects on humans was more limited with a 24% reduction in the prevalence of antibiotic resistant bacteria from lower antimicrobial use in animals. The authors also noted that reducing the need for antibiotics in livestock production is likely to have a beneficial effect on containing the rise in AMR in food producing animals.

4. Framework to evaluate the economic costs and benefits of antibiotics in livestock production

This section outlines the basic economic framework for a cost/benefit analysis of antibiotics in livestock production. There are a range of economic techniques that can be used to analyse the economic implications of antibiotics in the production system given the trade-offs between maintaining animal health and welfare, productivity and the need to contain the rise in AMR. The choice of technique will depend on several factors such as the nature of the problem, data availability, as well as the amount of resources available to undertake the analysis. Given these considerations the cost/benefit framework is the most cost efficient approach for this type of analysis.

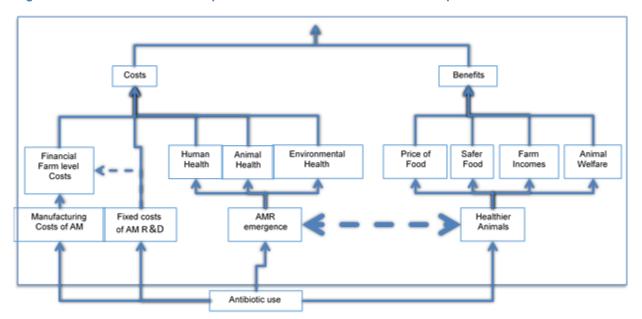
The theoretical background that underpins cost-benefit analysis lies in microeconomics and welfare economics. In essence, the foundations of cost-benefit analysis (CBA) are based on the concept of economic – changes in overall economic wellbeing of producers and consumers in a country as a result of a policy change such as efforts to improve animal health. The concept of economic surplus provides the economic rationale for much of the economic analysis on animal health issues (Berentsen et al., 1992; Sinden and Thampapillai, 1995; Harrison, 1996). The laws of supply and demand are at the core of cost-benefit analysis. In essence, this implies that the producers marginal cost curve is the supply curve – the schedule of extra cost of providing an extra unit of production (e.g. an extra animal to the market). If production costs fall, as in the case of reduced disease incidence, the producer could supply the same quantity for a lower market price. If expenditure on animal health falls then the cost of a given output would fall, or alternatively output would increase for the same cost level.

The cost/benefit framework has been widely used in animal production to examine long term disease control programmes and the costs of different actions over an extended period of time. As the costs and benefits may differ over time, it is important that future costs and benefits are discounted to make them comparable due to the time value of money. This approach can include the adjustments that must be made in terms of changes in management and resource use on the farm in order to optimise the use of antibiotics in livestock production. This approach can be applied at the individual animal level or at the farm/herd level. These results can then be extrapolated to the regional and/or national levels, depending on the policy objective. Drawing on the outcome of reliable epidemiology studies is critical in order to find the optimal level of antibiotic usage in animal production, bearing in mind the need to find the optimum balance between animal health, animal productivity and the need to contain the rise in AMR.

With the cost-benefit methodology it is important to distinguish between the short and long run, especially in the case of livestock production. For example, in the case of livestock production there is generally a time lag which varies by species before there can be a production response to price changes. In the long run, the elasticity of supply is much larger than in the short run. More specifically, while land can be a constraint for increasing beef production, other resources such as capital and feed stock can be a more important constraint in increasing poultry and pig production. Moreover, environmental regulations and compliance issues are becoming a more limiting constraint to expanding production in response to higher market prices. It should be noted that a fall in livestock production costs can lead to a gain in welfare for both consumers and producers. However, in the long run consumers tend to be the main beneficiaries of lower production costs resulting from improved animal health programmes (Harrison and Tisdell, 1995; Harrison, 1996).

The quantification of the economic impact of reducing antimicrobial use in food animal production, while maintaining good animal health and welfare is complex. Figure 2 attempts to simplify the issue and to capture the major economic impacts associated with antibiotic use and antibiotic resistance. More specifically, it shows the potential benefits and costs from the use of antibiotics in livestock production in the short run, as well as the longer run potential economic impacts of the rise in AMR on human, animal and environmental health. More specifically, the RHS of this figure shows the potential benefits of antibiotics in livestock production and includes better animal health and welfare, more animal food products, cheaper food and safer food, and consequently potentially higher and more stable farm income. However, there is considerable debate over the use of antibiotics in the production system and the issue of safer food. While the responsible use of antibiotics is important in treating sick animals and preventing

the spread of infectious pathogens, in the longer run, the excessive use of antibiotics can contribute to the emergence and spread of AMR resulting in additional costs to livestock producers, as well as extra expenditures to deal with the negative externalities on human health and environmental health.





Source: Adapted from Rushton et al. (2016).

Figure 2 shows the impact of a change in the production system which could result in healthier animals and consequently a reduced need for antibiotics on the farm. These changes could also result in increased productivity and higher animal welfare, and potentially higher returns to farmers and the industry. Moreover, it should be noted that the cost of resistance associated with the use of antibiotics is close to zero for the individual farm in the short term. However, in the longer term, the situation would change as the emergence and spread of resistant pathogens could potentially cause considerable loss in production on the farm and at the national level, in addition to the negative externalities and cost to human healthcare systems in many countries.

As regards the potential costs associated with the use of antibiotics in livestock production, the LHS of the chart identifies the possible costs in the short run and in the longer run. For example, in the short run the costs are likely to be relatively low and mainly relate to the direct costs of purchasing the antibiotics and the administration of the drugs on the farm. However, the longer term costs are likely to be much higher due to the direct and indirect impacts associated with the use of antibiotics, in particular the costs associated with the emergence and spread of AMR and the potential impact on human and animal health. As resistance increases, the costs of managing and treating animals for a disease outbreak is also likely to increase, resulting in a rise in production costs on livestock farms. Furthermore, antibiotics can leak (waste, unused, and excreted) into the environment and this can potentially cause a rise in AMR which can then be transmitted to animals and humans.

While the main focus of this report involves identifying and quantifying the costs and benefits of antibiotics in livestock production, primarily poultry and pig production, due to the lack of harmonised information and data at the farm level, it has drawn on existing case studies, and supplements these findings with new information on AMU in China and Brazil.

18 EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

More specifically, several case studies on antibiotic use in animal production have been undertaken in European countries, and these studies provide interesting insights on the use of antibiotics in production. Two separate studies on Brazil and China were commissioned by OECD. The results are discussed in the following section.

The costs and benefits of antimicrobials in animal production vary by country, species and type of production system. This report draws together the major findings and insights on a comparable basis for selected countries. The analysis focusses on the short term benefits and costs (snapshot) of antibiotics in livestock production and discusses the optimal level of use and balance between animal health and welfare, sustainable production, while restraining the drivers of AMR. Additional insights are provided on the potential transmission of resistance between different food animals, food animals and humans, and vice versa.

5. Main findings of case studies from selected OECD countries, Brazil and China

The responsible and prudent use of antibiotics in veterinary medicine is a key element of national action plans to combat the threat from antimicrobial resistance. As part of the implementation of the GAP, many European countries have set national targets on the use of antibiotics in food animal production. While these targets are often set at the industry level, several countries continue to refine their implementation targets to the species level. A good awareness and understanding of the technical and economic impacts arising from the use of antimicrobials in animal production is essential in order to achieve the desired outcome.

This section synthesises the findings of farm level studies that have examined changes in antibiotic use in food animal production in several European countries and their likely impact on technical performance and farm profitability. The livestock producers that participated in these surveys were the more modern and technically advanced farmers. The 2017 ESVAC report shows that the Nordic countries have had the lowest use of veterinary antimicrobials for many years and that these countries have strict regulatory measures on the level of permitted antibiotics in food-producing animals. The findings show not only the overall technical impact, but also the major benefits and costs of antibiotic use in the production system. However, it should be noted that the use of antibiotics varies significantly with different food-producing species, as well as at the different stages of the life cycle of the animal (e.g. calf vs finisher). Moreover, it was shown that the implementation of on-farm biosecurity measures to reduce the incidence of animal diseases could have a positive spill over effect on reducing the need for antimicrobials as a preventative medicine in production.

Findings from case studies in several European countries

Multi country study: Belgium, France, Germany and Sweden

Collineau et al. (2017) examined the technical and economic impact of herd-specific interventions by pig farmers who reduced their antibiotic usage in production, while at the same time implementing alternative disease management measures. This study was carried out over the 2014-15 production year cycle. The initial farm visits were organised to define the herd-specific intervention plans that were aimed at implementing preventative measures to allow for reduced use of antibiotics on the farms. The monitoring process involved two to six farm visits, in addition to regular communication with the farmers and veterinarians. A total of 70 birth-to-finish pig farms were covered in this study across four countries: Belgium, France, Germany and Sweden.

A range of alternative interventions to antimicrobials were considered by farmers and veterinarians depending on their feasibility, health problems of the herd, and country specific-legislation. For example, zinc-oxide is permitted as a feed additive in some countries to prevent a disease outbreak, but not in others.

However, due to the specific needs of a herd, different sets of interventions in terms of number and type of measures were implemented. The range of alternative interventions to antimicrobials included:

- Improving external biosecurity measures
- Improving internal biosecurity measures
- Increasing herd vaccination
- Changing the quality and composition of the feed and drinking water
- Improving health care and welfare of the animals
- Modifying housing in order to provide a more stable indoor climate.

The findings indicated that all farmers significantly decreased their use of antibiotics during the period of the experiment. The study not only monitored the use of antibiotics during the life cycle of the pigs, but also compared the technical performance of the herds with the results from the previous year. For a subset of the farms, estimates were also made on the impact the lowering of antibiotic use would have on the profitability of the farms.

This study recorded an overall decrease in the use of antimicrobials, with an average reduction of about 47% across participating farms. This decrease was achieved without any reported adverse impacts on the overall technical performance of the herds: there were no significant changes in the mortality rates or daily weight gains compared to the previous period. Moreover, it was noted that those farms that decreased antimicrobial usage by more than the average achieved slightly better animal performance. It was also noted that the feed conversion ratio and daily weight gains during the fattening period had the biggest impact on profit margins. Moreover, the level of expenditure on antibiotics and the direct costs of interventions had a negative impact on profit margins.

The overall economic performance of the farms was also assessed. An economic analysis of the subset of 33 Belgian and French farms showed a net profit ranging from EUR 1.2 to EUR 4.5 per breeding animal per year, depending on the type of model (deterministic or stochastic). Moreover, the rate of mortality for piglets, weaners and fatteners, the daily weight gain, and feed conversion ratio did not significantly change, although the number of pigs weaned per sow increased slightly.

While this study raises interesting questions, the findings are based on a relatively small sample size of 70 farmers across four countries. They provide an insightful snapshot of the technical and economic impacts of antibiotic use to prevent disease on farms. However, for more comparable results, similar harmonised studies would need to be undertaken for longer periods of time and across a larger number of countries and production systems. Finally, participants in such studies are usually based on voluntary participation and, in many cases, participants are often the more modern farmers in the industry.

Switzerland and Denmark

Carmo et al. (2017) compared veterinary antimicrobial consumption for cattle and pigs in Switzerland and Denmark from 2007 to 2013. The objectives of this study were to compare the patterns and trends of antimicrobial consumption in cattle and pigs, and to compare the relative consumption of different antimicrobial classes in the different species and countries. Although both countries have a similar animal health status, Switzerland had higher antimicrobial consumption in livestock per kilo of animal biomass compared to Denmark. The authors noted that additional factors beyond animal health status drive antimicrobial consumption and that benchmarking such consumption at the species level can lead to more tailored and effective optimisation measures.

More specifically, antimicrobial consumption in cattle in Switzerland was more than double the level in Denmark. But over the period 2008-2013, the consumption of antibiotics in Switzerland fell by about 25% compared to a 21% fall in Denmark. In the case of pigs, antimicrobial consumption in Switzerland was also higher than in Denmark. However, over the study period the level of consumption in Switzerland fell by 32% compared to a 2% decrease in Denmark. For all classes of antibiotics, except penicillin, consumption

20 | EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

was higher for cattle in Switzerland compared to Denmark. Lastly, the relative consumption of penicillin in swine was higher in Denmark than in Switzerland. These differences can be attributed to factors such as the infection status on the farm, animal husbandry practices, housing conditions, on-farm biosecurity, veterinary medicine prescription practices, product availability, and education and knowledge of farmers and veterinarians.

Denmark introduced in 2010 a unique system named the Yellow Card Initiative (YCI) to limit growth of antimicrobial use in pig production. The principal objective was to reverse the increase in antimicrobial consumption in pig production, and the related potential risks to human and animal health. CY was established by the Danish Veterinary and Food Administration (DVFA) they focussed uniquely on pig holdings as they consumed more than 80% of the antimicrobial agents used in livestock production in Denmark.

YCI focussed on lowering the consumption of antimicrobials in pig production. More specifically, if the average antimicrobial consumption in a holding within a nine-month period exceeded the threshold limit, the DVFA could issue an order or injunction (the yellow card) compelling the farmer, in collaboration with the veterinary practitioner, to reduce antimicrobial consumption on the farm below the threshold limit within the following nine months.

In 2016, the DVFA further developed the YCI by adding a multiplication factor for some antimicrobial agents. The multiplication factors are determined by the DVFA as a risk mitigation for each class of antimicrobials. Fluoroquinolones, which have been under restrictions by Danish Law since 2002, as well as 3rd and 4th generation *cephalosporins* are regarded as the highest priority antimicrobials in the treatment of human disease; YCI attributes them a multiplication factor of ten, the highest one possible. Since 2010 the Danish pig industry has voluntarily phased out the use of 3rd and 4th generation *cephalosporins*.

Initially, tetracyclines were given a multiplication factor of 1.2, leading to a decrease in their use. In January 2017, the factor for tetracyclines was increased to 1.5 to promote a further decrease in usage in pig production.

In 2016, the European Medicines Agency (EMA) recommended that colistin should only be used as a second line treatment in animals. Although Denmark was well below the consumption threshold suggested by EMA, the Danish government increased the multiplication factor for colistin from one to ten as a precautionary measure. This was also done for fluoroquinolones and 3rd and 4th generation *cephalosporins*. The use of colistin for pigs in Denmark is now negligible.

An important mechanism in the development of responsible and prudent use of antimicrobials is creating awareness amongst stakeholders. It is crucial that farmers and veterinarians are fully aware of their role and participate in finding solutions. YCI and other initiatives have made a major contribution to raising the awareness of pig farmers and veterinarians on AMR developments. In Denmark, the differentiated YCI has been an effective tool to promote the more prudent use of antimicrobials and to discourage the use of HPCIA.

In Switzerland, the Federal Food Safety and Veterinary Office (FSVO) introduced in 2006 a comprehensive surveillance and monitoring system to assess AMR in livestock and meat, and has established a comprehensive database on the sales of antibiotics for veterinary use. This database has helped improve the awareness and education of farmers and veterinarians on the risks associated with AMU and the development of resistant pathogens, contributing to the National Strategy on combatting the rise in AMR. In addition, the commercialization of vaccines has played a role in the pig sector, while the Bovine Viral Diarrhoea (BVD) eradication programme introduced in 2008 has contributed to the downward trend of BVD in the cattle sector. Over the last decade the use of antibiotics in animal production has fallen by 40%, largely due to the reduced number of treatments (Swiss Antibiotic Resistance Report, 2016).

In summary, this study shows there has been a substantial decrease in antimicrobial consumption in cattle and pig production in Denmark and Switzerland. Over the period of study, the overall decrease in antimicrobial consumption in Switzerland was estimated at 30% for pigs and 25% for cattle, while in Denmark the decrease was estimated at 2% for pigs and 7% for cattle. The decrease in antimicrobial use can be largely attributed to the range of measures implemented in both countries, such as the YCI for pigs in Denmark and the awareness and educational programmes in Switzerland. These initiatives helped to

increase understanding of the risks associated with antimicrobial usage and the potential consequences for human and animal health.

The Netherlands

The production system for livestock and livestock products in the Netherlands is one of the most intensive in the world, and is characterised by high inputs and good disease management that result in high productivity and high output. The Netherlands has some of the most stringent legislation on antimicrobials use in animal production. For example, the use of antibiotics is banned as a means of preventative use in animal production, there are strong restrictions on the use of critically important antimicrobials, and only veterinarians can prescribe the use of antibiotics following the completion of diagnosis tests. In 2008, a new policy was established which aimed to lower the use of antibiotics in food animal production. This policy was unique in that it involved a public-private partnership approach that involved all major stakeholders: farmers, veterinarians and regulators. Some key aspects of this policy include the monitoring of all antibiotic use in livestock production by 2015), greater transparency, and improved animal health through better disease management on farms.

A Wageningen University (2016) study showed a significant reduction in antimicrobial usage in the different food animal species in the Netherlands. In overall terms, the volume of veterinary antibiotic sales fell by 58% between 2009 and 2014. More specifically, antibiotic use declined by well over 50% in the pig, broiler and dairy sectors from 2009 to2014 (Table 1). Since 2013, the Netherlands does not allow medically important antibiotics in livestock production to be used, which has resulted in lowering the AMR risk in most species. In view of the fact that the ban on antimicrobial growth promoters (AGPs) was implemented in the European Union in 2006, the decrease in AMU reported in this study was the result of lower usage for therapeutic, prophylactic, and metaphylactic purposes.

Table 1. Reduction in antibiotic use per sector 2009-2014

Sector	2009	2014	%
Sow / piglets	25	11	56
Sow / piglets Fattening pigs Broilers	16	8	50
Broilers	37	16	57
Veal calves	34	21	38
Dairy cattle	5.8	2.4	58

Number of daily doses per animal year

Source: Netherlands Veterinary Medicines Authority.

This study also examined the technical and economic performance of herds with lower antibiotic usage across the different species and production systems. While there were differences across the different species, the lower usage of antibiotics in the production systems had no substantial effect on technical production factors, such as mortality and growth rates, over the period of the study. The technical results from 80 pig farms and 21 broiler farms reported that farms where antibiotic use was reduced by 50% or more did not show any better (or worse) performance than the benchmark farms (short-term static results). Furthermore, there were no reported adverse effects on animal health and welfare on the farms or on the level of farm profitability.

The study noted that while farm incomes fluctuated over the period of the study, these fluctuations were due mainly to changes in feed and meat prices. While most farmers who participated in the survey indicated that reducing their antibiotic usage had little impact on their income, some farmers reported improved technical results and higher animal gross margins. The overall outcome suggests that the decrease in the use of antibiotics in pig and poultry production did not impact animal health costs on the farms as a result

of the slightly higher costs of preventative measures, such as vaccinations and improved animal housing, water quality and hygiene measures.

In summary, this study shows it is feasible to improve animal health and lower antibiotic use by adopting a series of relatively simple and inexpensive management practices, such as greater attention to animal housing and animal behaviour, improving the quality of drinking water, and adopting better internal and external biosecurity and hygiene measures. Moreover, it concluded that antibiotic use can be reduced with modest improvements in disease preventative measures and careful selection of antibiotics for therapeutic purposes on food animal farms. In essence, the Netherlands has taken a pragmatic approach to optimizing the use of antibiotics on farms, and has implemented clear reduction targets, a ban on in-feed mixing of antimicrobials, and the regular monitoring of antibiotic use in the herd accompanied by comprehensive awareness and education programmes for stakeholders. Equally important are the strictly professional relationship between farmers and veterinarians, and the implementation of strict guidelines on the use of antibiotics in animal production.

Sweden

The overall level of animal disease is low in Sweden compared to other countries due to the proactive approach taken by both the Swedish food industry and government agencies. This has resulted in the absence of almost all the major animal diseases and therefore less need for antibiotics. Sweden was one of the first countries in Europe to phase out the use of antibiotics as a growth promoter (in 1986) and it presently has one of the lowest levels of antibiotic use in animal production in Europe. Figure 3 shows that sales of antimicrobials for food animals after an initial increase in the early 1990s, has since steadily fallen.

Backhans et al. (2016) examined the factors influencing the use of antimicrobials in farrow-to-finish pig herds in Sweden. The use of antimicrobials in pig production in Sweden is low as many of the serious pig diseases, such as porcine reproductive and respiratory syndrome (PRRS), are not present on Swedish farms due to the implementation of preventative measures. The main objective of this study was to examine the farm/farmer-related factors that influence antimicrobial use on farms and how biosecurity levels, herd size, farmers' attitudes to antimicrobial use, and advice from veterinarians influence such use. The hypothesis tested was that the high level of farm biosecurity is associated with low antimicrobial use, and that farmers who are aware of antimicrobial resistance generally use less antimicrobials in the production process. The use of antimicrobials is mainly limited to individual treatments of pigs, with low overall levels of usage in herds.

This study was undertaken under the European research project MINAPIG (evaluation of alternative strategies for raising pigs with minimal antimicrobial usage). A total of 60 farrow-to-finish herds were selected with at least 100 sows and 500 finishing pigs per year. The herds were visited once in 2013 when data on production parameters, biosecurity practices, and other herd characteristics were collected by the researchers.

The results of this study suggest that the association between antimicrobial use and biosecurity were notsignificant when farmer characteristics were taken into account. Individual characteristics such as age and education were considered to be more important. The authors noted the lack of association between antimicrobial use and biosecurity measures on the farms, but noted the results from a study by Postma et al. (2015) that showed better biosecurity measures resulted in less medicinal treatment for certain clinical diseases. The study also noted that given the high health status of pig herds in Sweden the association with antimicrobial use may be more difficult to identify than in other countries. The most important biosecurity measures, such as the all-in all-out system and lower stocking densities, have been implemented in the majority of herds studied. The authors concluded that further improvements in biosecurity measures are less important in terms of antimicrobial use than in other countries.

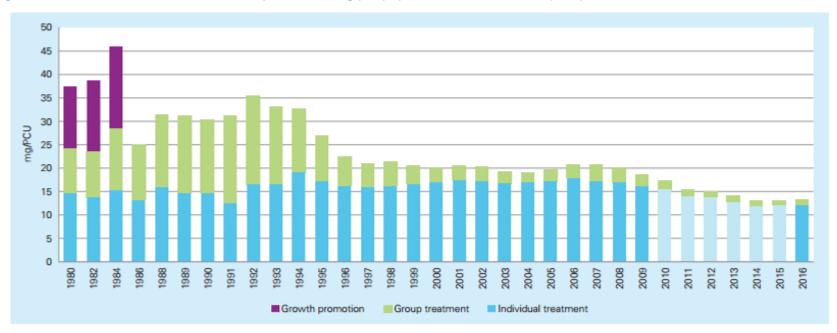


Figure 3. Sales of antibiotics for animals expressed as mg per population correction unit (PCU)

Note: Data from 2010-2015 are uncertain because of a lack of completeness mainly affecting injectable products. This is indicated by a paler colour for antibiotics for individual treatment. In the present figure, all products (including tablets) are included, while in data presented in the European surveillance of veterinary antimicrobial consumption tablets are excluded when calculating mg/PCU. Source: Swedres-Svarm (2017).

24 EVALUATING THE ECONOMIC BENEFITS AND COSTS OF ANTIMICROBIAL USE IN FOOD PRODUCING ANIMALS

Between 2007 and 2016, the total sales of veterinary antibiotics fell by 40% in Sweden, with the biggest drop of 70% due to the decrease in the use of tetracyclines. As Sweden had banned the use of antibiotics as a growth promoter in animal feed in 1986, this decrease represents a further substantial decline from an already low base. In reviewing the volume of antibiotic sales figures, it is also necessary to carefully examine changes in the number of livestock over the period and to adjust the sales data to trends in livestock numbers. Over the 2007-16 period, the sales of antibiotics for individual animal treatment fell by about 50%, while the sales of antibiotics for group treatment fell by 97% (2017 Report SWEDRES /SVARM).

In overall terms, the sale of veterinary antibiotics for animal production decreased by 70% between the mid-1980s and 2016. This decline can be attributed to several factors, of which the most important are the strict regulations on antibiotic use in food animal production, the complete ban on the use of antibiotics for animal growth promotion in 1986, and the greater efforts to enhance awareness and understanding of the risks associated with the over and inappropriate use of antibiotics in animal production. In 2005 Sweden established the SvarmPat programme, which is a special co-operation project between Farm and Animal Health and the SVA. The primary goal of this project is to limit the emergence and spread of antibiotic resistance in pathogenic bacteria from farm animals.

Sweden has a long-term policy to combatting the growth in AMR, and domestic AMR policies are built around a National Strategy that is closely linked to EU and international recommendations, e.g. GAP. Like many countries, the objective is to reduce the growth in AMR through a combination of preventative measures, good operating practices, and identifying alternatives veterinary medicines to prevent disease outbreaks. More specifically, the policy includes increasing knowledge on AMU/AMR through enhanced surveillance, implementation of preventative measures to prevent the spread of resistance, ensuring the responsible use of antibiotics, developing new diagnostic methods, vaccines and treatment options, increasing awareness on antimicrobial resistance and countermeasures in society, improving coherence and efficiency amongst the various stakeholders, and raising awareness on multilateral processes for the prudent and responsible use of antibiotics.

Belgium

Rojo-Gimeno et al. (2016) examined the high level of antibiotic use in pig production in Belgium. The study adopted a quasi-experimental longitudinal approach to assess the economic impacts of substituting antimicrobials for good management practices, in particular biosecurity strategies. The farrow-to-finish pig farms examined in this study were selected from the Flemish Farm Accounting Data Network (FADN) and the technical parameters on general management, vaccinations, biosecurity, and antibiotic use were recorded before and after these measures were implemented on the farms. The direct economic effects of improved biosecurity, improved vaccinations, and reduced antibiotic use were estimated using the standard cost accounting approach based on a combination of interviews with farmers, while data on prices and costs were taken from the relevant farm databases and analysed in the farm production economic model.

Of the 65 farms that participated in the experiment, 50 were farrow-to-finish pig farms. The experiment was carried out between 2010 and 2014, and each farm was visited three times to collect specific information and data on the different production parameters. Following the first visit a specific advisory plan on measures to improve internal and external biosecurity, vaccinations, management and on approaches to reduce antibiotic use was designed and implemented by the farmers. All the technical performance results were collected and analysed after the final visit.

Of the 50 farrow-to-finish pig farms, 48 remained throughout the study period. During the course of the study the dosage of antimicrobial in fattening pigs (from birth to slaughter) was reduced on average by 52%. In terms of the various technical parameters the visited farms performed better than the control farms. Moreover, in relation to the economic analysis, the total direct net costs fell on the visited farms (median) by EUR 7.68/sow/year, mainly due to savings from lower antibiotic usage. On the other hand, the increased biosecurity and vaccinations resulted in higher estimated costs of EUR 4.76/sow/year and EUR 5.94/sow/year, respectively. In summary, the overall profitability of the farms following a reduction in the use of antibiotics was estimated at EUR 2.45/finisher pig/year, or EUR 39.21/sow/year.

In summary, optimising the use of antibiotics, improving biosecurity measures, the use of selective vaccinations, and improved husbandry measures have contributed to an overall reduction in the net direct

costs on the farms. This reduction was largely attributed to the lower use of antibiotics as a prophylactic treatment. The study concluded that the use of antibiotics is not necessarily cheaper (despite the perceptions of many farmers that this is so) than was investing in alternative interventions such as biosecurity and vaccination measures.

Conclusions

The findings of the case studies of livestock producers in several European countries are based on surveys of commercial producers who have modern facilities and good management and know-how. Moreover, it should be noted that the starting point for antibiotic use is relatively low as the European Union banned the use of antimicrobials for growth promotion in 2006. Following this ban, many countries experienced a significant decline in the volume of antimicrobial sales and usage, especially in livestock production. Farmers have also became more aware of the need to increase investment in livestock facilities and livestock management so as to improve their on-farm biosecurity measures. In addition, over the last decade or so many livestock producers have given greater attention to finding alternative approaches and interventions to preventing disease outbreaks and this has resulted in further reducing the need for antibiotics in production. For example, countries such as Denmark, Sweden, the Netherlands and France have reduced their antibiotic use in livestock production by over 60% over the last 12 years.

The case studies mainly focussed on antibiotic use in the pig and poultry sectors as these sectors tend to have the most reliable records, and account for the bulk of antibiotic use in food animal production. These studies have collected and analysed the survey data and information from livestock producers on AMU and AMR. However, these studies were based on voluntary participation by producers and tend to represent the more efficient producers in the sector. Also, as the surveys were carried out over a limited time span, usually one year, the findings should be interpreted within this context.

A number of important lessons nevertheless can be drawn from these case studies. First, reducing the use of antibiotics as a prophylactic in pig and poultry production had no adverse impact on the technical or economic performance of the farms. This can be partly attributed to the high level of attention given to disease prevention on these farms, and consequently less need for preventive antibiotics. In terms of the economic impact there was a small increase in gross margins due to lower input costs associated with the lower use of antibiotics (lower drug costs and administration costs). For example, in the Belgian study (Rojo-Gimeno et al. 2016), the net increase in overall profitability of the farm due to a reduction in the use of antibiotics was estimated at EUR 2.45 per finisher animal per year.

Second, where the level of biosecurity and management were less robust, additional efforts and costs were incurred by farmers due to the need to invest in alternative interventions, including the vaccination of animals, and improving the management and biosecurity measures. The extra costs incurred partly offset the gains arising from the cost savings from the lower use of antibiotics.

Third, the studies acknowledge the key role of veterinarians and extension services in providing relevant and specific advice and guidance to producers at the local level. This has been a critical component on many farms due to the importance of having a better understanding of the alternative interventions to antibiotics and the potential consequences of the rise in resistant pathogens. While commercial livestock producers are concerned about making a livelihood, they are also concerned about finding the right balance in terms of animal health and welfare, productivity, as well as the economic and technical sustainability of the farm.

Fourth, younger and better educated farmers tend to be more aware of the AMR issue and of the potential long-term consequences of resistant pathogens to human health and to animal health and productivity. Younger farmers tend to also make greater efforts to acquire knowledge and know-how on possible alternatives to antibiotics that can be adopted on their farms.

Finally, these studies indicate that livestock producers are becoming more aware of the greater interest and concern of consumers on how food, especially meat and animal products, are produced. The growing interest by consumers in food production is expected to influence future animal production practices and inputs such as antibiotics that are used in the production process. In the European case studies discussed above the focus has shifted somewhat from productivity (and competitiveness) to greater attention to animal health and animal welfare with a longer term view to developing animal production systems that are less reliant on antimicrobials. Moreover, changes in consumer preferences also influence these changes, with a steady and growing demand by consumers (albeit from a low base) for animal products that are produced from animal production systems that use "low or no antimicrobials" in their production.

b) Findings of the studies from China and Brazil

The BRIICS account for over 80% of global production of livestock and livestock products, as well as a high share of global consumption of antimicrobials. Research studies have shown that the use of antibiotics is generally higher in large livestock-producing countries, driven by several factors including the species, the size of the livestock population, and the stocking density, with the highest usage of antibiotics in countries that have the highest concentration of large scale high density pig, poultry and cattle operations. Several studies have concluded that the global use of antibiotic in food animal production would continue to rise due to growing demand, mainly from the BRIICS where food animal production continues to increase to meet consumer demands. Recent estimates of antibiotic use in livestock production suggest that China and Brazil together account for over 50% of global antibiotic use.

China¹

Globally, China is the largest producer of pork, poultry and eggs, and the third largest producer of milk products (Shen et al., 2017). Overall, the livestock sector contributes slightly less than one-third (about 28%) of gross agricultural output. For almost 50 years, antibiotics have been widely used as feed additives in livestock production. China is the largest producer and exporter of antimicrobial drugs, with exports estimated to account for about 70% of antimicrobials traded in global markets (Wu, 2018). China produces about 200 different classes of antimicrobials, although production has fallen in recent years after reaching a peak in 2011. In 2013, China exported 38% and 16% of domestically produced antimicrobials and veterinary antimicrobials, respectively. Since 2011, the amount of antibiotics consumed in human medicine has fallen, following the introduction of reforms on the use of antimicrobials in hospitals. In food animal production, policies to reduce the use of antimicrobials in production were introduced in 2014.

In China, there are no records of any cost/benefit case studies on AMU at the farm or industry levels. In the absence of farm level case studies it is difficult to make comparisons with the findings of the case studies from the European countries. However, the studies on China provide some insights into the factors driving demand for antibiotics and the regulatory and policy responses to increasing concerns on the increase in AMR.

In 2001, the Chinese Ministry of Agriculture introduced a "code for the use of antibiotics as feed additives in livestock feed". The use of antibiotics was divided into two categories; i) for the prevention of diseases and growth promotion (non-prescription); and ii) for the treatment and control of disease (for which a prescription is required). In 2013, the total usage of antimicrobials was estimated at 162 000 tonnes, of which 52% was used for animals. More specifically, almost 85 000 tonnes of antimicrobials were used in animal production, producing an estimated 85 Mt of animal products. This amounted to about 987 mg of antimicrobials per kilo of animal product, compared to 100 mg/kg of animal product in the European Union (Wu, 2018).

Government regulations on antimicrobial use in animal production is the responsibility of the food safety system in China. The Food Safety Law came into force in 2009 and was further revised and updated in 2015. The system is co-ordinated by the Chinese Food and Drug Administration (CFDA) and implemented by several ministries, including the Ministry of Agriculture (MoA), the Ministry of Health (MoH), and the General Administration of Quality Supervision Inspection and Quarantine (AQSIQ). In the MoA, the Veterinary Bureau is responsible for the administration of all policies related to veterinary medicines.

In 2015, the MoA introduced a national five-year plan to manage the use of veterinary medicines in animal production and to phase out the use of certain antibiotics such as norfloxacin, pefloxacin and ofloxacin in food animals. Moreover, in 2016 the MoA phased out the use of colistin sulfate for growth promotion. The National Action Plan (2016-2020) was implemented in 2016 and its main aim is to contain the growth in AMR. In March 2017, the MoA introduced the "National Campaign to curb the rise in antimicrobial

¹ This section draws on the background paper prepared by Dr. Z. Wu, "Antibiotic use and antibiotic resistance in food producing animals in China (OECD Food, Agriculture and Fisheries Paper N°133).

resistance in bacteria of animal origin (2017-2020)". This campaign has focussed on the gradual removal of antibiotics for growth promotion in animal production.

Several additional policy measures have been introduced to deal with concerns related to the threat from AMR. First, a National Plan was introduced in 2009 to monitor the drug tolerance of animal-origin bacteria, and, in 2013 the national surveillance system became operational. Second, in 2014 a prescription system was introduced and 11 classes of antimicrobials, considered to be HPCIA in human health, were classified as prescribed medicines. Third, the antimicrobial use policy was further tightened with the implementation of two National Action Plans in 2015 and in 2016. In the Five-Year National Action Plan of Comprehensive Management for Veterinary Medicine (Antimicrobials) (2015-19), the consolidation of production and use of antimicrobials was a high priority.

More specifically, the MoA has phased out eight veterinary drugs that were widely used for growth promotion in food animal production. Specifically, in 2015 the MoA phased out four antimicrobial drugs – *lomefloxacine*, *pefloxacine*, *ofloxacin* and *norfloxacin* – from use in animal feed, and in 2017 colistin sulphate was phased out as a feed additive to promote animal growth. The MoA is currently reviewing the use of *olaquindox*, *phenalgin* and *roxarsone* in animal feed based on risk assessment. Further proposals are under discussion to further phase out the use of antibiotics for growth promotion by classifying antimicrobials into three categories: non-restrictive, restrictive and special use only drugs. In practice, only antibiotics that have been proven to be safe, effective and show low levels of antimicrobial resistance will be classified as non-restrictive. Finally, the MoA introduced in December 2017 new maximum use levels of zinc as a feed additive in pig production: 110 mg/kg for piglets and an overall limit of 1 600 mg/kg over the lifecycle of the animal.

In the 2017-20 Action Plan, the MoA set the following policy targets for 2020:

- Reduce antimicrobial use by 50% in animal production
- Reduce antibacterial use by phasing out antimicrobial drugs for growth promotion that are HPCIA for human health and those with greatest potential of cross transmission of AMR
- Develop new veterinary drugs and withdraw the high risk drugs that are currently used in animal production
- Improve the monitoring of antimicrobial use and AMR via enhancing technical standards and networking
- Educate users and veterinarians on the correct scientific use of antimicrobial drugs.

The relatively high use of antibiotics in food animal production in China is believed to be partly related to production conditions and partly to the continued use of antimicrobials as growth promoters. Often, small farms are associated with poor animal sanitary conditions. On many medium and large animal farms the management of intensive livestock systems is weak. Therefore, antimicrobials are frequently used as a type of insurance to prevent animal diseases and to offset the effects of overcrowding and poor sanitation in pig and poultry production. The situation is further complicated as antimicrobials are widely perceived as an important contributor to enhancing animal growth. At this juncture, only 14 antimicrobials can be used in animal feed for growth promotion. AGPs are estimated to account for 60%-70% of all antimicrobials used in animal production in China (Wu, 2018).

There are no official statistics available on antimicrobial use by individual species in China. However, based on market surveys of antimicrobial use in animal production, the breakdown is estimated at 62% in the pig sector, 23% in the poultry sector, and the remaining 15% for other animals. In pig production, antimicrobials are used as pre-mixes by feed manufacturers and on farms as AGPs or to prevent and treat animal diseases. In the case of poultry production, experts estimate that antibiotics are over-used by 60%-90% (Wu, 2018). Moreover, the over-use of antibiotics can be 2-3 times or more than the recommended dosage due to the widespread perception of the poor quality of domestically-produced veterinary drugs.

Reliable information on the costs of antibiotics in food animal production is difficult to ascertain in China. For several decades, antibiotics have been used as AGPs in animal feed either by feed manufacturers or by livestock farmers who prepare their feed on the farm. In addition, antibiotics have been used as an important veterinary medicine in preventing and treating animal diseases. More specifically, antimicrobial

costs account for 70% to 80% of total veterinary medicine costs in livestock production. On average, this amounts to an additional cost of CNY 20 per tonne of pig feed, and CNY 15-20 per tonne of poultry feed. In terms of veterinary medicine costs per head, on average, they amounted to CNY 19 for pigs, CNY 1.5 for broilers, CNY 1.9 for hatched chicken and CNY 193 for dairy cows.

In terms of total production costs for pigs and broilers, the most important cost is feed, while labour costs have been low and are now estimated at close to 10%. As regards antimicrobial costs, while the nominal cost per head has increased, their share of total costs has fallen from 2% to 1.4% in pig production and 3.3% in broiler production over the period 2010-2016. Of the two main uses (therapeutic and growth promotion), antimicrobial feed use accounted for 23% and 42% of total antimicrobial costs for pig and broiler production, respectively.

Moreover, the cost per animal of veterinary medicines can vary substantially by farm size as shown in Table 2. For example, the costs on pig farms tend to increase as the scale expands, while on broiler farms the overall trend is unclear. More specifically, the cost was higher on medium-sized broiler farms than it as on the small- or large-sized farms.

	Year	Average	Small size	Medium size	Large size
Pigs (per head)	2011	18.86	16.55	17.75	22.28
	2012	18.97	16.83	17.68	22.39
	2013	19.55	17.29	18.43	22.93
	2014	19.88	16.94	17.87	24.83
	2015	19.26	17.12	18.13	22.54
Broilers (per 100 birds)	2011	82.34	81.62	84.11	81.29
	2012	76.07	59.48	83.04	85.69
	2013	81.25	76.32	84.73	82.71
	2014	72.78	67.72	76.27	74.36
	2015	28.43	21.72	37.18	32.38

Table 2. Medicinal costs on pig and broiler farms in China (CNY)

Note: For both the pig and broiler sectors, small, medium and large sizes in the table are classified by number of animals. They are, respectively, 30-100, 100-1 000 and >1 000 head for the pig sector and 300-1 000, 1 000-10 000 and >10 000 head for the broiler sector

Brazil²

Brazil is one of the largest producers and exporters of poultry, beef and pig meat globally. In 2017, exports of meat and meat products exceeded USD 15 bn, of which, poultry meat accounted for slightly less than half (about 46%), with beef exports accounting for a further USD 6 bn., and pork a further USD 1.6 bn. In 2017, the value of poultry meat and beef exports increased by 5.5% and 13.7%, respectively, but the value of pork exports fell by about 5%.

The animal production system varies substantially between species and region, ranging from fully integrated systems to co-operatives and independent farms. In terms of poultry production, over 90% of production is based on fully integrated production systems and are mainly concentrated in southern Brazil. Cattle production is concentrated in the midwest where the majority of farms are based on extensive pasture systems involving low inputs (technologies), and consequently low cost systems. In recent years, however, there has been a trend to more intensive high density systems and these now account for about 13% of total production. The profile of pig production is more complex and varies substantially by region. For example, the larger farms (> 1 000 sows) are located in the midwest with the majority of production in fully integrated systems. The medium-sized producers (up to 500 sows) are concentrated in the south, with production through co-operative-type systems or fully integrated along the chain. Lastly, small scale

² This section draws on the background paper prepared by Professor Marisa Cardos (OECD Food, Agriculture and Fisheries Paper N°134, 2019).

independent producers (< 200 breeding sows) are located in the southeast and northeast regions with production mainly for local markets.

Production is largely based on highly integrated animal production chain structures with strict internal and external biosecurity measures for each stage of production. Within this closely integrated system the use of antibiotics is closely monitored. Compared to EU countries, the restrictions on the use of antibiotics in food animal production are limited and antibiotics are widely used in production, including the use for growth promotion due to their perceived economic benefits.

Antibiotics are used in animal production for therapeutic, prophylactic and metaphylactic purposes, as well as for growth promotion. In Brazil, only 13 antimicrobials can be used in animal feed for growth promotion and the species are specified in the regulations. Official data on the volume of antimicrobials use are not published in Brazil, but sale volumes are available from the National Union of Animal Health Products Industries. According to these data, the estimated sales of animal medicines increased by about one-third between 2013 and 2017, while antimicrobials declined by 10% over the period (Sindan, 2018). Since 1998, Brazil has prohibited several classes of antimicrobial drugs for growth promotion in animals, namely avoparcin, amphenicols, tetracyclines, beta lactames (benzyl penicillin group, cephalosporins), quinolones, systemic sulphonamides, nitrofurans, olaquindox, carbadox, spiramycin, erythromycin and colistin.

In 2017, Brazil ratified the recommendations of the United Nations high level meeting on combating AMR (2016) and the G20 Leader's Statement on the growing threat of AMR to public health and economic growth. The use of antimicrobial drugs in feed are regulated by the Normative Instruction 65 of 2006 (MAPA, 2006) which set the procedures for the manufacture and use of veterinary medicines in animal feed. However, the use of AGPs are not covered by this regulation. On 23 October 2017, the Normative Instruction 41 was published and the National Program for Prevention and Control of Antimicrobial Resistance for Livestock and Agriculture (AgroPrevine) was established under the co-ordination of the Ministry of Agriculture and Livestock (MAPA, 2017). This program covers antimicrobial resistance in livestock and promotes awareness of the interdependence between human, animal and environmental health through better education, surveillance and monitoring.

On 16 May 2018, the National Plan of Action for the Prevention and Control of Antimicrobial Resistance in Agriculture (PAN-BR Agro) was launched, based on the "One Health" approach. The National Plan is sectorial and focuses on the promotion of responsible and prudent use of antimicrobials, and restricts the use of antimicrobials that impact human health (HPCIA) in veterinary medicine for therapeutic purposes, based on risk analyses. A number of objectives and interventions have been proposed for the promotion of the rational use of antimicrobials in animals, increased veterinary supervision and the implementation of good agricultural practices, including sanitary management practices to prevent infection and reduce the use of antibiotics. The National Plan is to be implemented over the period 2018-2022.

Information and data on the use of antimicrobials in animal production in Brazil is sparse and only a few reliable studies are currently available on this issue. Bokma et al. (2014) examined the use of antibiotics in pig and poultry production in Brazil and attempted to forecast the trends in usage for a 3-5 year period. The study was based on a series of interviews with stakeholders along the animal chain, including farmer organisations, meat production companies, feed companies, antibiotic producers, veterinary services and researchers on animal health. Overall, it found that antibiotics are generally freely available without any need for a prescription. Broiler production for export markets, the European Union in particular, is separated from the domestic market and produced without any antibiotic growth promoters. The study concluded that the use of antibiotics for therapeutic purposes in animal production is low due to generally good production conditions and lower stocking densities.

While the overall volume of antibiotics used in food animal production is not available, several surveys have been undertaken and provide some insight into the volume of use for different species. For example, Machado (2016) undertook a limited survey of pig farms and, based on this survey, he estimated the use of antimicrobials at 367.7 mg/kg of pig meat produced. Dutra (2017) estimated that pigs are exposed to antimicrobials for about two-thirds of their life. While there are no comprehensive studies on the costs of antimicrobial in pig production, the Brazilian Association of Pork Producers (ABCS) estimated the cost at about 1.5% of total production costs.

In terms of broiler chicken production, the National Centre for Advanced Research in Applied Economics (CEPEA-ESALQ/USP) estimated the cost of veterinary medicines in 2017 at 3.3% of total production costs,

of which antimicrobials represented the highest amount. As regards cattle production, the CEPEA-ESALQ/USP estimated that antimicrobials represented about 0.16% of total production costs, mainly concentrated in the more intensive high density systems (87% of beef comes from extensive production).

Several studies on the potential impact of a ban on antimicrobials in feed have been undertaken by the Animal Science Department, Federal University of Rio Grande do Sul. One of these studies by Rampi et al. (2016) involved a meta-analysis of 67 studies to estimate the economic impact of withdrawing growth promoters from pig diets. The overall results of this study indicated that withdrawing AGPs resulted in a negative impact on animal performance. More specifically, animals fed without AGPs showed a 4% increase in feed requirements compared to those receiving feed treated with AGPs. In practice, this meant that an additional 9.73 kg of feed was needed to reach the same slaughter weight of AGP-fed animals. In overall terms, this raised the feeding cost by 3.8% per animal. For the overall pig industry in Brazil, the authors estimated this could result in losses of up to BRL 277 million.

A similar meta-analysis study was undertaken by Cardinal et al. (2018) for broiler production in Brazil. A total of 150 scientific articles were analysed and the most frequent antibiotics used were identified. The study concluded that the consumption of feed did not differ between those that received AGPs in the feed and those without. The flocks that were given feed without AGPs showed a 1.9% lower weight gain and a 3.6% increase in feed compared to those that had received AGPs in the feed. The authors concluded that the withdrawal of AGPs from broiler feed could result in annual losses of up to BRL 639 million for the Brazilian broiler chicken sector.

Although surveillance of the veterinary use of antibiotics has started, it will take many years to establish a reliable and functioning reporting system. Moreover, the continued intensification in pig and poultry production with larger farms and mechanical ventilation systems has increased demand for therapeutic antibiotics in order to maintain good animal health and well-being. However, in view of the growing public health concerns and the risks associated with antibiotic use and AMR, public pressure is likely to restrain the classes of antibiotics that can be used as an additive in animal production.

Conclusions

China is the largest global producer and consumer of antibiotics. Over the last four decades there has been a surge in the use of antibiotics in livestock production driven by the rapid growth in animal production and the intensification of production. The consumption of antimicrobials in China is estimated to be at least five times higher than the average usage level in EU countries. Moreover, about 85% of consumption is in the pig and poultry sectors, and over two-thirds has been administered to enhance animal growth. Until recently, there were few regulations or policies on the use of antibiotics in the food system in China. However, over the last two decades the use of antibiotics has been more tightly monitored and regulated with specific targets aimed at reducing the use of antibiotics in animal production. Brazil is also a major producer and exporter of poultry meat, pig meat and beef, and antimicrobials are an important input in ensuring a competitive and productive animal production sector.

There are several lessons that can be drawn on antimicrobial use in China. First, the high use of antibiotics is closely related to the animal production conditions, with relatively poor hygiene and sanitary systems in many livestock production operations. As the cost of antibiotics is very low, they are often used to compensate for the poor level of management and low investment in on-farm biosecurity measures.

Second, as there have been few regulations on the use of antibiotics in animal production, producers have tended to include these drugs as an additive in livestock feed to enhance their production efficiency. By far, the bulk of antibiotic use in China has been for growth promotion with only about one-third used for treating sick animals and for preventing disease.

Third, public concern over the rise in AMR is growing in China, as there have been several recorded outbreaks of resistant pathogens in food-producing animals. In 2015, for example, colistin-resistant pathogens were recorded in pig production which were transmitted to humans, resulting in several deaths.

Fourth, the economic value of antimicrobials in animal production are perceived to exceed the short-term costs at the farm level. Antimicrobials continue to be widely used and are often perceived to provide a type of low cost "insurance" against a potential disease outbreak. On the other hand, in Brazil, the use of

antimicrobials as an additive in feed is primarily aimed at increasing animal productivity and the competitiveness of the farm operation.

The Chinese government has introduced a National Action Plan (2016) on AMR which sets out targets to lower antimicrobial use in food-producing animals, phase out the use of HPCIA for growth promotion, and limits the number of classes of antibiotics that can be used in animal production. In Brazil, the adopted Plan is sectorial for "Livestock and Agriculture", and the PAN-BR Agro is in line with the livestock recommendations of the GAP/WHO.

6. Policy options and best practices to limit the rise in AMR in foodproducing animals

The policy options and best practices outlined in this section are intended to complement the GAP recommendations to combat AMR by drawing on the cost/benefit case studies of several countries. The findings from these case studies are further developed and expanded with input from the OECD Expert Steering Group on AMR. The results of the case studies provide many interesting insights and are influenced by factors such as specific industry and country conditions, the type and degree of modernisation of farms, and the level of education and management skills of farmers.

It should be noted that these case studies provide a useful snapshot of the situation on the farm at a point in time (usually one production cycle), but that these studies should be repeated over a number of years for a more comprehensive understanding of the economic and technical impacts on production. Nevertheless, the economic insights that can be drawn can provide better targeting of policies to influence farmer behaviour to a more optimal use of antimicrobials and more sustainable animal production systems.

Many countries have made good progress in their strategies to reduce the need for antibiotics in animal production without adversely affecting animal productivity and profitability, animal health and animal welfare standards. For example, the evidence from countries such as Sweden, Belgium, Denmark, the Netherlands and Germany suggest that these objectives can be achieved with modest changes to their existing animal production systems. While the risks associated with antimicrobial resistance are global, the solutions tend to be more specific to each country, the production system and animal species. From the research to date, it is clear that there is no one size fits all situations, but that potential solutions need to adopt an integrated multidisciplinary and multi-sectoral approach, bearing in mind that this is a long-term challenge to develop sustainable solutions to combat the increase in AMR.

The lessons learned, best practices and policy options that can be drawn from these studies focus primarily on the economic dimension associated with antimicrobial use in animal production and are discussed below.

1. Enhance the availability of information on the economic benefits and costs of antimicrobials in food-producing animals

A better understanding by farmers and veterinarians of the economic optimal level of antibiotic use in animal production is critical in modern animal production systems. The outcome of the case studies indicated that the economic benefits from antimicrobials in feed are significantly lower than those experienced in the 1970s and 1980s. In many cases, farmers are not always fully aware of the limited economic benefits that modern livestock farming can get from the systematic use of antimicrobials in feed. In some countries, the high volume of antimicrobial use in livestock production is a legacy of past practices, which continue due to the perceived benefits from their use in production, especially where management and sanitary practices are below optimum.

However, in less modern animal production facilities, the study suggests that the economic benefits from the use of antibiotics can be substantial. In many of these cases it would appear that antibiotics may be "substituting" for weak management, poor nutrition, and weak or non-existent biosecurity measures on the farm. Moreover, in countries with many small- and medium-sized producers, animal feed is often purchased from external feed mills and farmers may not always be aware that antimicrobials are in the feed.

To reach the optimal economic level of antimicrobial input in animal production the following areas need to be addressed:

- Provide specific training and better information on the economic impact of antimicrobials in the production system to the key stakeholders, especially farmers and veterinarians.
- Provide examples of "best practice" in terms of optimal level of use on animal farms from research in other countries and from other animal enterprises.
- Improve the diagnostic tests of animal diseases in order to optimise the use of preventative and affordable veterinary medication, as well as information on the antimicrobial classes best suited to control the disease.
- This study evaluates the short-term static costs and benefits of antimicrobials in animal production. However, similar studies would need to be undertaken over a longer period of time and farm types to provide farmers with the necessary economic information to adequately access the real value of antimicrobials in animal production.

2. Improve the availability of information and knowledge on alternative interventions, as well as the relative costs and benefits of these interventions

There is a range of alternative technologies to antibiotics that can be used in food animal production to prevent a disease outbreak. Animal production systems usually involve the use of many different technologies to enhance the overall results in dealing with disease. In some circumstances these technologies may have some offsetting effects in terms of disease control on the farm. This section outlines several alternative interventions that are currently available to farmers, but seldom used.

Research suggests that combining different preventive interventions are often used to substitute for antibiotics in the production system, depending on their availability and relative cost. The most frequent alternative interventions used are vaccines, but new technologies are available. These have been summarised by the OIE (2016) and include:

- Gene-encoded natural antibiotics including host-derived antimicrobial peptides such as defensins and cathelicidins
- Prebiotic and probiotics
- Bacteriophages
- Recombinant synthesized enzymes such as phytases and carbohydrates
- Phytogenic feed additives.

The alternatives to antibiotics in livestock production were also discussed at the 2nd International Symposium on Alternatives to Antibiotics (ATA): Challenges and Solutions in Animal Production, organised by the United States Department of Agriculture Research Service, with support from the OIE and held at the OIE Headquarters in Paris in December 2016.

Studies also reveal that some pig producers have resorted to using zinc oxide to prevent certain diseases in their herds. While zinc oxide has proven to be successful in some cases, in many countries there are concerns over the possible adverse environmental effects. In some countries the use of zinc oxide has been banned for use in animal production. For respiratory diseases in farm animals, vaccines are still the most commonly used alternative intervention. For example, farmers in Denmark and the Netherlands have at once increased their use of vaccines in pig production, while reducing their use of antimicrobials.

A major drawback of vaccines is that they may not be accessible in all countries at a competitive price to existing antimicrobials and this may have hindered their uptake. In addition, experts have noted that exports of animals and animal products could potentially be restricted from certain markets if certain vaccines are used in production. In terms of the newer technologies, some of these are still being evaluated for their economic and technical performance on the farm.

3. Need for flexible regulations to facilitate adjustment at farm level

Many OECD countries have taken a regulatory approach to reducing the use of antibiotics as growth promoters in animal production and have seen a dramatic reduction in the overall use of antibiotics in production. For example, the European Union introduced a ban on the use of antibiotics for animal growth promotion in 2006 and this has contributed to a significant reduction in antibiotic use since that time. Other countries, however, have taken a voluntary approach where the decision on antimicrobial use is left to the individual farmer or to the industry. In some of these countries, the use of antibiotics has increased over the last decade. Overall, the studies show that the most effective approach to optimising the use of antibiotics involve finding the right combination of regulations and producer-driven initiatives.

Studies also show that moving toward an optimal economic level of antibiotic use requires several conditions on the farm, including good disease diagnostics, good monitoring of antibiotics use, and strict limits on the use of certain types of molecules that are classified as the highest priority or last resort antibiotics. In cases where intervention has been targeted at the species level, this has resulted in improved farmer compliance with regulations and in better animal health and animal well-being. In some countries, recent surveys have shown that sales of a broad spectrum of antibiotics are declining, while the use of a narrow spectrum antibiotics have tended to rise.

In adopting a regulatory-type approach to nudging producers to more sustainable levels of antimicrobial use, this may involve a number of elements including:

- The existence of quality veterinary services and legislation
- Good co-operation and understanding of the regulations by all stakeholders supported by appropriate enforcement, adequate expertise, and a well-functioning surveillance system
- Certain molecules that are the highest priority critically important for human health should be the highest priority for countries to abolish growth promoters in animal production
- Access to alternative interventions at a reasonable price.

4. Optimise the mix of management and biosecurity measures on the farm

Economic optimisation of animal production usually involves a range of activities such as animal breeding, feeding, housing and management that are combined to ensure good animal health and welfare, and efficient production. The studies show that measures that improve the general health status of the herd also tend to lower the need for antibiotics. While veterinary costs (medicines and advice) are generally not a large share of production costs on most farms, they can be substantial for some farms types in some circumstances. The case studies show that one of the most important items in animal production is the need to improve the internal and external biosecurity on many farms. This a critical element to reducing the incidence of disease and the need for preventative actions involving the use of antimicrobials. Other measures may also involve greater attention to the correct stocking density, the adoption of an all-in and all-out system, good housing and climate, as well as appropriate hygiene controls on humans and vehicles entering and leaving the farm.

Breeding animals for higher resistance, better nutrition and better overall herd management on the farm are also important. For example, in 1986 when Sweden changed its animal production system with the phasing out of antibiotics for growth promotion, no adverse clinical effects were reported in the production of poultry or beef cattle. There was no apparent economic impact on the financial returns on livestock farms as this change was accompanied by additional efforts to improve animal health, nutrition, hygiene standards, and the management of the farms.

Overall, the studies show that the economic impact of reducing the use of antibiotics in animal production can be positive in most modern production systems. However, these results depend on farm type, species and existing standards of management and biosecurity on the farm. These results could be applicable to similar animal production systems and livestock enterprises in different countries. While the package of disease preventative measures may vary from country to country, several elements are critical in all situations:

- Good internal and external biosecurity on the farm
- Increase the natural immunity of animals by improving animal housing, nutrition and the stocking density on the farm.
- Improve overall farm management.

5. The need to take an inter-sectoral or "One Health" approach to combat negative externalities arising from AMR

While this report focusses on farm-level case studies to develop a snapshot of the economic impact of antibiotic use in the production of food animals, it does not examine the medium- to long-term negative spill-over effects on human health and the environment. The Global Action Plan advocates the adoption of a "One Health" approach to combat adverse long-term externalities on public health. In practice, the use of antibiotics in animal production contributes to a rise in antibiotic resistance, and the increase in resistant pathogens can pose serious human, social and economic risks to public health and well-being, animal health and well-being and environmental health. The scientific evidence on the linkages and causal pathways between the emergence and spread of resistant bacteria between animals and humans, and *vice versa*, has made good progress in providing insights into this problem. On livestock farms, the transmission of resistant bacteria to food-producing animals can result in economic losses and raise concerns on disease management strategies on the farms. Much work has been done to estimate the economic burden of human health care due to the rise in antimicrobial resistance, and many of the lessons learned can be applied to animal production.

There has been good co-operation and co-ordination in many countries amongst all stakeholders, including government ministries, industry, the food industry, veterinarians and farmers. However, in other countries there is considerable scope for improving co-operation to deal with the global challenge from the increase in AMR. Finding pragmatic and sustainable solutions to this challenge requires a concerted effort to further improve coherence and the sharing of knowledge and experiences amongst all public and private stakeholders at the national and international levels.

Annex A. Expert Steering Group (ESG) on AMR in Food Producing Animals

Professor Jonathan Rushton

Professor of Animal Health and Food Systems, Economics Institute of Infection and Global Health, University of Liverpool, N8 Research Partnership, Adjunct Professor Institute of Rural Futures University of New England, Armidale, Australia

Dr. Diana Viske Animal Health Analyst Swedish Board of Agriculture Jonkoping, Sweden

Dr. Stacy Sneeringer Research Economist Structure, Technology, & Productivity Branch Resource & Rural Economics Division Economic Research Service, USDA, United States

Dr. Elisabeth Erlacher-Vindel Head of the Antimicrobial Resistance and Veterinary Products Department World Animal Health Organisation (OIE) 2 rue de Prony 75017, Paris, France

Prof. Jeroen Dewulf Professor in Veterinary Epidemiology Ghent University Bruges, Belgium

Dr. Daniela Battaglia Antimicrobial Resistance Working Group FAO, Rome, Italy

Dr. Michele Cecchini Principal Administrator (AMR), Public Health Division Directorate for Employment, Labour and Social Affairs ELS), OECD

Dr. Michael M. Ryan Senior Agricultural Policy Analyst, Agriculture and Trade Division Trade and Agriculture Directorate (TAD), OECD

References

- Aarestrup, F.M., Jensen, V.F., Embourg, H.D., Jacobsen, E., and Wegener, H.C. (2010). Changes in the use of antimicrobials and the effects on productivity of swine farms in Denmark". *American Journal of Veterinary Research*, 2010, 71(7):726–733.
- Backhans, A., Sjolund, M., Lindberg, A., and U. Emanuelson. (2016). "Antimicrobial use in Swedish farrow-to-finish pig herds is related to farmer characteristics". *Porcine Health Management. BioMed Central.* The Open Access Publisher.
- Black WD. "The use of antimicrobial drugs in agriculture. Canadian Journal of Physiology and Pharmacology, 1984, 62:1044–1048.
- Bondt, N. and H. Kortstee. "Good Practices: Use of Antibiotics". 2016 L.E.I., Wageningen UR, Netherlands."<u>https://www.government.nl/topics/antibiotic-resistance/documents/reports/2016/01/27/good-practices-use-of-antibiotics</u>.
- Bokma, M., Bondt, N., Neijenhuis, F., Mevius, D., and Stephanie Ruiter. 2014. "Antibiotic use in Brazilian broiler and pig production: an indication and forecast of trends. *Report No 714.* Wageningen UR Livestock Research, LEI, Netherlands.
- Cardinal, K.M. *et al.* " Simulação doimpacto produtivo da retirada de antibióticos promotores de crescimento da ração de frangos de corte' . In: Conferencia FACTA-WPSA Brasil. Campinas May 16th to 17th 2018.
- Cecchini M, et al. (2015). "Antimicrobial resistance in G7 countries and beyond: Economic Issues, Policies and Options for Action". Paris: OECD Publishing, 2015.
- Codex Alimentarius (2011). "Guidleines for Risk Analysis of Foodborne Antimicrobial Resistance", Rome, Italy.
- Collineau, L., et al. (2017) "Herd–specific interventions to reduce antimicrobial usage in pig production without jeopardising technical and economic performance". *Preventive Veterinary Medicine* 144 (2017) 167-178.
- Cordoso, M., (2019), "Antimicrobial use, resistance and economic benefits and costs to livestock producers in Brazil". *OECD Food, Agriculture and Fisheries Paper* N°132, OECD, Paris.
- Cui D, et al. "Use of and microbial resistance to antibiotics in China: A path to reducing antimicrobial resistance". *Journal of International Medical Research*. 2017:0300060516686230.
- Davis, M.F., Price, L.B., Meng-Hsin Liu, C. and E.K. Silbergeld, 2011. "An ecological perspective on U.S. industrial poultry production: the role of anthropogenic ecosystems on the emergence of drug-resistant bacteria from agricultural environments". *Current Opinion in Microbiology*. 14(3):244–250.
- Dijkhuizen, A.A., Huirne, R.B., and A.W. Jalvingh (1995), "Economic Analysis of Animal Diseases and their Control". Wageningen Agricultural University, Wageningen, Netherlands.
- Dutra, M C. 2017. "Uso de antimicrobianos na suincultura no Brasil: Análise crítica e impacto sobe marcadores epidemiológicos de resistência". Tese (Doutorado em Ciências), Faculdade de Medicina Veterinária e Zootecnia Universidade de São Paulo, São Paulo, 2017. <u>http://www.teses.usp.br/teses/disponiveis/10/10134/tdehttp://www.teses.usp.br/teses/disponiveis/10/10134/t</u>
- ECDC 2009. Joint opinion on antimicrobial resistance (AMR) focused on zoonotic infections. Scientific Opinion of the European Centre for Disease Prevention and Control; Scientific Opinion of the Panel on Biological Hazards; Opinion of the Committee for Medicinal Products for Veterinary Use; Scientific Opinion of the Scientific Committee on Emerging and Newly Identified Health Risks". *EFSA Journal, 2009, 7*(11):1372.
- European Medicines Agency (2016 "Sales of veterinary antimicrobial agents in 29 European countries in 2014". European Surveillance of Veterinary Antimicrobial Consumption, 2016. (EMA/61769/2016).
- Federal Office of Public Health and Federal Food Safety and Veterinary Office (2016 "Usage of Antibiotics and Occurrence of Antibiotic Resistance in Bacteria from Humans and Animals in Switzerland". Swiss Antibiotic Resistance Report 2016. November 2016. Bern.
- FAO/OIE/WHO 2003 Joint Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific Assessment: Geneva, 1–5 December 2003.
- FAO (2016). The FAO Action Plan on Antimicrobial Resistance 2016-2020. FAO, Rome.
- FAO (2016). Drivers, Dynamics and Epidemiology of Antimicrobial Resistance in Animal Production. FAO, Rome.

- FAO/OIE/WHO. Joint Expert Workshop on Non-Human Antimicrobial Usage and Antimicrobial Resistance: Scientific Assessment: Geneva, 1–5 December 2003. Geneva, World Health Organization, 2004 (http://www.who.int/foodsafety/publications/micro/en/amr.pdf).
- Harrison, S.R. and Tisdell, J.G. (1995). "The Role of Animal Health programs in Economic Development". Paper presented at the third conference of the International Institute for Development Studies. Helsinki, Finland.
- Harrison, S.R. (1996). "Cost Benefit analysis with applications to animal Health Programmes: Basics of CBA". Working Paper No. 18. The University of Australia, Brisbane, Australia.
- Hennessy, D.A., J. Roosen and H.H. Jensen (2005), "Infectious disease, productivity, and scale in open and closed animal production systems", *American Journal of Agricultural Economics*, Vol.87, pp. 900-917.
- Hoelzer, K., Wong, N., Thomas, J., Talkington, K., Jungman, E. and A. Coukell (2017). "Antimicrobial drug use in food- producing animals and associated human health risks: what, and how strong, is the evidence?". BMC Veterinary Research (2017) 13:211. The Pew Charitable Trusts, Washington, DC 20004.
- Huang X, Yu L, Chen X, Zhi C, Yao X, Liu Y, et al. 'High Prevalence of Colistin Resistance and mcr-1 Gene in Escherichia coli Isolated from Food Animals in China". *Frontiers in Microbiology*. 2017 2017-April-04;8(562).
- Hu Y, Cheng H. "Use of veterinary antimicrobials in China and efforts to improve their rational use". *Journal of Global Antimicrobial Resistance*. 2015;3(2):144-6.
- Huijsdens XW, van Dijke BJ, Spalburg E, van Santen-Verheuvel MG, Heck MEOC, Pluister GN, et al. "Communityacquired MRSA and pig-farming". Ann Clin Microbiol Antimicrob [Internet]. 2006;5:26. <u>http://www.ncbi.nlm.nih.gov/pubmed/17096847</u>
- LandersT.F., Cohen, B., Wittum, T.E., Larson, E.L. (2012). "A review of Antibiotic Use in Food animals: Perspective, Policy and Potential". *Public Health Reports*, 2012; 127 pp 4-22
- Laxminarayan, R., Matsoso, P., Plant, S., Brower, C., Rottingen, J.A., Klugman, K., Davies, S. (2015). "Access to Effective Antimicrobials: A Worldwide Challenge". *Lancet 387:* 168-75.
- Machado, G. 2016. "Futuro dos sistemas de produção de suínos no Brasil'. In PorkExpo 2016. http://aveworld.com.br/relatorio/fad485567025dbc6960bf3890c934a30.pdf .
- MAPA (2018). Ministério da Agricultura Pecuária e Abastecimento. Notícias. <u>http://www.agricultura.gov.br/noticias/superavit-de-us-81-86-bilhoes-</u> <u>dohttp://www.agricultura.gov.br/noticias/superavit-de-us-81-86-bilhoes-do-agronegocio-foi-o-segundo-maior-</u> <u>da-historia</u>.
- MAPA (2018). Ministério da Agricultura Pecuária e Abastecimento. 2018b. Notícias. <u>http://www.agricultura.gov.br/assuntos/insumos-</u> <u>agropecuarios/insumoshttp://www.agricultura.gov.br/assuntos/insumos-agropecuarios/insumos-</u> <u>pecuarios/arquivos-de-insumos-pecuarios/Substnciasproibidas.pdf</u>.
- MAPA. Resultado PNCRC 2016 . <u>http://www.agricultura.gov.br/assuntos/inspecao/produtos-animal/plano-de-nacionalhttp://www.agricultura.gov.br/assuntos/inspecao/produtos-animal/plano-de-nacional-decontrole-de-residuos-e-contaminantes/documentos-da-pncrc/resultados-pncrc2016-englishversion.pdf/view.</u>
- MAPA Instrução Normativa 65, de 21 de novembro de 2006. <u>http://www.agricultura.gov.br/assuntos/insumoshttp://www.agricultura.gov.br/assuntos/insumos-agropecuarios/insumos-pecuarios/alimentacao-animal/arquivos-alimentacaoanimal/legislacao/INSTRUONORMATIVAN65.2006.pdf</u> Acessed on August 9th 2018.
- MAPA, Ministério da Agricultura Pecuária e Abastecimento. Instrução Normativa 41, de 23 de utubro de 2017.
- http://www.lex.com.br/legis 27542328 INSTRUCAO NORMATIVA N 41 DE 23 DE OUTUBRO DE 20 17.aspx.
- MAPA. Ministério da Agricultura Pecuária e Abastecimento. 2018. PAN-BR Agro. <u>http://www.agricultura.gov.br/assuntos/insumos-</u> <u>agropecuarios/insumoshttp://www.agricultura.gov.br/assuntos/insumos-agropecuarios/insumos-</u> <u>pecuarios/programas-especiais/resistencia-antimicrobianos/pan-br-agro.</u>
- Ministry of Agriculture. Bureau of Veterinary, Ministry of Agriculture PRC. 2009中国动物卫生状况报告 (Animal health In China): 中国农业出版社; 2011.

Morel, C., (2019). "Transmission of antimicrobial resistance between animal agriculture and humans", OECD Food, Agriculture and Fisheries Paper N°134, OECD, Paris, France, 2019.

OIE (2016). Report of the 2nd International Symposium on Alternatives to Antibiotics. OIE, Paris, France.

- OIE (2018). List of Antimicrobial Agents of Veterinary Importance. OIE, Paris, France. <u>http://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_OIE_List_antimicrobials_Ma_y2018.pdf</u>.
- OIE (2016). The OIE Strategy on Antimicrobial Resistance and the Prudent Use of Antimicrobials. OIE, Paris, France.
- OIE (2017). Annual Report on the Use of Antimicrobial Agents in Animals: Better Understanding of the Global Situation. OIE, Paris, France.
- OECD (2015). "An Overview of Work on AMR and Preliminary Scenario Analysis". Paper presented to the Workshop on the Economics of Antimicrobial use in the Livestock Sector and Developments of Antimicrobial Resistance. OECD, Paris.
- OECD (2017). Producer Incentives in Livestock Disease Management: A Synthesis of Conceptual and Empirical Studies. Draft Report, OECD, Paris.
- OECD (2018). OECD-FAO Agricultural Outlook 2018-2027, OECD Publishing, Paris,
- OECD (2016). "Antimicrobial resistance Policy Insights". Paris: OECD Publishing, Paris, France.
- O'Neill, J. (2016). "Tackling Drug-Resistant Infections Globally: Final Report and Recommendations". *The Review on Antimicrobial Resistance*". Wellcome Trust, HM Government, London.
- O'Neill, J. (2015). "Agriculture and the Environment: Reducing Unnecessary Use and Waste. *The Review on Antimicrobial Resistance*. Wellcome Trust, HM Government, London.
- Postma, M., Vanderhaeghen, W., Sarrazin, S., Maes, D., and J. Dewulf. "Reducing Antimicrobial Usage in Pig Production without jeopardizing Production Parameters". *Journal of Zoonoses and Public Health*, 2016.
- Pruden, A. et al. (2013). "Management Options for Reducing the Release of Antibiotics and Antibiotic Resistance Genes to the Environment". Environmental Health Perspectives 121:878–
- Rampi, J.Z. *et al.* Simulação do impacto econômico da retirada dos antibióticos promotores de crescimento na suinocultura brasileira. In: PorkExpo 2016. Curitiba October18th to 20th 2016. Proceedings.
- Rojo-Gimeno, C., Postma, M., Dewulf, J., Hogeveen, H., Lauwers, L. and E. Wauters. "Farm-Economic Analysis of Reducing Antimicrobial use whilst Adopting Improved Management Strategies on Farrow-to-Finish Pig Farms". *Journal of Preventive Veterinary Medicine 129*, 2016.
- Rushton, J. (2013). "An Overview Analysis of Costs and benefits of Government Control Policy Options". In proceedings of *Livestock Disease Policies: Building Bridges between Science and Economics*. International Workshop held in OECD, Paris, France, 3-4 June 2013, Pages 39-51.
- Rushton, J., J. Pinto Ferreira and K.D. Stark (2014), "Antimicrobial Resistance: The Use of Antimicrobials in the Livestock Sector", OECD Food, Agriculture and Fisheries Papers No 68, OECD Publishing.
- Rushton, J. (2015). "Antimicrobial use in animals: How to Assess the Trade-Offs". *Zoonoses and Public Health* 62, 10-21.
- Sinden, J.A. and Thampapillai, D.J. (1995). Introduction to Cost-Benefit Analysis, Longman, Melbourne.
- Sindan. Sindicato Nacional da Indústria de Produtos para Saúde Animal. 2018. Estatísticas. Available at: http://www.sindan.org.br/.
- Sneeringer, S., J. MacDonald, N. Key, W. McBride and K. Mathews, "Economics of Antibiotic Use in U.S. Livestock Production", ERS-200, U.S. Department of Agriculture, Economic Research Service, Washington, November.
- Swedres/Svarm (2016). "Consumption of antibiotics and occurrence of antibiotic resistance in Sweden". Public Health Agency of Sweden and the National Veterinary Institute. Uppsala.
- Tang, K..L., Caffrey, N.P., Nobrega, D.B., Cork, S.C., Ronksley, P.E., Barkema, H.W., Polachek, A.J., Ganshorn, H., Sharma, N., Kellner, J.D. and William A Ghali (2017). "Restricting the use of antibiotics in food-producing animals and its associations with antibiotic resistance in food-producing animals and human beings: a systematic review and meta-analysis". *Lancet Planet Health* 2017. http://dx.doi.org/10.1016/S2542-5196 (17)30141-9.

Teillant, S., Laxminarayan, R. (2015). "Economics of Antibiotic Use in US Swine and Poultry Production". *The Magazine of Food, Farm and Resource Issues*. 1st Quarter, 2015.

UNEP(2017), "Antimicrobial Resistance: Investigating the Environmental Dimension". UNEP, Nairobi.

- Van Boeckel T.P., Browser C, Gilbert M., Levin S.A., and T.P. Robinson (2015). "Global Trends in Antimicrobial Use in Food Animals". Proc National Academy of Science, 5 May 112(18): pp. 5649-54.
- Van Boeckel T.P., Glennon E.E., Chen D., Gilbert M., Robinson, T.P., Grenfell, B.T., Levin, S.A., Bonhoeffer, S., and Ramanan Laxminarayan (2017). "Reducing Antimicrobial Use in Food Animals" Science/AAAS -- Insights, 29 September 2017, Vol 357 Issue 6358, Washington D.C.
- World Bank (2016). "Drug-Resistant Infections: A Threat to Our Economic Future. Part VI. Antimicrobial Use in Animals and AMR, pp 65—78", Washington, DC.
- Wu Z. (2017). "Balancing food security and AMR: a review of economic literature on antimicrobial use in food animal production". *China Agri Econ Rev.* 2017;9(1):14-31
- Wu, Z., (2019). "Antibiotic use and antibiotic resistance in food producing animals in China", OECD Food, Agriculture and Fisheries Paper N°133, OECD, Paris, France, 2019.
- WHO (2015). "Antimicrobial Resistance: Global Report on Surveillance", Geneva.
- WHO (2015). "Global Action Plan on Antimicrobial Resistance", Geneva.
- WHO (2001). "Global Strategy for Containment of Antimicrobial Resistance", Geneva.
- WHO (2003). "Impacts of antimicrobial growth promoter termination in Denmark". The WHO international review panel's evaluation of the termination of the use of antimicrobial growth promoters in Denmark. Geneva.
- Xiao Y. (2017). "A National Action Plan to Contain Antimicrobial Resistance in China: Contents, Actions and Expectations". *AMR Control.*
- Zhang Q-Q, Ying G-G, Pan C-G, Liu Y-S, Zhao J-L. (2015) "A comprehensive evaluation of antibiotics emission and fate in the river basins of China: Source analysis, multimedia modelling, and linkage to bacterial resistance". *Environmental Science & Technology.* 2015;49(11):6772-82.