Organisation for Economic Co-operation and Development

TAD/CA/APM/WP(2018)19/FINAL

Unclassified

English - Or. English

6 May 2019

TRADE AND AGRICULTURE DIRECTORATE
COMMITTEE FOR AGRICULTURE

Cancels & replaces the same document of 21 March 2019

Working Party on Agricultural Policies and Markets

Antibiotic Use and Antibiotic Resistance in Food Producing Animals in China

13-15 November 2018
OECD Conference Centre, Paris

This paper is a revised version of document TAD/CA/APM/WP(2018)19/REV1, prepared by Dr. Ziping Wu, which was discussed at the 75th session of the Working Party on Agricultural Policies and Markets held on 13-15 November 2018. Delegations agreed to declassify that document, under the responsibility of the Secretary General. The intention is to publish this paper in the Agriculture, Food and Fisheries paper series.

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JT03447106

Note by the Secretariat

The paper TAD/CA/APM/WP(2018)19/REV1 was prepared by Dr. Ziping Wu, Agri-Food and Biosciences Institute (AFBI), Queens University, Belfast, Northern Ireland. This document provides information on the current use of antimicrobials in animal production and changes in policies to deal with the rise in AMR in China. The Secretariat has revised and updated the paper based on comments received at the APM and written submissions from delegations [TAD/CA/APM/WP(2018)19/REV2].

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Acronyms

ACA: Acetic Acid

AGP: Antimicrobial growth promoter

AMR: Antimicrobial resistance

ARGs: Antimicrobial resistance genes

CHINET: Chinese national surveillance network for AMR

CPFX: Ciprofloxacin

FAO: Food and Agricultural Organisation, United Nation

FMD: Foot and mouth disease

HPAI: High pathogenic avian influenza

HPS: Hantavirus pulmonary syndrome

MERS: Middle east respiratory syndrome

MoA: Ministry of Agriculture, China

MRLs: Maximum residue levels

NCDR: National Commission for Development and Reforms, China

OIE: World Animal Health Organisation

PCU: Population Correction Unit

PRRS: Porcine reproductive and respiration syndrome

RMB: Ren Min Bi Chinese currency unit

Antibiotic Use and Antibiotic Resistance in Food Producing Animals in China[1]

Dr. Ziping Wu

Executive Summary

China is an important player in international markets for animal products, antibiotics, and in global efforts to combat antibiotic resistance (AMR). As a key measure to ensure food security, over half of all antibiotics used annually are for food animal production in China. This paper reviews the use of antibiotics and the emergence of AMR in Chinese food animal production. With rapid growth in food, animal production, relatively poor animal production conditions and increasing production intensity, has resulted in an increase in antibiotic use in China in both absolute and relative terms over the past four decades. This increasing trend, however, has been deterred by recent government policies and improvements in public awareness of AMR. Four key government policies including; the maximum residue level monitoring and control, permitted lists, proper use of the withdrawal period, and prescription only use have been introduced to reduce antibiotic use in animal production to combat the rise in AMR. Among the key measures, antibiotic classification and prescription policies may have played an important role in reducing antibiotic use in animal production in recent years. Antibiotic use in China, as measured in terms of mg/PCU, is more than 5 times higher than the international average. One of the main reasons for the relative higher usage is the widespread misuse associated with growth promotion in the feed and veterinary use on farms. The high veterinary usage is also partly related to shortage in veterinarian support and guidance at farm level. As in many other countries, antibiotics are mainly used in pig and broiler production in China. The cost of antibiotics are estimated at only 1.4-3.3% of total production costs in Chinese pig and broiler production; therefore, its potential insurance return is very high and difficult to find suitable substitutes. A combination of economic and regulatory approaches will be needed to control antibiotic use in China. Further research will be needed to clarify a policy baseline at national and farm level, and evaluating existing policy instruments in controlling antibiotic use in China. In combating AMR, not only the reduction of antibiotic use, but also the transmission of AMR pathogens in animals, humans and the environment needs to be considered. Control of post antibiotic use in soils and waterways in China are also critical elements in the policy framework.

[1] This document was prepared by Dr. Ziping Wu, Agri-Food and Biosciences Institute (AFBI), Queens University, Belfast, UK BT7 3LQ. Sincere appreciation to Prof. Guanguo Ying of the Chinese Academy of Sciences for his kind advice and Prof. Hongbin Xiao for providing part of the data used in this study.

1. Introduction

1. Antimicrobials have been used as sub therapeutic growth promoters (AGP) in animal feed, as well as to prevent and treat animal diseases in livestock production in China. Zhang *et al.* [1] estimated that China consumed over 84 200 tonnes of antimicrobials in food animal production in 2013, which suggests that China may be the largest consumer of antimicrobials in animal production in the world.

2. The widespread use of antimicrobials and the associated negative impact of AMR on human and animal health, and the environment, have become a major concern in China. As a key government policy, the Chinese Government in August 2016 unveiled its National Action Plan to combat AMR. The Action Plan aims to reduce antimicrobial use, including antimicrobials used in animal production. Moreover, the Government pledged to mobilize its administrative efforts including developing new antimicrobials, allowing sales of antimicrobials only by prescription, setting up a surveillance system, and improving training and education of farmers and veterinarians [2].

3. The misuse of antimicrobials in animal production and cross transmission of AMR pathogens between animals and humans have been a focus of discussion with respect to antimicrobial use in animal production. The discovery of AMR to colistin in food animals in 2015, the last resort antimicrobial reserved for human use, has now reached global attention [3].

4. This paper provides a brief outline of antimicrobial use in China and emerging AMR issues in food animal production. In Section 2, Chinese food animal production is discussed. It is followed by a review of antimicrobial use in food animal production and reports on some AMR cases in Sections 3 and 4.

2. Food animal production in China

5. Animal husbandry is one of the key agricultural sectors in China. In 2016, China produced 85.4 million tonnes of meat, including 53 million tonnes of pork and 18.9 million tonnes of poultry meat, 36 million tonnes of milk and 30.9 million tonnes of eggs. Between 1980 and 2015, meat, milk and egg production in China increased annually by 5.8%, 10% and 7.2%, respectively, compared to cereal production, which only increased by 1.9% annually. Globally, China has become the largest producer of almost all major agricultural products, except milk. In 2013, China accounted for 28% of global meat production including, 48% of pork and 17% of poultry meat in the world. At the same time, it's per capita meat consumption was 25% more than in Japan, and energy intake was about 10% above the international average [4]. In China, the growth rates in poultry meat, beef and lamb production have exceeded that of pork production. As a result, the proportion of pork production has fallen from over 80% of total meat production in the 1980s, to about 60% in recent years. In 2016, pork production accounted for 62% of total meat produced, followed by poultry meat (22%), beef (8%) and sheepmeat (5%)[5].

2.1. Animal production and structural change

6. The growth of animal production in China over the last four decades has been attributed to changes in both demand and supply. On the demand side, an increase in household income and rapid urbanisation was closely associated with a rapid increase in demand for meat

and dairy products. On the supply side, the growth was related to the adoption of modern animal production technologies; including improvements in genetics and feeding and changes in production structures [6].

7. The growth in animal production has also been linked to the development of commercial large-scale production. This is different from the crop sector, where farm expansion is largely constrained by the land tenure system. The livestock sector has undergone rapid structural change in China over the last two decades. This is clearly reflected by changes in the number of farms involved in animal production and the rapid increase in the proportion of large and medium sized livestock farms over the last 20 years. In the pork sector, the proportion of pig farms that slaughtered 50 or more pigs accounted for 13.6% of total slaughtered in 1996; this increased to 27.2% in 2002, 65% in 2011 and 70.8% in 2014. In the broiler sector, farms that slaughtered 50k or more chickens accounted for 21.6% of total national chickens slaughtered in 2007, and the proportion increased to 44.7% in 2014, while the contribution of small producers (less than 2 000) has fallen from around 20% to 14% [7].

8. Table 1 shows the herd/flock size and farm structures of pig and broiler producers in 2014. More specifically, small pig producers (slaughtered less than 50 pigs per annum) and small broiler producers (<50k chickens per annum) accounted for 95% and 98.1% of total pig and broiler farms, respectively. These farms, however, only produced 29.2% of pigs and 14.3% of chickens slaughtered, while large-scale farms (those producing 500 or more pigs a year or 50k chickens) contributed 41.8% and 42.3% of slaughtered pigs and chickens, respectively.

Table 1. Pig and broiler production structure in China in 2014

Pig farms			**Broiler farms**		
Size (heads)	**% of total slaughtered**	**% of total farms**	**Size (heads)**	**% of total slaughtered**	**% of total farms**
1-49	29.2	94.7	**<2k**	14.3	98.1
50-100	11	3.2	**2-10k**	12.4	1.2
100-500	18	1.636	**10-50k**	28.6	0.6
500-1k	11.9	0.3537	**50-100k**	12.9	0.096
1-3k	10.8	0.1342	**100-500k**	12.6	0.031
3-5k	5.1	0.0276	**500k-1m**	5.6	0.004
5-10k	4.9	0.0147	**>1m**	13.6	0.003
10-50k	7.1	0.0091			
>50k	2	0.0005			
Total number of farms		49,538,409			22,065,408

Source: China Livestock Production and Veterinary Service Yearbook, 2016

9. Growth of meat production, particularly pork and poultry meat, has slowed down in recent years. One reason for the slowdown is related to the country's relatively high level of

meat consumption. According to FAO Nutrition Statistics, although the prevalence of malnutrition in China is still high at 9.7% of the population in 2014-16, the average Chinese energy intake was already 3 108 kcal/capita/ day which is about 30% above the adequacy level, and its protein intakes reached 98g/capita/day in 2013. The daily consumption level is already higher than in Japan, where intake is estimated at 2 726 kcal/capita/day energy supply and 86.6 g/ capita / day protein in 2013. In particular, meat consumption per capita was about 20% higher than in Japan. As a result, 10.8% of men and 14.9% of women in China are now classified as overweighed or obese[4] and the focus of consumers is now changing towards higher quality food and food safety issues.

10. The slowdown has also been affected by other economic factors and environmental concerns. On the economic side, production has been squeezed by relatively high prices for inputs such as animal feed, which has been higher in China in recent years due to a combination of government support policies, rising labour costs, and relative low product prices. For example, the average nominal cost of pig production has increased from 3.13 yuan/kg in 1991 to 14.16 yuan in 2015, and now exceed the production costs in the USA, Denmark and several other EU countries [8]. As regards the environmentally, concerns over pollution caused by animal waste have led to the closure of many pig and poultry farms in city suburbs and major animal production regions in 2017[2]. The introduction of the Environmental Protection Tax from 1st January 2018 on animal farms above 50 cattle, 500 pigs or 5000 birds (slaughtered per year) will further add to the cost of production.

2.2. Progressive improvement in animal health

11. Improvement in animal health has also contributed to the growth in food animal production in China. Animal health management in China is mainly carried out internally (on farm) by farm operators, and externally (outside of farms) by the government administration system. Prior to the 1980s, animal production (except for large draught animals such as cattle, which were usually raised by the former collectives for power on farms), has always been carried out by farm households in their backyards as a subsidiary sector. After the implementation of the household responsibility system in the late 1970s and early 1980s, animals were produced by farm households and specialised companies/animal farms. As discussed above, animal production has become more specialised and the farm size has expanded dramatically over the last 20 years. The upscaling of animal production required many changes including the need for better farm management and biosecurity, especially in terms of animal health and productivity. A key aspect of the animal management system is to manage the increased risks to domestic production from international animal diseases.

12. To meet these two challenges, China has established a new Government animal health administration system with 300,000 staff and 73,000 veterinarians involved in veterinary drug administration, animal health supervision and surveillance, research and technical support, and inspection and quarantine institutions related to international trade of agricultural products from the Central Government to the township level [9]. With Government investment, the infrastructure has been significantly upgraded including disease surveillance systems, diagnosis and control. It has also made rapid progress in integrating international animal health standards into national regulations. Consequently, animal health has improved, but the accountability of the administration of the system still needs to be improved to better match the market changes[10].

[2] Some reports estimated that it result in 5%-10% production loss.

13. Zoonosis is one of the key potential transmission routes of AMR genes between animals and humans. The prevalence of major animal diseases including zoonosis in China is shown in Table 2. All major animal diseases appear to be better controlled except for HPAI and Brucellosis.

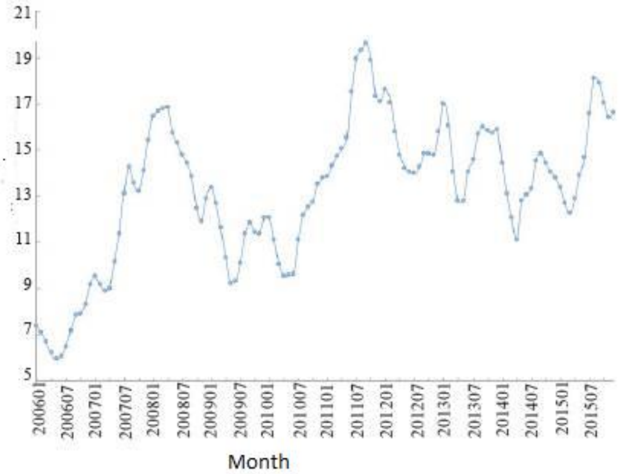
Table 2. The occurrence of major animal diseases in China in selected years: 2000-2014 (Units: head)

Year /Diseases	HPAI	FMD	Swine fever	PRRS	Newcastle Disease	Brucellosis
2000	0	0	42121	3182	1963504	678
2003	0	0	75934	5280	1144480	662
2006	93531	836	69691	114048	1195795	2031
2009	2951	813	39277	6885	302173	4676
2012	49635	365	1048	1378	114205	81906
2014	60479	74	837	1347	14000	28735

Sources: Figures for 2000-09 are from [10] and others from [9].

14. Animal diseases have been one of the key factors affecting food animal production in China. In pig production, for example, outbreaks of porcine reproduction and respiration syndrome in 2006, and foot &mouth disease and swine fever in 2010 are regarded as the main reasons for the decline in pork production in 2006-07 and 2010-11, and the subsequent price hikes in these two periods (Fig 1)[11]. These outbreaks are likely to have affected not only pork production, but also the use of veterinary medicines including antimicrobials.

Figure 1. Monthly pork price changes in China, 2006-15 (Yuan/kg)



Source: Guo, H.W., Analysis of pig production and its development trend. Chinese Journal of Animal Science, 2017. Chinese Yearbook of Animal Husbandry and Veterinary Services (several editions).

3. The use of antibiotics in food animal production

3.1 Government regulations and antimicrobial use

15. As this relates to both animal and human health, antimicrobial use in animal production is an important part of the food safety system in China. The Chinese Food Safety Law, which came into force in 2009, and revised in 2015, is the legal basis of the system. The system is coordinated by the Chinese Food and Drug Administration (CFDA) and is implemented by a number of Government Ministries. At the animal production stage, the Ministry of Agriculture (MoA) mainly manages it. At the food consumption stage, it is the responsibility of the Ministry of Health (MoH), and of the General Administration of Quality Supervision Inspection and Quarantine (AQSIQ), if it is related to the international trade of agriculture and food products. Therefore, almost all policies, laws, directives or orders concerning antimicrobial use in animal production originate in the MoA, or are based on MoA's involvement. In the MoA, the Bureau of Veterinary is responsible for administration of all policies related to veterinary medicines and drugs.

16. Antimicrobials have been widely used as feed additives and as a veterinary medicine to prevent and treat animal disease. At the beginning of this century, antimicrobials were treated the same as other veterinary drugs in China. At that time, as the main pressures for the veterinary drug control were from international trade and GATT/WTO negotiations and distrust in the domestic market over veterinary medicine, including antimicrobials, the focus was on the potential risks of drug residues in animal products and counterfeit drugs. The Government Policy focused on drugs, which were, banned in the importing countries, the maximum residue levels (MRLs) of veterinary drugs for agricultural products (particularly those exported) and quality control of veterinary medicine and drugs. This was reflected in the regulations on animal production use issued by the MoA and other Government Ministries in the years after 1980. It is reported that since 1999 when the residue surveillance scheme started, the surveillance network has tested veterinary drug residues of 24 classes of antimicrobials including ceftiofur, thiamphenicol and macrolides in nine different animal organs, amounting to 14000 batches annually. The failure rate of MRL level of veterinary drugs in the tests has fallen from 1.43% in 1999 to 0.11% in 2015[3].

17. With the growing concerns over the risks associated with AMR, other policy measures were gradually adopted. First, a national action plan to monitor the drug tolerance of animal-origin bacteria was initiated in 2009 and the national surveillance system became operational in 2013. Second, a prescription system was introduced and 11 classes of antimicrobials with high rates of AMR and important in human healthcare were classified as prescription only medicines in 2014. Third, the antimicrobial use policy was further tightened with the implementation of two national action plans in 2015 and 2016. In the Five Year National Action Plan of Comprehensive Management for Veterinary Medicines (Antimicrobials) (2015-19), the consolidation of production and uses of antimicrobials became the focus of the action plan.

18. Over the last three years, the MoA has banned eight veterinary drugs for use in food animal production. In 2015, the MoA announced that four antimicrobials, lomefloxacine, pefloxacine, ofloxacin, norfloxacin, were banned for use in animal feeds from 30 September

[3] See http://www.moa.gov.cn/fwllm/qgxxlb/qg/201602/t20160226_5030184.htm

2015, and colistin sulphate was banned as a feed additive on 30 April 2017[4]. More recently, the MoA announced that consultation on phasing out the use of olaquindox, phenalgin and roxarsone from May 2019, based on risk assessment, and that another consultation on managing veterinary use of antimicrobials by class was completed in 2017[5]. The consultation document also proposed a new way of managing clinical antimicrobial use: all antimicrobials are classified into three categories (non-restrictive, restrictive and special use only) and only those proved safe, effective and showing a low level of antimicrobial resistance will be non-restrictive. On December 15, 2017, the MoA announced a new maximum use level of zinc as a feed additive for pig production for piglets (110mg/kg), and over the whole life of the pig (1600mg/kg)[6].

19. In the follow up action plan for 2017-20, the MoA clarified the policy targets to be reached by 2020, including:

- to halve antimicrobial use in animal production by prescription;
- to reduce antibacterial use through the phasing out of antimicrobials that are important for human healthcare and those with potential of cross transmission of AMR and antimicrobials used as AGPs;
- to optimize the variety structure of antimicrobials, to develop and apply 100 or more safe and effective new veterinary drugs while withdrawing 100 high risk drugs, and to maintain the pass rate of veterinary drugs above 97%;
- to improve the monitoring system of antimicrobial use and AMR via enhancing technical standards and networking; and,
- to educate users and veterinarians on the scientific use of antimicrobials.

20. All these new measures and announcements suggest that China is following the WHO/OIE recommended list of critically important antimicrobials and is more closely integrated with the global consensus on fighting AMR.

21. In summary, antimicrobial use in animal production in China has been restricted in five main ways. First, based on risk assessment, the use of some antimicrobials was totally withdrawn and banned in animal production and for the treatment of animals. Second, only selected antimicrobials can be added as animal feed additives. Out of the two main categories of antimicrobials used in animal production (i.e. antimicrobials (8 classes and 56 drugs) and antimicrobial compounds (3 classes and 45 drugs)), including β-lactam, aminoglycosides, tetracyclines, sulphonamide, quinolones etc. only 14 antimicrobials and compounds can be added to animal feed as AGPs[7]. For example, in the category of macrolides, which includes kitasamycin, tylosin, spiramycin, erythromycin and oleandomycin, kitasamycin is the only antibiotic approved by the Chinese government for use as feed additives. Thirdly, to reduce MRL and risks to humans and the environment, those permitted veterinary drugs are required to have withdrawal periods prior to slaughter. Fourth, prescriptions are required for some veterinary antimicrobials that are important for animal and human health. Finally, there are

[4] No 2428, MoA Announcement, July 26, 2016

[5] In Jan 11, 2018, MOA announced that the consultation completed and three veterinary drugs will be banned as planned (No 2638, MoA Announcement)

[6] No 2625, MoA Announcement, Dec. 15, 2017

[7] With the implementation of MoA Announcement 2638, only 11 antimicrobials and compounds are allowed.

MRLs for some veterinary drugs in animal products and national standards in testing MRLs[8]. The detailed information for these measures is available from the following websites.

a) Antimicrobials banned in feed and veterinary use (http://kss.zgdwbj.com/?p=198)
b) Drugs allowed to be used in animal feeds (http://www.moa.gov.cn/fwllm/qgxxlb/qg/201602/t20160226_5030184.htm)
c) Regulation on withdrawn period of veterinary drugs (http://www.moa.gov.cn/zwllm/nybz/200803/t20080304_1028652.htm)
d) Antimicrobials require prescription for animal use (http://www.moa.gov.cn/fwllm/zxbs/xzxk/spyj/201706/t20170606_5662448.htm) and
e) MRLs of veterinary drugs in animal products (http://www.moa.gov.cn/zwllm/tzgg/gg/200302/t20030226_59300.htm)

The main Government regulations on antimicrobial use in China are listed in Table 3.

[8] Four types of MRLs for veterinary drugs are available in China: (1) for 88 veterinary drugs, no MRLs are required, (2) for 94 drugs, tests of MRLs are needed, (3) for 9 drugs, no residue is allowed and (4) 31 drugs including clenbuterol are banned.

Table 3. List of main regulations on antimicrobial uses in animal production

Tittle of Regulation	Main Contents	Office Issued
Guideline for Veterinary Drugs Used as Feed Additives (2001)	Use rules for 33 as AGPs and 24 as veterinary additives, first issues in 1994, amended in 1997 and 2001	MoA, No 168
http://www.foodmate.net/law/qita/163454.html		
List of Veterinary Drugs and Chemical Compounds Forbidden in Feeds and Water (2002)	Banned 21 classes of drugs including Chloramphenicol	MoA, No 193
http://www.moa.gov.cn/zwllm/tzgg/gg/201104/t20110422_1976324.htm		
Guideline for Maximum Residue Levels of Veterinary Dugs in Animal Originated Food (2002)	MRLs of different veterinary drugs for different food	MoA, No 235
http://www.moa.gov.cn/zwllm/tzgg/gg/200302/t20030226_59300.htm		
Regulation on withdrawn periods of veterinary drugs (2003)	Withdraw periods for 202 veterinary drugs (mainly antibiotics) and those do not need withdrawn period	MoA, No 278
http://www.moa.gov.cn/zwllm/nybz/200803/t20080304_1028652.htm		
List of Permitted Feed Additives (2003)	191 permitted additives. Early version issued in 1999 ceased its use	MoA, No 318
http://www.moa.gov.cn/zwllm/tzgg/gg/200401/t20040109_154399.htm		
Regulations on Administration of Veterinary Drugs (2004)	Rules to research, produce, market, trade, use and management of veterinary drugs	State Council, No 404
http://www.lawinfochina.com/display.aspx?lib=law&id=3524&CGid=		
Monitoring Plan on Drug Tolerance of Animal-Origin Bacteria (2009)	Sampling and testing for drug products commonly used on animals and likely to be abused	MoA Vet No22
http://www.syj.moa.gov.cn/fagui/201006/t20100606_1535658.htm		
Guideline for Managing Veterinary Drugs Required Prescription and Non-prescription (2014)	11 antimicrobials and its compounds including β-lactam, cephalosporins, tetracycline, etc. are listed as prescription drug	MoA, No 1997
http://www.moa.gov.cn/fwllm/zxbs/xzxk/spyj/201706/t20170606_5662448.htm		

Five Year National Action Plan of Comprehensive Management for Veterinary Medicine (Antimicrobials) (2015-19) (2015)	Close monitoring and management of production, marketing and use of antimicrobials	MoA, No 6 (quality)
http://www.moa.gov.cn/zwllm/tzgg/tz/201507/t20150723_4759838.htm		
National Action Plan for Combating AMR (2016)	Developing new drugs, monitoring AMR, responsible use, research and education	14 ministries including MoH and MoA
http://extwprlegs1.fao.org/docs/pdf/chn169656.pdf		
National Action Plan for Combating AMR from animal sources (2017-2020) (2017)	Targets and measures	MoA, Vet No N22
http://www.moa.gov.cn/govpublic/SYJ/201706/t20170623_5726086.htm		

3.2 Estimates of the total use of antimicrobials in food animal production

22. Estimating the total use of antimicrobials in animal production in China is still a major challenge. As in many countries, there are no official statistics on antimicrobial use in China. At the National Level, official data on antimicrobial production, trade, and survey data are limited (See Table 4). However, there are four figures often cited in public media and academic studies from time to time. The first figure is from Van Boeckel et al. [12]. It claims that China consumed 23% of world antimicrobial consumption in animal production in 2010, which is equivalent to 14 524 tonnes of antimicrobials in effective ingredients. The other three estimates are from Chinese sources. Zhang et al. (2015) estimated that 84 240 tonnes of antimicrobials were used in animal production in China in 2013. , and this accounted for 52% of total antimicrobials used that year[1]. The third figure frequently cited is that 97 000 tonnes, or 46.1% of total production of antimicrobials in China are used in animal production[9]. As the survey was carried out in 2007, it is believed that this figure reflected the antimicrobial use in China before 2007. The last figure is the production of veterinary antimicrobials from those manufacturers approved by the MoA in China. It is normally reported in the Yearbook of Chinese Animal Production and Veterinary Services.

23. According to the 2014 edition of the yearbook, China produced 197 000 tonnes of antimicrobials, which included 59 500 tonnes of veterinary antimicrobials in 2013[10]. The veterinary production figures were also cited by Prof. Xu, Shi-Xin, China Institute of Veterinary Drug Control (IVDC), a national authority on antimicrobial use in animal production, in an

[9] The figures are suspected to be those from a survey in 2007 as they are the same as those in [10,11]. According to my personal communication with the main author of the initial report in Zhejiang University, the source report on the estimation has never been published and the figure was leaked.

[10] The yearbook also suggested that 53000 tonnes of veterinary antimicrobials were produced and 9900 tonnes of them were exported in 2014.

interview of Famer’s Daily concerning veterinary use of antimicrobials in Feb 2016[11]. In the recent issue of the National Action Plan for Combating AMR from Animal Sources (2017-2020), the Chinese Government has urged a reduction in antimicrobial use, but no specific reduction targets have been set. This may suggest that the total antimicrobial use in animal production in China, or the baseline for the reduction is still not clear.

24. Of the four estimates discussed above, the one from Van Boeckel [12] was based on limited data in the IMS Health MIDAS database. We are not able to judge its quality as little information is available on the way it was derived in their various publications [13, 14]. The second and third figures were based on market surveys of antimicrobial manufacturers, which may be subject to sampling errors[12]. The last figure was from the official statistical reporting system but confined by the jurisdiction of the MoA in managing veterinary medicine. Due to limited information, it is difficult to provide a clear picture of antimicrobial use in animal production in China. However, as market supply and demand are broadly balanced, the existing data helps to reveal some interesting features of antimicrobial use.

a. Animal production in China may have used more antimicrobials than those reported as veterinary antimicrobials

25. China is the largest producer and exporter of antimicrobials globally and accounts for approximately 70% of antimicrobials traded on international markets. In the past, antimicrobial use was more constrained by the lack of supply, but over the last decade or so, demand side factors are mainly responsible for driving the rise in use. By the end of 2009, China had become the largest antimicrobial producer in the world with capacity to produce around 200 antimicrobial drugs. Total antimicrobial production in China has fallen in recent years after the initial increase that peaked in 2011 (Table 4). The main factors affecting production are the changes in international and domestic demand. In 2013, China exported 38% of total antimicrobials, and 16% of veterinary antimicrobials domestically produced. Chinese exports have mainly concentrated on intermediates and raw materials for final antimicrobial products and traditional (older generation) antimicrobial products. In this market, China has faced strong competition from India on exports of 7-ACA products, but still dominates the market for those antimicrobials derived from fermentation processes[15]. Human consumption of antimicrobials has being falling since 2011, and this has been attributed to the Government’s reforms in hospital antimicrobial use policy. After 2014, more concrete policies on reducing antimicrobial use in animal production came into force.

26. Antimicrobial use in animal production in China can be derived from the balance of supply and demand of antimicrobials. Taken the balance in 2013 as an example, it was officially reported that 197 000 tonnes of antimicrobials were produced, 87 698 tonnes exported and 11 836 tonnes imported. Assuming there is no inventory being kept, total domestic antimicrobial use for humans and animals in that year was 121 100 tonnes and the total use of antimicrobials from domestic produced veterinary sources was 49 800 tonnes. This leaves 71 300 tonnes (59%

[11] See http://www.moa.gov.cn/fwllm/qgxxlb/qg/201602/t20160226_5030184.htm

[12] Detailed information on the data collection and analysis for Zhang et al. (2015) is available in the paper published. Briefly, the study wasbased on database in the CFDA and IVDC and assisted by China Pharmaceutical Industry Association. A Stratified sampling process was used, sales of 237 drug manufacturers were surveyed and survey data were cross validated by the reported data. Therefore, data reported in the study is believed to be relatively accurate.

of total domestic consumption) for human consumption, and this would seem to question the survey results reported by Zhang et al. [1] that animal consumption of antimicrobials in 2013 accounted for 52% of total antimicrobials in China (antimicrobial use in animal production was estimated at 84 200 tonnes). As China has rarely imported veterinary antimicrobials[13], if the estimate of Zhang et al. [1] (reported in Table 4) are accurate, it is likely that the use of human antimicrobials in animal production in 2013 is estimated in the range 13 172 to 34 400 tonnes[14]. This suggests that a One Health approach is preferable in any analysis of antimicrobial use and policies to contain the rise in AMR.

27. There are several possible reasons for Chinese farmers to use human antimicrobials in feed and for veterinary use. First, most of the antimicrobials used for animal feed in China are those of 1^{st} and 2^{nd} generation. China is the largest producer of these types of antimicrobials in the world and they tend to be suitable for both humans and animals. Second, domestically produced antimicrobials are usually much cheaper compared to imported antimicrobials. Finally, human antimicrobials are generally regarded as having better quality control and as being more effective, and there are no restrictions on substitution. In fact, as discussed earlier, the quality of veterinary antimicrobials has been a concern of the National Authorities. Using human antimicrobials in animal production is reported in many Chinese research papers [16].

Table 4. Antimicrobial output, exports and uses in food producing animals in China (10,000 tons crude weight)

Year	Total Output	Total Domestic Use	Net Export	Veterinary antimicrobials*		
				Output	Export	Use
2007	13.4	21.0[17]				9.70[17, 18]
2008	15.4					
2009	18.2					
2010	21.8			3.18	0.65	1.45[12]§
2011	22.3			4.70	0.60	
2012	21.2			5.25	0.73	
2013	19.7		7.59	5.95	0.97	
2013[1] ‡	24.8[1]	16.2[1]	8.74[1]			8.42[1]
2014			8.03	5.30	0.99	
2015			7.68			
2016				5.47		5.04¢

Source: except those specified, total output figures are from China's Antibiotics Markets: An In-depth Analysis and Prospect 2015-2020 http://www.chyxx.com/research/201502/306230.html, which claims to be obtained from China Medical and Health Import and Export Association. Net exports are from China Customs Yearbook and * from Ministry of Agriculture.

13 Because of concerns in national biosecurity, antimicrobial imports is tightly controlled in China.

14 Zhang et al. did not report veterinary production and exports, but their figure of antimicrobial use for animal production was 84200 tonnes which is about 70% higher than the figure directly derived from statistics (i.e. 49800 tonnes). The lower bound of human antimicrobials used in animal production is calculated by assuming that 52% was used for animal use and there were no imports and inventory changes in 2013, and the higher bound is the difference between 84200 and 49800 tonnes.

Note: § figures in effective ingredients, Based on IMS Health MIDAS database. Ϯ Zhang *et al* [8] estimated that total production in 2013 in China was 248 thousand tonnes, imports and exports were 600 and 88000 tonnes, respectively. ¢ Veterinary antimicrobial sales.

b. Antimicrobial use in animal production in China increased until 2014, but has fallen in recent years

28. There is no historic data on antimicrobial use in humans and animals in China. Hu *et al.* revealed that China might have used approximately 6 000 tonnes of antimicrobials in animal production in 2001[18]. A survey carried out in 2007 indicated that China consumed 97 000 tonnes of antimicrobials, of which, 46% use was for animal production in 2006 [17]. Another survey by Zhang *et al.* estimated that 84 200 tonnes or 52% of total antimicrobial use was for animal production in 2013[1]. It appears that antimicrobial use increased significantly from 2001 to 2006, then fell in the period from 2006 to 2013. However, we believe that both the proportion and the total amount of antimicrobials used in animal production may have increased in the period between 2006 and 2013. A qualitative analysis of the main factors that affected the amount of antimicrobials used over the period are listed in Table 5.

Table 5 Factors affecting antimicrobial use in animal production in China in 2006-13

Factor	Evidence	Expected Effects on Antimicrobial Use in the period
1. Animal production:		
(1) Animal health	Improved slightly but mainly uncertainties	- / insignificant
(2) Total production	Production increased	+
(3) Production intensity	Intensity enhanced	+
2. Policy instruments		
(1) prescription	No prescription needed before 2014	insignificant
(2) drug ban	Revised a few times	insignificant
(3) permitted list	From 2003	- / insignificant
(4) withdrawn period	From 2003	- / insignificant
(5) MRLs	From 2002	- / insignificant
3. Prices	General trend of falling antimicrobial price	+
4. Other factors		
(1) AMR	Possible increase in AMR	+
(2) Technology advance	New medicine, new way uses etc. but shortage of evidence	-

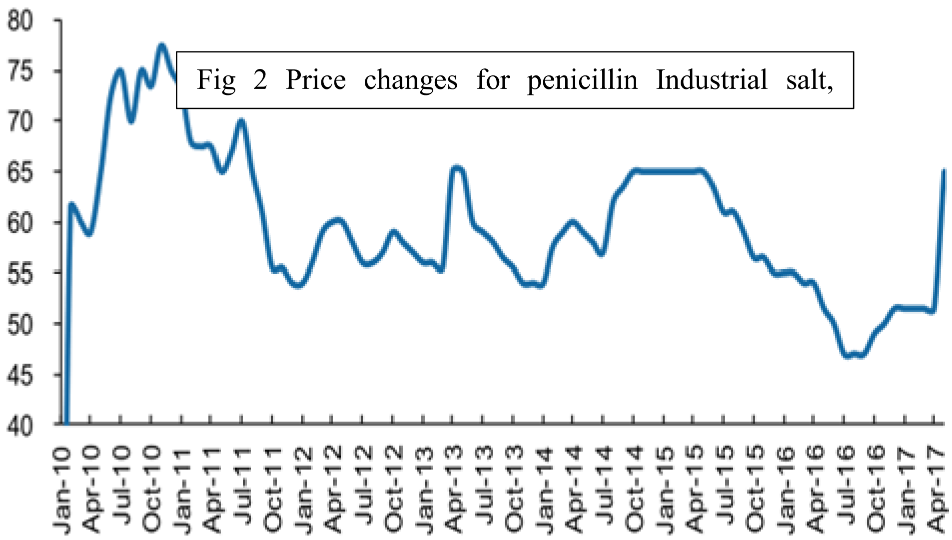
29. Four factors are likely to have affected the rise in antimicrobial use in animal production. In the period 2006-13, many of these factors potentially affecting antimicrobial use in animal production were insignificant or uncertain, while those factors increasing its use were more definitive. The three broad factors are the demand from animal producers, price and policy changes.

30. First, demand is the main factor influencing antimicrobial use. More specifically, there are two main factors in animal production driving antimicrobial use: total animal production and animal farm size. These two factors have favoured more antimicrobial use over this period.

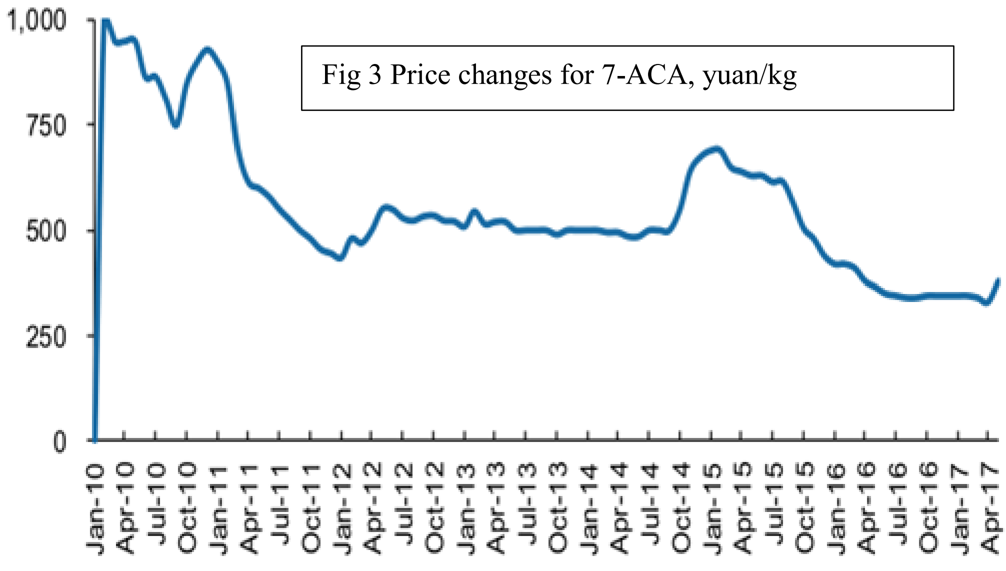
Over the period 2006 -2013, the annual production of meat, milk and eggs increased by 2.7%, 1.4% and 2.5%, respectively.

31. More importantly, the expansion in farm size accelerated during this period and antimicrobial use appears to have increased with the increase in farm size. A survey in Zhangjiajie City of Hunan province indicated that only 65% of small scale free range pig and poultry farms used antimicrobials, while all medium and large scale farms used antimicrobials in 2015 [19]. The study found that more classes of antimicrobials and quantities (per animal) were used in large farms, particularly those raising more than 10 000 pigs.

32. Second, antimicrobial prices also favour higher antimicrobial use. Although, historic price information for veterinary antimicrobial use in China is not available, Figures 2-4 illustrates nominal monthly price changes of the main intermediates/raw materials used to produce antimicrobials over the period 2010 to 2017. They indicate the downward pressure on antimicrobial prices including veterinary antimicrobials.

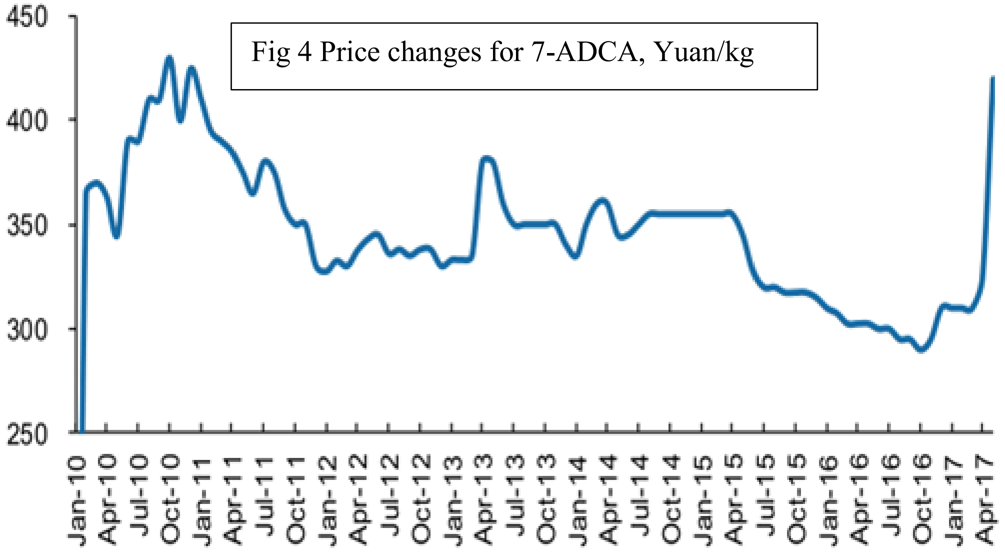


Source: adapted from the market research report (http://www.chyxx.com/industry/201708/550654.html)



Source: ibid.

Fig 4 Price changes for 7-ADCA, Yuan/kg



Source: ibid.

33. Finally, there is no clear evidence that antimicrobial use in animal production in China was restricted by Government regulations prior to 2014. The main policies used in the period 2007-13 such as permitted lists, minimum withdrawal periods and MRL levels were more concerned with the direct toxic risks of antimicrobials to humans and animals rather than on reducing antimicrobial use. Therefore, it is not expected that antimicrobial use be significantly affected by policies and regulations during this period.

34. The key AMR mitigation measure i.e. the use of prescriptions for antimicrobials in animal production was introduced in 2014, after the prescription system introduced in 2010 for human health proved successful in reducing antimicrobial use. Reforms in human antimicrobial use in 2010 separated doctor's pay from prescription drug sales, developed a system of differential drug sales and set restrictions on hospitals in terms of the number of classes of antibiotics and dosage [17]. These measures have significantly reduced antimicrobial use in the human health system. As a result, human consumption of antimicrobials has fallen gradually since 2011, after initially reaching a peak around 2010[1, 20]. While animal consumption may have peaked around 2015-16, after the prescription system had been fully adopted in animal production, the overuse of antimicrobials in animal production became an important societal concern.

3.3 Antimicrobial use in China has strong regional characteristics

35. There are big variations between different regions in antimicrobial use for humans and animals in China. It is reported that antimicrobial emission concentration in the waterways of the populous Eastern region of China was six times that of the Central and West regions. The Southern regions tend to use more antimicrobials than those in North China[1]. The main reasons for the regional differences in antimicrobial use may be partly related to the distribution of population, as the Eastern regions are more densely populated. The difference between the North and Southern regions are quite similar to the situation in Europe, where southern regions with relatively high temperatures may be more conducive to greater disease transmission so higher usage is needed.

36. In a wider perspective, the average concentration in Chinese rivers was about 303 nanograms per litre, compared with 9 nanograms in Italy, 120 nanograms in the United States, and 20 nanograms in Germany [1]. Measured in terms of antimicrobial use per person, China consumed 157 grams per person in 2013, which was 5 times more than that in the USA and UK[21]. Regarding antimicrobial use in animal production, measured in mg per Population Correction Unit (PCU), China consumed 51.5 mg/kg in 2001 and 703 mg/kg in 2007 [18].

37. The relative high usage in animal production is believed to be partly related to animal production conditions and partly to the use of antimicrobials as AGPs. As discussed earlier, small producers are still dominant in animal production in China, though more intensive and larger, scale animal farming has expanded (Table 1). These small farms are usually associated with poor animal housing and hygiene conditions. Most operators in medium and large size animal farms also tend to lack management experience for intensive livestock farming. Therefore, antimicrobials are often used as an insurance to prevent an outbreak of animal disease that are associated with overcrowding and poor sanitation in pig and poultry production. The situation is further exacerbated as antimicrobials are widely regarded as an important growth stimulant. China started its AGP use in the early 1970s. At present, 14 antimicrobials can be added to animal feed to enhance growth. It is estimated that AGP use accounts for roughly 60-70% of antimicrobials used by food producing animals in China[22, 23].

38. The high usage is also related to the misuse of antimicrobials in production. Antimicrobial misuse includes the ineffective and inappropriate use of the drugs, timing, dose and duration. In addition to the over use of antimicrobials, additional concerns relate to the use of counterfeit and substandard products, violations of the drug withdrawal time, improper use of antimicrobials when they are not needed, the use of the wrong class of antimicrobials, preference for new and highly effective drugs, long-term and continuous use. The misuse is also partly related to the fact that an incentive mechanism for proper use has not been developed[24], and partly to the absence of veterinarians' instructions and difficulties in the enforcement of regulations[25, 26]. Moreover, the number of rural veterinarians has fallen sharply in recent years as many vets chose to move into urban cities to meet the high demand emanating from the rising number of pet animals. The advisory role commonly played by the vets is increasingly taken over by the salespersons of companies that sell their products directly to the farmers.

3.4 Sectoral use of antimicrobials

39. There are no official statistics on antimicrobial use by individual species in China. A widely cited market survey of the 36 main antimicrobials used in animal production in 2014 suggested that these antimicrobials accounted for 57.2% of the national total in 2013. Of the total antimicrobials used in animal production, 62% were used in the pig sector, 23% in poultry sector and remainder 15% were used for other animals, indicating that pig and chicken sectors are the main users of antimicrobials in China (Table 6).

Table 6. Antimicrobial uses by animal species (percentage)

	Pig	Chicken	Others
Sulfonamides	50.5	35.2	14.3
Tetracyclines	66.3	23.4	10.3
Fluoroquinolones	62.6	21.9	15.5
Macrolides	63.0	22.3	14.7
β-Lactams	63.6	21.8	14.6
Others	63.2	22.2	14.6
Total	62.0	23.2	14.9

Source: [1]

40. As measured in mg/PCU, antimicrobial use by the pig and broiler sectors are much higher than in other countries and almost 5 times higher than the international average (Table 7).

Table 7. Annual antimicrobial use (mg/kg) in selected species of different countries

Country	Year	Pig	Broiler	Cattle	Multi-species average
Austria[27]	2010	26.1			62.9
Denmark[28]	2014	48	13	32	44.2
France[29]	2014	152	151	56	107
Netherlands[29]	2015	53	45	83	64.4
Sweden[30]	2014	12.3			11.5
UK[31]	2016	183	17	26	45
China	2013	545	622		

Note: Chinese figures are calculated by the author, based on Chinese statistics on animal mass production and antimicrobial usage by animal species as reported in Zhang et al (2015) and assumed no live animal trade. In poultry sector, antimicrobial use for hatched chicken in egg production period is forbidden.

Pigs

41. Antimicrobials are used as premixes by feed manufacturers and on farms as AGPs or veterinary drugs to prevent and treat animal diseases. A survey of 60 pig farms in 2007-8 in Henan province suggested that antimicrobials have been used in all stages of pig production, from weaning, to growing and fattening, by additives in animal feed, to animal drinking water and direct injection. Mixing in feed is the most popular way and almost all farms use antibiotics at the weaning stage (100% of farms). However, the use of antibiotics tend to be reduced in the pig growing cycle (Table 8). The main classes used in pig production are reported in Table 9.

Table 8. Different ways of antimicrobial use in various stages of pig production in total farm surveyed (%)

Way of Use	Weaning	Growing	Fattening
Mixed in feed	100	87	75
Added to drinking water	58	20	17
Injection	48	40	32

Source: [32]

Table 9. The top three antimicrobials used in different stages of pig production in Chinese farms

Way of Use	Weaning	Growing	Fattening
Mixed in feed	Aureomycin/penicillin (58%), bacitracin (22%), lincomycin (15%)	Tylosin (45%), Lincomycin (30%), Aureomycin (17%)	Tylosin (80%), Lincomycin (32%), Aureomycin (8%)
Added to drinking water	Tetracycline (30%), Penicillin (3%), Tiamulin (3%)	Tetracycline (10%), Penicillin (5%), Lincomycin (2%)	Tetracycline (10%), penicillin (3%), sulfadimidine (2%)
Injection	Ceftiofur (50%), Sulfamonomethoxine (30%), Florfenicol (10%)	Ceftiofur (55%), Sulfamonomethoxine (21%), Tylosin (15%)	Ceftiofur (40%), Sulfamonomethoxine (20%), Florfenicol (13%)

Source: ibid
Note: Figures in brackets are the percentage of farms that used the medicine.

Poultry

42. A survey carried out by Chen and Yue in 2012 [16] covering 25 poultry farms in Zhong Xiang county, Chongqing, suggested several issues with the use of antimicrobials on broiler farms.

- Due to constraints of education and lack of support from veterinarians, antimicrobials have been widely misused for virus prevention and treatment, long term and repeated uses of the same medicine, and by over and under dosing. It is estimated that misuse rates are as high as 60%-90% of total use. In the case of overuse, the over usage can be 2-3 times or even more than 10 times of the standard dose, partly due to perception of poor quality of veterinary drugs and partly due to the irrational marketing by manufacturers.
- Medicines banned on the MoA list such as chloramphenicol were still used by some farmers, suggesting difficulties in the enforcement of regulations.
- Human antimicrobials were used for veterinary purposes. The survey suggested that all broiler farms have used tetracycline as a feed additive and, at the same time, over 80% of farms have used gentamicin, CPFX and penicillin, which are also used in human health.
- Raw materials of veterinary medicines were used directly. Multiple antimicrobials were irrationally used in treating diseases. An analysis of 236 veterinary prescriptions suggested that antimicrobial costs accounted for 77.5% of total medical costs and over half of prescriptions have used two or more antimicrobials in which β-lactams were the most popular and quite often improperly paired with other antimicrobial such as cephalexin and penicillin, lincomycin and erythromycin (which have the same spectrum of antimicrobial coverage).
- The recommended medical withdrawal period as required by Government, regulations were not always followed.

43. Many of the problems found in this survey are believed to continue, although the situation may have improved.

4. Costs and benefits of antimicrobial use

44. Information on costs of antimicrobial use in animal production is difficult to get at the farm level. Antibiotics have been used as AGPs in animal feed by either feed manufacturers or farmers themselves. They are also used to prevent and treat animal diseases. A survey by a market research company in 2014 estimated that about 3-3.5 billion RMB yuan[15] of antimicrobials were added to animal feed, and this included 0.5 billion yuan of antimicrobials to deal with Gram negative bacteria and 2.5-3 billion yuan to deal with Gram positive bacteria. At farm level, an additional 28-30 billion yuan of veterinary medicinal costs were incurred, of which, 43% was spent in the pig sector, 33% in poultry, 13% in eggs and roughly 10% in dairy cows. Here, antimicrobial costs accounted for 70-80% of the veterinary medicinal costs. On average, about 20 yuan of antimicrobials were added to every tonne of pig feed concentrates and 15-20 yuan was added to poultry concentrates[16]. On the farm, the estimated veterinary medicine costs per head (on average) for pig, broiler, hatched chicken and dairy cows were, 19, 1.5, 1.9 and 193 yuan, respectively[22].

45. Looking at the bigger picture regarding pig and broiler production costs, the changes in antimicrobial costs on farms are shown in Tables 10 and 11.

Table 10. Changes in typical costs and income in Chinese commercial pig farms (yuan/head)

	2010	2011	2012	2013	2014	2015	2016
Income	1296.53	1913.56	1707.43	1707.25	1564.88	1809.22	2210.58
Costs	1169.71	1470.05	1587.56	1616.90	1592.14	1605.15	1809.99
(1) variable costs	90.8%	90.9%	90.0%	88.9%	88.0%	87.7%	88.8%
Feed	62.2%	55.4%	55.8%	57.5%	59.4%	56.6%	48.0%
Medical	1.5%	1.3%	1.2%	1.2%	1.2%	1.2%	1.1%
Mortality	1.0%	1.0%	0.9%	0.9%	0.8%	0.8%	0.8%
(2) labour cost	7.5%	7.7%	8.7%	9.8%	10.6%	10.9%	9.9%
Antimicrobial costs per head (yuan)							
Feed	10.00	10.08	10.21	10.32	10.48	10.58	10.79
Medical	12.86	14.15	14.23	14.66	14.91	14.45	15.16
Total	22.86	24.22	24.44	24.98	25.39	25.03	25.95
As % of total costs	2.0%	1.6%	1.5%	1.5%	1.6%	1.6%	1.4%

Source: Own calculation based on Price Dept. of NCDR (Eds.) Compilation of Costs and Revenues of Agricultural Products, various years.
Note: Antimicrobial costs per head is estimated based on feed consumption and medical costs data. It is assumed that 75% of medical costs are those for antimicrobials and 20-yuan worth of antimicrobial is added in each tonne of the pig feed concentrates.

15 As in Dec 27, 2017, one US$ = 6.56 RMB yuan

16 Antimicrobial use is banned for feeds used for milking cows and hatched chicken

Table 11. Costs, revenues, and antimicrobial costs for broiler production Yuan/100 birds

	2010	2011	2012	2013	2014	2015	2016
Income	2353.07	2592.01	2672.98	2682.90	2682.90	2716.78	2737.76
Costs	2121.11	2303.13	2492.37	2559.25	2559.25	2472.36	2442.53
(1) variable costs	92.1%	92.1%	90.8%	89.1%	89.1%	87.4%	87.2%
Feed	72.4%	69.6%	71.8%	71.1%	71.1%	69.0%	67.4%
Medical	3.4%	3.7%	3.3%	3.3%	3.3%	3.1%	3.4%
Mortality	1.6%	1.6%	1.6%	1.3%	1.3%	1.3%	1.4%
(2) labour	5.8%	6.4%	7.7%	9.2%	9.2%	10.7%	11.0%
Antimicrobial costs per 100 birds (yuan)							
Feed antibiotics	16.02	16.73	18.69	18.99	18.99	17.79	17.18
Med antibiotics	54.56	63.08	62.28	63.55	63.55	56.86	62.72
Total	70.57	79.81	80.97	82.54	82.54	74.65	79.90
As % of total costs	3.3%	3.5%	3.2%	3.2%	3.2%	3.0%	3.3%

Source: ibid.

46. Of the total costs for pig and broiler production in China, feed costs are still dominant, but the cost of labour is increasing. The share of labour costs in total costs for pig production has increased from 7.5% to around 10% between 2010 and 2016, and for broiler production, the increase was larger rising from 5.8% to 11% over the same period. As for antimicrobial costs, the nominal cost per head increased, but the share in total costs fell slightly from 2% to 1.4% in the pig sector, and remained stable at 3.3% in the broiler sector over this period. Of the two main uses, on average, antimicrobial feed use accounted for 23% and 42% of total antimicrobial costs for pig and broiler production in the period between 2010 and 2016, respectively[17].

47. Antimicrobial costs for feed and medicinal purposes accounted for a small percentage of total costs, while simply measuring its benefit by its income-cost ratio, antimicrobial use in pig and broiler production reached 33:1 and 70:1 for pigs and broilers in the period 2010-2016, respectively. The use of antimicrobials for preventing animal diseases have played an important insurance role in animal production in China, the low cost and high income-cost ratio may suggest that some economic policies such as taxing antimicrobials may have a limited effect in reducing their overall use. Furthermore, as antimicrobials used for treating animal diseases tend to have small own price and substitution elasticities, a combination of both economic and regulatory approaches may be needed to effectively reduce antimicrobial use in animal production [33].

48. The share of antimicrobial costs in pig and poultry production costs in China appears to be somewhat low compared to other countries. There are several possible reasons. First, antibiotics in China appear to be cheaper than in many developed countries. . For example, tetracycline, an important antimicrobial in the WHO/OIE list. Some types of tetracycline such as oxytetracycline are still used as AGPs in China, while in the USA it can only be used for

[17] Cost proportion between feed and veterinary antimicrobial uses may be different from its volume proportion due to different varieties and prices of antimicrobials were used. Some suggested the AGP use may account for 60-79% of total antimicrobial use in animal production by its volume / weight [21, 22].

therapeutic purposes. On 7 February 2018, the online price in China ranged from 50-200 yuan /kg, while in the USA the price ranged from 800 to 1500 yuan /kg. Second, it may be related to the different prices used in calculating the cost of antimicrobials used as feed additives and medicine in this estimation[18]. It should be noted that there are many difficulties in making these calculations. For example, should the purchase cost of antibiotics used to calculate the antibiotic feed costs also take account of costs in mixing the antibiotics with other feed components? In the treatment period, should antibiotic costs only include medicine costs or part of services provided by veterinarians? Finally, there are still big differences in defining production costs between China and developed countries.

49. Veterinary medicine costs per animal appear to be significantly different by farm size in China (Table 12). On pig farms, medicinal costs per head increase as scale expands; however, the trend on broiler farms is less clear. The cost was highest in medium size broiler farms than the other two types. It suggests that the assumption of greater intensification in production leading to more antimicrobial use may need to be further scrutinized and the links between farm size and veterinary medicine costs needs to be better understood.

Table 12. Medical costs in Chinese pig and broiler farms (yuan)

	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

Source: Price Dept. of NCDR (Eds.) Compilation of Costs and Revenues of Agricultural Products, various years.
Note: for both pig and broiler sectors, small, number of animals classifies medium and large sizes in the table. They are, respectively, 30-100, 100-1000 and >1000 heads for pig sector and 300-1000, 1000-10000 and >10000 heads for broiler sector.

[18] It was reported in 2016 Chinese Yearbook of Livestock Production and Veterinary Services that China has sold 12 billion yuan of veterinary antimicrobials in 2015. A validation of the sales by data used in this calculation suggests that both pig and broiler sectors spent 25.3 billion yuan in antimicrobials including those used for feed additives and medical costs and the pig sector costs accounted for more than 70% of 25.3 billion yuan.

5. Reported AMR cases

50. With the high usage, wide spread misuse and relatively uncontrolled environment, China has been regarded as potentially a high AMR prevalence country. The WHO AMR country situation analysis (2014) indicated that China is amongst the high AMR countries[34]

51. A large number of AMR studies in China are available, but most of these studies are focused on either the human health system, animal production system or the natural environment. Few researches have used the "One Health" concept to cover all areas of antimicrobial usage. Using a combination of market surveys and analyses of antimicrobial emissions in the Chinese river basins, Zhang et al. found a close correlation of bacterial resistance rates in hospitals and the aquatic environment. They concluded that around 58% of the antibiotics were excreted by humans and animals into the environment [1].

52. Most AMR studies focus on human health systems. China has developed a national AMR surveillance system in human health, CHINET, since 2005 [35, 36], and the Government has taken actions in controlling antimicrobial use in hospitals after 2011[37]. In animal AMR studies, however, the national surveillance system was not developed until 2013.

53. It is commonly accepted that resistant organisms originating in animals can spread to humans by multiple routes. It may spread via human contact with animals, or animal products colonised by resistant organisms, or ingested food that is incompletely cooked. For AMR from animal origins, the MoA in China, in 2013, started to operate an AMR surveillance scheme in animals and animal products in animal slaughterhouses. This scheme is based on the national animal disease surveillance network developed in the 1980s. In 2013, the scheme covered 15 animal production regions. The main bacteria monitored in the scheme include; escherichia coli (e coli), enterococcus, salmonella, MERS, campylobacter, pasteurella and HPS, and the main antimicrobials are penicillin, erythromycin, tylosin, tetracycline and vancomycin.

54. No official resistance report from the network is openly available at this time. However, some studies based on the information from the system have revealed that the resistance levels in animal-origin bacteria in China has increased. One study reported that there is an increasing trend of bacterial resistance to cefotaxime, florfenicol and mequindox from the 1980s to 2014[3]. In 2016 and 2017, the network also reported the emergence of resistance to plasmid-mediated colistin (a drug used as an AGP in animal production in China), in food-producing animals and in hospitals. Moreover, the resistance has become more significant in recent years [3, 38].

55. Jiang et al. (2011) used E coli as a bio-indicator of AMR to test 22 antimicrobials across eight antimicrobial classes on pig and poultry farms in south China. They found that E. coli isolates had very high rates of resistance to single antimicrobials such as ampicillin (99.5%), doxycycline (95.6%), tetracycline (93.4%) and also multi-AMR, most commonly to 5-6 different antimicrobials and one for all 22 antimicrobials [39]. By using serotyping, antibiotic susceptibility testing (15 anti-biotics) and pulsed-field gel electrophoresis (PFGE) technology, another study of poultry and pig farms in north China isolated Salmonella from both poultry and pig carcasses. The PFGE results suggested that Salmonella in poultry carcasses were from cross-contamination in the abattoir. Antibiotic resistance rates for 15 antimicrobials in 2012 were significantly higher than those in 2009. In 2012, 41.5% and 42.2% of Salmonella were resistant to ciprofloxacin and ceftiofur, respectively [40]. The main conclusions of this study were also confirmed by other studies carried out in this region [41]. The presence and spread of the CTX-M-27 in S. enterica serovars Typhimurium and Indiana from food-producing animals is a potential threat to public health [42].

56. The AMR organisms from animals can also spread from animal waste in an uncontrolled environment. In China, due to the absence of relevant regulations (until recently), the residue levels of a variety of veterinary antimicrobials have been consistently reported at high levels in animal waste[43]. Use of animal manures in agricultural fields is believed to be a main contributor to extended-spectrum β-lactamase-producing E coli spread in both hospitals and animals [44]. Zhu et al. (2013) identified 149 AMR pathogens in pig manure and found that the diversity and abundance of antimicrobial resistance genes (ARGs) in pig manure and soils fertilized by the manure were significantly higher in pig farms that used all major classes of antimicrobials except vancomycin, than antimicrobial free manure and soil [45][19]. Another study on animal waste also suggested that the number of ciprofloxacin resistant bacteria was significantly greater in ciprofloxacin 0.04mg/kg and 0.4 mg/kg exposure as compared with no-ciprofloxacin control and the ciprofloxacin 4 mg/kg exposure in a 2-month period, suggesting importance of using proper dosages [46].

57. The ARGs have also been found in rural surface water and fishponds that are often linked with animal waste when proper sewage treatment systems were lacking. A study of the prevalence of veterinary antibiotics and AMR to E. coli in the livestock production region of Northern China, where 12 veterinary antibiotics are often used, reported that high levels of eight antimicrobials (up to 450 ng L^{-1}) were found in the surface water system. Among different ARGs, significant correlations were found among the resistance rates of sulfamethoxazole-trimethoprim, chloromycetin and ampicillin, as well as between tetracycline and chlortetracycline, suggesting a possible cross-selection for resistance among these drugs[43]. Another study in south China of fish ponds which are mainly used in aquaculture, also found high concentrations of antibiotics and abundant ARGs including resistance genes for tetracycline, sulfonamide and plasmid-mediated quinolone, suggesting that fish ponds have served as reservoirs of both antibiotic residues and resistance genes [47].

58. AMR in animal production has changed over time. Before 2005, staphyloccus, streptococcus and E coli were the three main pathogens with high levels of resistances to selectrin, tetracyclin, kanamycin and streptomycin. There are increasing concerns on the concentration of salmonella and its multi-resistance to the key antimicrobials in animal production[23]. Additionally, some recent reports indicate that 40% of isolated Klebsiella pneumonia strains possessed high-levels of resistance to amikacin and gentamicin from dogs and cats in South China[48].

59. Although quantitative analyses of AMR and antimicrobial use is rare, the misuse of antimicrobials including the over and under dosing of animals, and using antimicrobials as feed additives are commonly regarded as the main reasons for increasing levels of AMR in food animals and the transmission of resistance to humans.

6. Summary and Conclusions

60. Although difficult to quantify, antimicrobial use in animal production is believed to be a key contributor to the growth of animal production and ensuring food security in China over the last four decades. Understanding antimicrobial use in animal production is important

[19] It is reported that in 2016 there were 2283 organic fertilizer producers with an annual production capacity of 34.8 million tonnes and about 10 million tonnes were marketed. Only one third of animal waste was treated before being spread on farmland. As of March 2017, China implemented a new national standard of testing for residues of tetracyclines in organic fertiliser (GB/T 32951-2016). It may suggest that the control of antimicrobials in organic fertiliser will be tightening soon.

not only for ensuring food security in China, but also to the global endeavours to combat AMR. First, China is the largest antimicrobial user in the world and one of the main players in the international market for antimicrobials and agricultural products. Second, the clarification of the status quo on antimicrobial use in animal production is a useful starting point to help develop a robust national policy on AMR. Furthermore, China's experience in regulating antimicrobial use in animal production may also provide useful lessons to many other developing countries.

61. In response to growing demand associated with the rapid increase in household incomes and the urbanisation process, animal production in China has adopted modern production technologies; including genetic and feeding improvements and larger farm size, resulting in unprecedented growth in the sector. It is believed that antimicrobial use in animal production has also increased with the expansion of animal production and with more intensive livestock production over the last four decades. Only in recent years, when more concrete Government measures to regulate practices were introduced and this has seen a fall in the use of antimicrobials. It is also expected that when more policy initiatives are introduced and consumers become more conscious of food safety, antimicrobial use in animal production in China will fall further.

62. China uses almost 5 times more antimicrobials compared to the international average in pig and broiler production (mg/PCU). The main reason for this is related to the misuse of antimicrobials in animal production, including AGPs, the widespread violation of government policies on antimicrobial use and misuse related to the lack of knowledge and skills in using antimicrobials. From an economic standpoint, antimicrobials are used as an insurance to keep animals safe and many farmers have tended to use more than is necessary. Therefore, government policy should be focused on reducing antimicrobial use, through gradually phasing out antimicrobials as a growth promoter, reinforcing the implementation of good policies and practices, providing sufficient technical support in diseases surveillance, diagnosis and control to ensure animal biosecurity and safety. As antimicrobial costs are relatively small (estimated at 1.3% and 2.4% of total cost for pig and broiler production in 2016), but the insurance benefits are perceived to be large. This a combination of economic and regulatory approaches may be needed.

63. In China, a key issue in reducing antimicrobial use relates to --- how to balance food security concerns and AMR risks[49]. More empirical studies are needed to understand why antimicrobial use has been at such a high level, and how to reduce the usage from this high level without adversely affecting food security.

64. Antimicrobials have been mainly used in premixes as an on-farm animal feed additive and for the prevention and treatment of animal diseases. Therefore, antimicrobials are used as an insurance to prevent diseases in response to the prevalence of certain diseases. Antimicrobial use is generally perceived as a low cost option, but having a high insurance affect in prevention an animal disease outbreak, and low own price and substitution elasticities in treating animal diseases.

65. The Chinese animal health system is in the process of upgrading its infrastructure and integrating with international governance structures, but still needs to be better suited to the changing domestic production structures and increasing risks of exotic diseases. The animal health situation has improved in China with new regulations and policies on antimicrobial use in animal production over the last two decades. Earlier, the policy did not distinguish between the administration of antimicrobials from other veterinary medicines and was mainly focused on reducing residues in animal products. However, antimicrobial use in animal production has been tightened gradually and a new antimicrobial policy emerged after 2014. Apart from residue control, the main instruments included in the new policy are: (1) an AMR surveillance system,

(2) classification of antimicrobials into non-restrictive, restrictive and special use only, (3) introduction of prescription system for different classes of antimicrobials, (4) regularly updating the lists for permitted, withdrawal and prohibited antimicrobials to be used in animal production based on risk analysis, and (5) introduction of withdrawal periods for different antimicrobials used in the late animal production period. As the quality of antimicrobial used is also relevant to AMR, quality control of veterinary antimicrobial manufacturing is also an important Government priority.

66. More research is needed to quantify antimicrobial use in animal production and develop a baseline for an appropriate reduction strategy. It is generally perceived that China uses more antimicrobials in animal production than in human health. China accounts for about half of the global antimicrobial use in animal production, although its share may have fallen in recent years. A portion of antimicrobials used in animal production were from those produced for human consumption in China. As in other countries, antimicrobials are more intensively used in pig and broiler production. The high usage is associated with their widespread misuse, including the use as AGPs. It is also related to the backyard animal production conditions, a lagging veterinary medical service system, poor level of disease diagnosis, and counterfeit and poor quality of veterinary drugs. The impact of different policies on the control of antimicrobial use needs to be further reviewed and there are more policy options such as controlling the use from the supply side, and using price premiums on the demand side.

67. AMR can emerge and can be transmitted between animals and humans via the environment in several different ways. In China, the misuse of antimicrobials is regarded as a key source of AMR, and animal manure, water systems and soil have proved to be the key mediums in the transmission of AMR from animal origin. While the reduction in antimicrobial use in animal production is a high priority, AMR transmission also needs to be addressed in developing a robust AMR policy.

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