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Antibiotic use and antibiotic resistance in food-producing animals in China

Ziping Wu



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ANTIBIOTIC USE AND ANTIBIOTIC RESISTANCE IN FOOD-PRODUCING ANIMALS IN CHINA

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The People's Republic of China is an important player in international markets for animal products, antibiotics, as well as in global efforts to combat antibiotic resistance (AMR). This paper reviews use of antibiotics and the emergence of AMR in Chinese food animal production. The rapid growth in food, animal production, and the relatively poor animal production conditions as well as increasing production intensity led to a sharp increase in antibiotic use in both absolute and relative terms. This trend, however, has been reversed by recent government policies and public awareness of AMR. Four government policies are particularly important in attempting to decrease the use of antibiotics: the imposition of maximum residue levels, establishing a list of permitted antibiotics, the proper use of antibiotics during the withdrawal period, and establishing a list of prescription-only antibiotics use in animal production. Antibiotic use in China is more than five times higher than the international average. One of the main reasons for the relative higher antibiotic usage is the widespread misuse associated with growth promotion in the feed and veterinary use on broiler and pig farms. The relatively low cost of antibiotics, estimated at 1% to 3% of production costs, encourages such excess use in livestock production, but alternatives are often not available and more costly. This paper recommends a mix of economic and regulatory approaches to control the overuse of antibiotics in livestock production and limit the rise in antimicrobial resistance.

Key words: AMR, antimicrobial

JEL Codes: Q1

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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
CNY	Yuan renmimbi
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
Mt	Million tonnes
NCDR	National Commission for Development and Reforms, China
OIE	World Organisation for Animal Health
PCU	Population Correction Unit
PRRS	Porcine reproductive and respiration syndrome

1. Introduction

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 the People's Republic of China (hereafter "China"). Zhang et al. (2015) 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.

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 unveiled in August 2016 its National Action Plan to combat AMR with the aim to reduce antimicrobial use in animal production. The government also pledged to mobilize administrative efforts to develop new antimicrobials, allowing sales of antimicrobials by prescription only, setting up a surveillance system, and to improve the training and education of farmers and veterinarians (Xiao, 2017).

The misuse of antimicrobials in animal production and the 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 colistin resistant bacteria in food animals in 2015, the last resort antimicrobial reserved for human use, is now receiving global attention (Liu et al., 2016)

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, followed by a review of antimicrobial use in food animal production and reports on several AMR cases in Sections 3 and 4.

2. Food animal production in China

Animal husbandry is a key agricultural sector in China. In 2016, the country produced 85.4 Mt of meat, including 53 Mt of pork and 18.9 Mt of poultry meat, 36 Mt of milk, and 30.9 Mt 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, it accounted for 28% of global meat production, including 48% of pork and 17% of poultry meat. 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 (FAO, 2017). 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%) (NBSC).

Animal production and structural change

Growth in animal production over the last four decades is largely the result of changes in demand and supply. On the demand side, an increase in household income and rapid urbanisation has been closely associated with the rapid increase in demand for meat and dairy products. On the supply side, growth has been related to the adoption of modern animal production technologies, including improvements in genetics and feeding and changes in production structures (Yang, 2013).

Growth in animal production has also been linked to the development of large-scale commercial production. While farm expansion in the crop sector has been constrained by the land tenure system, the livestock sector has undergone rapid structural changes. This is clearly reflected 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, 44.7% in 2014, while the contribution of small producers (less than 2 000) has fallen from around 20% to 14% (CLPVSY).

Table 1 shows the herd/flock size and farm structures of pig and broiler producers in 2014. More specifically, small pig producers (less than 50 pigs slaughtered per annum) and small broiler producers

(less than 50k chickens slaughtered per annum) accounted for 95% and 98.1% of total pig and broiler farms, respectively. These farms, however, produced only 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.

Growth of meat production, particularly pork and poultry meat, has slowed in recent years. One reason is related to China's relatively high level of meat consumption. According to FAO Nutrition Statistics, although the prevalence of malnutrition is still high at 9.7% of the population in 2014-16, the average Chinese energy intake was 3 108 kcal/capita/ day, which is about 30% above the adequacy level, and protein intake was 98g/capita/day in 2013. The daily consumption level is higher than in Japan, where intake is estimated at 2 726 kcal/capita/day energy supply and 86.6g/capita/day protein in 2013. Meat consumption per capita was about 20% higher in China than in Japan. As a result, 10.8% of men and 14.9% of women in China are classified as overweighed or obese (FAO, 2017), and the focus of consumers is now changing to higher quality food and food safety issues.

The slowdown is also 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 increased in recent years due to a combination of government support policies, rising labour costs, and relatively low product prices. For example, the average nominal cost of pig production has increased from CNY 3.13/kg in 1991 to CNY 14.16 in 2015, and now exceed production costs in the United States, Denmark, and several other EU countries (Guo, 2017). As regards the environment, concerns over pollution due to animal waste led to the closure in 2017 of many pig and poultry farms in city suburbs and major animal production regions.[1] The introduction of the Environmental Protection Tax from 1 January 2018 on animal farms above 50 cattle, 500 pigs, or 5 000 birds (slaughtered per year) will further add to the cost of production.

Progressive improvement in animal health

Improvement in animal health has also contributed to the growth in food animal production in China. Animal health management is 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 to use as power on farms), has

[1] Some reports estimated that it results in 5%-10% production loss.

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 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.

To meet these two challenges, China 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 (MoA, 2009). With government investment, the infrastructure has been significantly upgraded to include 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 accountability of the administrative system still needs to be improved to better match the market changes (Wei, 2015).

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, with the exceptions of HPAI and Brucellosis.

Table 2. The occurrence of major animal diseases in China in selected years, 2000-2014

Units: Head

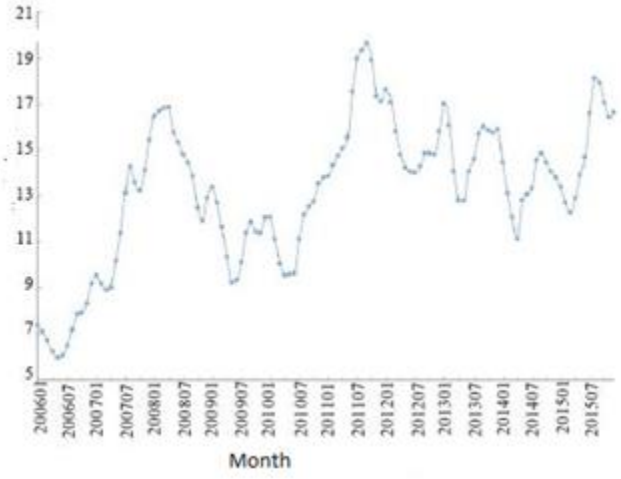
Year / disease	HPAI	FMD	Swine fever	PRRS	Newcastle disease	Brucellosis
2000	0	0	42 121	3182	1 963 504	678
2003	0	0	75 934	5280	1 144 480	662
2006	93 531	836	69 691	114 048	1 195 795	2 031
2009	2951	813	39 277	6 885	302 173	4 676
2012	49 635	365	1 048	1 378	114 205	81 906
2014	60 479	74	837	1 347	14 000	28 735

Source: Figures for 2000-09 are from Wei et al. (2015) and others from MoA (2009).

Animal diseases have been a key factor affecting food animal production in China. In pig production, for example, outbreaks of porcine reproduction and respiration syndrome in 2006, and foot and 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 during these two periods (Figure 1) (Guo et al., 2017). 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

CNY/kg



Source: Guo (2017). Chinese Yearbook of Animal Husbandry and Veterinary Services (several editions).

3. The use of antibiotics in food animal production

Government regulations and antimicrobial use

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, which is coordinated by the Chinese Food and Drug Administration (CFDA) and implemented by several government ministries. At the animal production stage, the Ministry of Agriculture (MoA) is the principal manager. 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. 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 the administration of all policies related to veterinary medicines and drugs.

Antimicrobials have been widely used as feed additives and as a veterinary medicine to prevent and treat animal disease. At the beginning of 21st century, antimicrobials were treated the same as other veterinary drugs in China. At the 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. 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 during the 1980s. 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. This amounted to 14000 batches annually. The failure rate of MRL level of veterinary drugs in the tests fell from 1.43% in 1999 to 0.11% in 2015.[2]

With growing concerns over the risks associated with AMR, other policy measures were gradually adopted. First, a national action plan to monitor drug tolerance of animal-origin bacteria was initiated in 2009 and the national surveillance system became operational in 2013. Second, a prescription system was

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

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 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 yearly action plans.

Over the last three years, the MoA has banned eight veterinary drugs for use in food animal production. In 2015, it announced that four antimicrobials – lomefloxacine, pefloxacine, ofloxacin, norfloxacin – were banned in animal feeds as of 30 September 2015, and colistin sulphate was banned as a feed additive on 30 April 2017.[3] More recently, the MoA announced that consultation on phasing out the use of olaquindox, phenalgin and roxarsone from May 2019, based on risk assessments, and that on managing veterinary use of antimicrobials by class were completed in 2017.[4] The consultation document also proposed a new way to manage clinical antimicrobial use: all antimicrobials are to be 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 would be non-restrictive. On 15 December 2017, the MoA announced a new maximum use level of zinc as a feed additive for piglets (110 mg/kg) and over the whole life of the pig (1 600mg/kg).[5]

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 by enhancing technical standards and networking.
- To educate users and veterinarians on the scientific use of antimicrobials.

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.

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 withdrawn and banned in animal production and for the treatment of animals. Second, only selected antimicrobials can be added as animal feed additives. 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, only 14 antimicrobials and compounds can be added to animal feed as AGPs.[6] 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

[3] No. 2428, MoA Announcement, 26 July 2016.

[4] On 11 January 2018, MOA announced that the consultation was completed and that three veterinary drugs would be banned (No. 2638, MoA Announcement).

[5] No. 2625, MoA Announcement, 15 December 2017.

[6] The implementation of MoA Announcement 2638 allows only 11 antimicrobials and compounds.

human health. Finally, there are MRLs for some veterinary drugs in animal products and national standards in testing MRLs.[7] Detailed information on these measures is available from the following websites.

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

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

Name of regulation	Main contents	Issuing office
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		

[7] 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.

Name of regulation	Main contents	Issuing office
Guideline for Managing Veterinary Drugs Required Prescription and Non-prescription (2014)	11 antimicrobials and its compounds including ◌ƒactam, 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		

Estimates of the total use of antimicrobials in food animal production

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 (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. (2015), which claims that China consumed 23% of world antimicrobial consumption in animal production in 2010, 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 2013, accounting for 52% of total antimicrobials used that year. The third figure frequently cited is that of 97 000 tonnes, or 46.1% of total production of antimicrobials in China.[8] As the survey was carried out in 2007, it is believed this figure reflected antimicrobial use in China before 2007. The last figure is the production of veterinary antimicrobials by manufacturers approved by the MoA and which is normally reported in the *Yearbook of Chinese Animal Production and Veterinary Services*.

According to the 2014 edition of the yearbook, China produced 197 000 tonnes of antimicrobials in 2013, which included 59 500 tonnes of veterinary antimicrobials.[9] The veterinary production figures were also cited by Professor Xu, Shi-Xin of the China Institute of Veterinary Drug Control (IVDC), a national authority on antimicrobial use in animal production, in an interview of the *Famer's Daily* in February 2016 on veterinary use of antimicrobials.[10] In a recent issue of the National Action Plan for Combating AMR from Animal Sources (2017-2020), although the Chinese government urged a decrease in antimicrobial use, no specific reduction targets were set. This may suggest that total antimicrobial use in animal production, or the baseline for the reduction, is still not clear.

[8] The figures are suspected to be those from a 2007 survey as they are the same as those in Wei (2015) and Guo 2017). According to the author's personal communication with the main author of the initial report at Zhejiang University, the source report on the estimation has never been published and the figure was leaked.

[9] The yearbook also suggested that 53 000 tonnes of veterinary antimicrobials were produced and 9 900 tonnes were exported in 2014.

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

Of the four estimates discussed above, the one from Van Boeckel appears to be estimated from the models rather than actually reported due to the data availability problem. In a later paper, they have used Zhang's estimates of the Chinese animal consumption as a baseline for the prediction of international consumption of antimicrobials in animal production (see Van Boeckel et al., 2017). The second and third figures were based on market surveys of antimicrobial manufacturers, and may be subject to sampling errors.[11] The last figure is from the official statistical reporting system but confined by the jurisdiction of the MoA in managing veterinary medicine. Due to the 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.

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

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 constrained by the lack of supply, but over the last decade or so, demand factors are mainly responsible for driving the increase in use. By the end of 2009, China had become the largest antimicrobial producer in the world with the capacity to produce around 200 antimicrobial drugs. Total antimicrobial production in China has fallen in recent years, after the increase that peaked in 2011 (Table 4), due primarily to changes in international and domestic demand. In 2013, it exported 38% of total antimicrobials and 16% of domestically-produced veterinary antimicrobials. Chinese exports have mainly concentrated on intermediates and raw materials for final antimicrobial products and traditional (older generation) antimicrobial products. In this market, it has faced strong competition from India on exports of 7-ACA products, but still dominates the market for antimicrobials derived from fermentation processes (Ltd CNPIC). Human consumption of antimicrobials has been falling since 2011, attributed to government reforms of hospital antimicrobial use policy. Since 2015, more concrete policies to reduce antimicrobial use in animal production has come into force.

Antimicrobial use in animal production in China can be derived from the balance of supply and demand of antimicrobials. Taking the balance in 2013 as an example, it was officially reported that 197 000 tonnes of antimicrobials were produced, with 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% of total domestic consumption) for human consumption, and this would seem to question the survey results reported by Zhang et al. (2015) 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,[12] if the estimate of Zhang et al. (2015) (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,[13] suggesting that a One Health approach is preferable in order to contain the rise in AMR.

There are several possible reasons why Chinese farmers use human antimicrobials in feed and veterinary use. First, most antimicrobials used for animal feed are 1st and 2nd generation. China is the world's largest producer of these types of antimicrobials, which are generally 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 passed better quality

[11] Detailed information on the data collection and analysis is available in Zhang et al. (2015). Briefly, the study was based 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. Therefore, data reported in the study is believed to be relatively accurate.

[12] Because of concerns in national biosecurity, antimicrobial imports are tightly controlled in China.

[13] Zhang et al. did not report veterinary production and exports, but their figure of antimicrobial use for animal production was 84 200 tonnes which is about 70% higher than the figure directly derived from statistics (i.e. 49 800 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 84 200 and 49 800 tonnes.

controls and to be more effective, and there are no restrictions on substitution. As discussed above, 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 (Chen and Yue, 2013).

Table 4. Antimicrobial output, exports and uses in food producing animals in China

10 000 tonnes crude weight

Year	Total output	Total domestic use	Net export	Veterinary antimicrobials*		
				Output	Export	Use
2007	13.4	21.0[2]				9.70[2, 3]
2008	15.4					
2009	18.2					
2010	21.8			3.18	0.65	1.45§ [4]
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¢

Note: § figures in effective ingredients, Based on IMS Health MIDAS database. ϯ Zhang et al. estimated that total production in 2013 in China was 248 000 tonnes, imports and exports were 600 and 88 000 tonnes, respectively. ¢ Veterinary antimicrobial sales
Source: 1. Zhang et al. (2015); 2. Hvistendahl (2012); 3. Hu (2015); 4. Van Boeckel et al. (2015); all other 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 data is obtained from the China Medical and Health Import and Export Association. Net exports are from *China Customs Yearbook* and * the from Ministry of Agriculture

Antimicrobial use in animal production in China increased up to 2015, but has since fallen

There is no historic data on antimicrobial use in humans and animals in China. Hu et al. (2015) revealed that China might have used approximately 6 000 tonnes of antimicrobials in animal production in 2001. A 2007 survey indicated that China consumed 97 000 tonnes of antimicrobials in 2006, of which, 46% was for animal production (Hvistendahl, 2012). Another survey by Zhang et al. (2015) estimated that 84 200 tonnes, or 52% of total antimicrobial use, was for animal production in 2013. It appears that antimicrobial use increased significantly from 2001 to 2006, then decreased from 2006 to 2013. However, it is possible that both the proportion and the total amount of antimicrobials used in animal production may have actually increased during this period. A qualitative analysis of the main factors that affected the amount of antimicrobials used are listed in Table 5.

Four factors are likely to have affected the increase in antimicrobial use. In the period 2006-13, many 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.

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.

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(Kimi and Dai, 2016). 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.

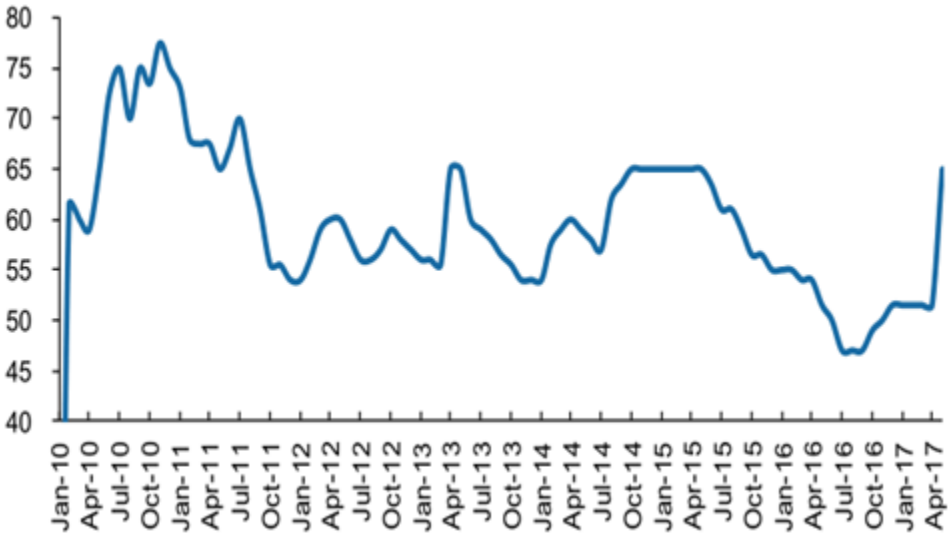
Table 5. Factors affecting antimicrobial use in animal production in China, 2006-13

Factor	Evidence	Expected effects on antimicrobial use
Animal production:		
Animal health	Improved slightly but mainly uncertainties	/ insignificant
Total production	Production increased	+
Production intensity	Intensity enhanced	+
Policy instruments		
Prescription	No prescription needed before 2014	Insignificant
Drug ban	Revised a few times	Insignificant
Permitted list	From 2003	/ insignificant
Withdrawn period	From 2003	/ insignificant
MRLs	From 2002	/ insignificant
Prices	General trend of falling antimicrobial price	+
Other factors		
AMR	Possible increase in AMR	+
Technology advance	New medicine, new way uses, etc., but shortage of evidence	-

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

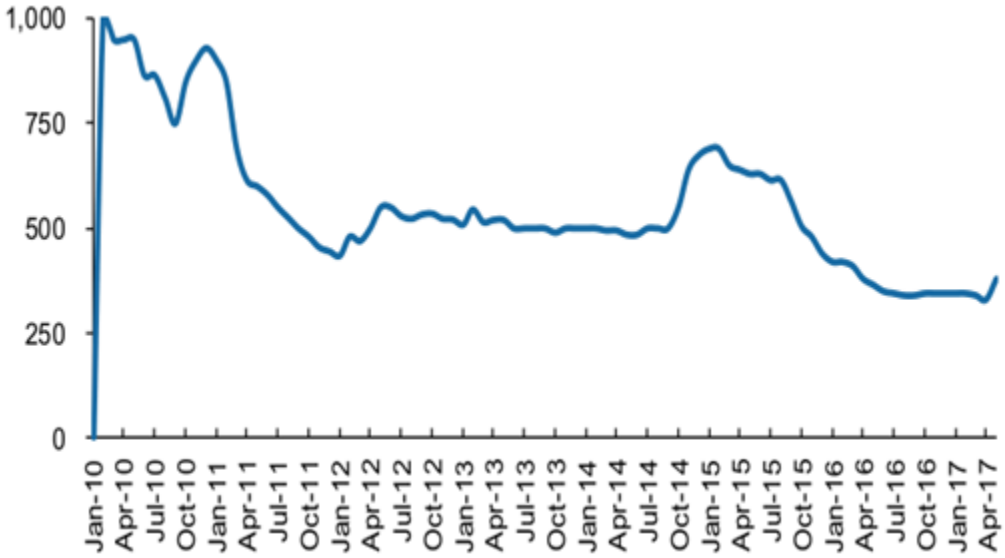
Finally, there is no clear evidence that antimicrobial use in animal production in China was restricted by government regulations prior to 2014. The main policies used in the period 2007-13 – such as permitted lists, minimum withdrawal periods and MRL levels – were more concerned with the direct toxic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

Figure 2. Price changes for penicillin Industrial salt, CYN/bou



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

Figure 3. Price changes for 7-ACA, CNY/kg



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

Figure 4. Price changes for 7-ADCA, CNY/kg



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

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 (Hvistendahl, 2012). These measures have significantly reduced antimicrobial use in the human health system, with human consumption of antimicrobials decreasing gradually since 2011, after a peak in 2010 (Zhang et al., 2015; anonymous source). While animal consumption may have peaked around 2015-16, the overuse of antimicrobials in animal production became an important societal concern with the adoption of the prescription system for antibiotic use in animal production.

Antimicrobial use in China has strong regional characteristics

There are big variations between regions in antimicrobial use for humans and animals. 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 western regions. Regions in the south tend to use more antimicrobials than those in the north (Zhang et al., 2015). 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 northern andsSouthern regions are 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.

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 (Zhang et al., 2015). Measured in terms of antimicrobial use per person, China consumed 157 grams per person in 2013, which was five times more than in the United States and the United Kingdom (Ying et al., 2017). 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 (Hu and Cheng, 2015).

The relatively 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 above, small producers continue to dominate animal production in China, though the number of more intensive and larger-scale animal farms have increased (Table 1). Small farms are usually associated with poor animal housing and hygiene conditions, and most operators of medium- and large-size animal farms tend to lack management experience for intensive livestock farming. Therefore, antimicrobials are often used as an insurance to prevent an outbreak of animal disease associated with overcrowding and poor sanitation. The situation is 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 (YUBOINFO; Wang, 2014).

The high usage is also related to the misuse of antimicrobials in production. This includes the ineffective and inappropriate use of the drugs, timing, dosage, and duration. 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, and long-term and continuous use. Misuse is also partly related to the fact that an incentive mechanism for proper use has not been developed (Cui et al., 2017), and partly to the absence of veterinarian instructions and the difficulties of enforcing regulations (Wang et al., 2016; Hu and Cheng, 2016). Moreover, the number of rural veterinarians has fallen sharply in recent years as many vets choose to move into urban cities to meet the high demand from the rising number of pet animal owners. The advisory role commonly played by the veterinarians is increasingly taken over by salespersons of companies that sell their products directly to the farmers.

Sectoral use of antimicrobials

There are no official statistics on antimicrobial use by individual species. A widely cited market survey of the 36 main antimicrobials used in animal production in 2014 suggested 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 the remaining 15% were used for other animals, indicating that the pig and chicken sectors are the main users of antimicrobials in China (Table 6).

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

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: Zhang et al. (2015).

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

Country	Year	Pig	Broiler	Cattle	Multi-species average
Austria[1]	2010	26.1			62.9
Denmark[2]	2014	48	13	32	44.2
France[3]	2014	152	151	56	107
Netherlands[3]	2015	53	45	83	64.4
Sweden[5]	2014	12.3			11.5
United Kingdom[6]	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
Sources: 1. Trauffler et al. (2014); 2. Bager et al. (2015); 3. Alliance to Save Our antibiotics (2016); 5. Hellman et al. (2016); 6. UK-VARSS (2016).

Pigs

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 were used at all stages of pig production – from weaning, to growing and fattening – by using additives in animal feed, animal drinking water, and by direct injection. Mixing in feed was the most popular method and all farms used antibiotics at the weaning stage. However, the use of antibiotics tended to decrease 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 at various stages of pig production in all farm surveyed (%)

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

Source: He et al. (2011).

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

Method 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%)

Note: Figures in brackets are the percentage of farms that used the medicine.
Source: He et al. (2011).

Poultry

A survey carried out by Chen and Yue in 2012, 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, this can be 2-3 times or even more than ten times of the standard dose, due partly to the perception of poor quality veterinary drugs and to the irrational marketing by manufacturers.
- Medicines banned by the MoA, such as chloramphenicol, were still used by some farmers, suggesting difficulties in enforcing regulations.
- Human antimicrobials were used for veterinary purposes. The survey suggested that all broiler farms had used tetracycline as a feed additive and, at the same time, over 80% of farms had 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 had 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.

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

4. Costs and benefits of antimicrobial use

Information on the costs of antimicrobial use in animal production is difficult to obtain at the farm level. Antibiotics have been used as AGPs in animal feed by feed manufacturers and/or by farmers mixing the feed on their farms. They are also used to prevent and treat animal diseases. A 2014 survey by a market research company estimated that about CYN 3-3.5 billion[14] of antimicrobials were added to animal feed; this included CNY 0.5 billion of antimicrobials to deal with Gram negative bacteria and CNY 2.5-3 billion to deal with Gram positive bacteria. At farm level, an additional CNY 28-30 billion of veterinary medicinal

[14] As in 27 December 2017, USD 1 = CNY 6.56.

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 CNY 20 of antimicrobials were added to every tonne of pig feed concentrates and CNY 15-20 was added to poultry concentrates[15]. On the farm, the estimated veterinary medicine costs per head (on average) for pig, broiler, hatched chicken, and dairy cows were CNY 19, CNY 1.5, CNY 1.9 and CNY 193, respectively.

Tables 10 and 11 present the bigger picture regarding pig and broiler production costs, and the changes in antimicrobial costs on farms.

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

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

Table 11. Costs, revenues, and antimicrobial costs for broiler production CNY/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 (CNY)							
Feed antibiotics	16.02	16.73	18.69	18.99	18.99	17.79	17.18
Medical 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: Own calculation based on Price Dept. of NCDR (Eds.) Compilation of Costs and Revenues of Agricultural Products, various years.

[15] Antimicrobial use is banned for feeds used for milking cows and hatched chicken.

Table 12. Medical costs on Chinese pig and broiler farms (CNY)

	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

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
Source: Price Dept. of NCDR (Eds.) Compilation of Costs and Revenues of Agricultural Products, various years.

Of the total costs for pig and broiler production, feed costs still dominate but the cost of labour is increasing. The share of labour costs in total costs for pig production increased from 7.5% to around 10% between 2010 and 2016; the increase was larger for broiler production, 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. Of the two main uses, on average antimicrobial feed use accounted for 23% and 42% of total antimicrobial costs for pig and broiler production, respectively, during this period.[16]

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, respectively, for the period 2010-2016. The use of antimicrobials to prevent 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 to treat 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 (Wu, 2018)

The share of antimicrobial costs in pig and poultry production costs in China appears to be 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 United States it can only be used for therapeutic purposes. On 7 February 2018, the online price in China ranged from CNY 50-200/kg, while in the United States the price ranged from CNY 800/kg to CNY 1500/kg. Secondly, different prices may be used to calculate the cost of antimicrobials used as feed additives and medicine.[17] It should be noted 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 into account the cost of mixing antibiotics with other feed components? During the treatment period, should antibiotic costs only

[16] The 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 (Ying et al., 2017; YUBOINFO).

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

include medicine costs or also services provided by veterinarians? Finally, there are still significant differences between China and developed countries on how to define production costs.

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; the trend on broiler farms, however, is less clear. The cost was highest on medium-sized broiler farms than on the other two types. This suggests that the assumption of greater intensification in production leading to more antimicrobial use may need to be further scrutinized, and that the links between farm size and veterinary medicine costs need to be better understood.

5. Reported AMR cases

With the high usage, wide-spread misuse and a relatively uncontrolled environment, China has been regarded as a potentially high risk AMR country. Indeed, the WHO AMR country situation analysis (2014) classed China amongst the high AMR countries (WHO, 2014).

Many AMR studies in China are available, but most 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. (2015) 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.

Most AMR studies focus on human health systems. Since 2005, China has developed a national AMR surveillance system on human health, called CHINET, (Hu et al., 2016; Xiao et al., 2011) and since 2012 the government has taken actions to control antimicrobial use in hospitals (Xiao, 2013). The national surveillance system for animal AMR was not developed until 2013.

It is commonly accepted that resistant organisms originating in animals can spread to humans by multiple routes. For example, 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 started to operate in 2013 an AMR surveillance scheme in animals and animal products in animal slaughterhouses 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 include; *escherichia coli* (*e coli*), *enterococcus*, *salmonella*, MERS, *campylobacter*, *pasteurella* and HPS, and the main antimicrobials are penicillin, erythromycin, tylosin, tetracycline, and vancomycin.

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 of animal-origin bacteria in China has increased. One study reported there was an increase in bacterial resistance to cefotaxime, florfenicol and mequindox from the 1980s to 2014 (Liu et al., 2016). In 2016 and 2017, the network reported the growinig resistance to plasmid-mediated colistin (a drug used as an AGP in animal production in China) in food-producing animals and in hospitals. This resistance has become more significant in recent years (Liu et al., 2016, Huang, 2017).

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 to multi-AMR, most commonly to 5-6 different antimicrobials and one for all 22 antimicrobials. 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 abattoirs. 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 (Lai et al., 2014). The main conclusions of this study were confirmed by other studies carried out in this region (Zhao et al., 2017). 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 (Zhang et al., 2016).

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 (Zhang et al., 2014). 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 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.[18] Another study on animal waste 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 two-month period, suggesting importance of using proper dosages (Huang et al., 2016).

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 Zhang et al., 2014). 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 (Xiong, 2015).

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 (Wang, 2013). 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 southern China (Xia, et al., 2017).

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

Although difficult to quantify, antimicrobial use in animal production is believed to have been a key contributor in the growth of animal production and to ensuring food security in China over the last four decades. Understanding antimicrobial use in animal production is important to not only to ensure food security in China, but to global endeavours to combat AMR. China is the largest antimicrobial user in the world and one of the main players in the international market for antimicrobials and agricultural products. 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, and China's experience in regulating antimicrobial use in animal production may provide useful lessons to other developing countries.

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

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

China uses almost five times more antimicrobials compared to the international average in pig and broiler production (mg/PCU). This is primarily due to the misuse of antimicrobials in animal production, including AGPs, the widespread violation of government policies on antimicrobial use, and misuse due 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 focus on reducing antimicrobial use by gradually phasing out antimicrobials as a growth promoter, and reinforcing the implementation of good policies and practices, providing sufficient technical support in diseases surveillance, diagnosis and control to ensure animal biosecurity and safety.

A key issue to reducing antimicrobial use relates to how to balance food security concerns and AMR risks (Wu, 2017). More empirical studies are needed to understand why antimicrobial use has been at such a high level, and how to reduce the usage without adversely affecting food security.

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 a type of insurance to prevent the spread of certain types of animal 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.

The Chinese animal health system is in the process of upgrading its infrastructure and integrating international governance structures, however it needs to be better suited to changing domestic production structures and able to face the 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. Prior to this, policies did not distinguish between the administration of antimicrobials from other veterinary medicines but focused on reducing residues in animal products. However, antimicrobial use in animal production has been tightened gradually and a new policy emerged after 2014. Apart from residue control, the main instruments included are: (1) an AMR surveillance system; (2) the classification of antimicrobials into non-restrictive, restrictive and special use only; (3) the introduction of a 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) the 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.

More research is needed to quantify antimicrobial use in animal production and to develop a baseline for an appropriate reduction strategy. China is generally perceived as using more antimicrobials in animal production than in human health, and it accounts for about half of global antimicrobial use in animal production, although its share may have fallen in recent years. A portion of antimicrobials used in animal production came from the production destined for human consumption in China. As in other countries, antimicrobials are more intensively used in pig and broiler production. This high usage is associated with its widespread misuse, including the use as AGPs. It is also related to 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.

AMR can emerge and be transmitted between animals and humans via the environment in several 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 decrease in antimicrobial use in animal production is a high priority, AMR transmission also needs to be addressed in developing a robust AMR policy.

References

Alliance to Save our Antibiotics. Farm antibiotic use in the Netherlands. 2016.

Anonymous. Misuse of Antibiotics in China's Animal Husbandry Industry: Causes and Economics Implications. http://pa-europecom.webhosting.be/www.pa-international.org/htdocs/documents/ChinaAMREconomicsReport.pdf2017.

Bager F, Birk T, Høg BB, Jensen LB, Jensen AN, de Knegt L, et al. DANMAP 2014-Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark. 2015.

Bureau of Veterinary, Ministry of Agriculture PRC. 2009中国动物卫生状况报告 (Animalhealth in China): 中国农业出版社; 2011.

Chen JX, Yue JQ. 养殖业抗生素使用现状及其对策 (Situation and measures of antimicrobial sue in livestock production). 中国畜牧兽医文摘 (Abstracts of Chinese Livestock Production and Veterinary Services). 2013;29(05):15-6.

CLPVSY Editorial Board. China Livestock Production and Veterinary Service Yearbook. Chinese Agricultural Publishing House; various years.

Cui D, Liu X, Hawkey P, Li H, Wang Q, Mao Z, et al. Use of and microbial resistance to antibiotics in China: a path to reducing antimicrobial resistance. J Int Med Res. 2017:0300060516686230.

FAO. Food and Agriculture Data. In: FAOSTAT, editor. Food and Agriculture Organization of the United Nations 2017.

Gao L, Hu J, Zhang X, Wei L, Li S, Miao Z, et al. Application of swine manure on agricultural fields contributes to extended-spectrum β-lactamase-producing Escherichia coli spread in Tai'an, China. Frontiers in Microbiology. 2015 2015-April-14;6(313).

Guo HW. Analysis of pig production and its development trend (我国生猪产业发展的背景和趋势分析). Chin J Anim Sci. 2017 (5).

Guo PT, Xu C, Ma Y. Pork price fluctuation in past 10 years and farm size changes (基于养殖规模变化解析我国近十年的生猪价格波动). Chin J Anim Sci. 2017 (12).

He M, Yi BC, Chen M. 豫南地区猪场抗生素使用调查 (A survey of antimicrobial use in pig farms in southern region of Henan province). 中国兽医杂志 (Chiense Veterinary Sciences). 2011;47(10):77-8.

Hellman J, Olsson-Liljequist B, Bengtsson B, Greko C. SWEDRES-SVARM 2014. Use of antimicrobials and occurrence of antimicrobial resistance in Sweden. Solna/Uppsala: Swedish Institute for Communicable Disease Control and National Veterinary Institute. 2016.

Hu Y, Cheng H. Health risk from veterinary antimicrobial use in China's food animal production and its reduction. Environmental Pollution. 2016;219:993-7.

Hu F-P, Guo Y, Zhu D-M, Wang F, Jiang X-F, Xu Y-C, et al. Resistance trends among clinical isolates in China reported from CHINET surveillance of bacterial resistance, 2005–2014. Clin Microbiol Infect. 2016;22:S9-S14.

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.

Huang T, Xu Y, Zeng J, Zhao D-H, Li L, Liao X-P, et al. Low-Concentration Ciprofloxacin Selects Plasmid-Mediated Quinolone Resistance Encoding Genes and Affects Bacterial Taxa in Soil Containing Manure. Frontiers in Microbiology. 2016 2016-November-01;7(1730).

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).

Hvistendahl M. China takes aim at rampant antibiotic resistance. Science. 2012;336(6083):795-.

Jiang H-X, Lü D-H, Chen Z-L, Wang X-M, Chen J-R, Liu Y-H, et al. High prevalence and widespread distribution of multi-resistant Escherichia coli isolates in pigs and poultry in China. The veterinary journal. 2011;187(1):99-103.

Kimi Y, Dai CT. 农村养殖业抗生素使用现状与应对措施—以张家界市为例 (Antimicrobial use and mitigation measures in rural livestock production: a case study in Zhangjiaojie). 现代农业科技 (Modern Agricultural Science and Technology). 2016 (18):246-50.

Lai J, Wu C, Wu C, Qi J, Wang Y, Wang H, et al. Serotype distribution and antibiotic resistance of Salmonella in food-producing animals in Shandong province of China, 2009 and 2012. International journal of food microbiology. 2014;180:30-8.

Liu Y-Y, Wang Y, Walsh TR, Yi L-X, Zhang R, Spencer J, et al. Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study. The Lancet Infectious Diseases. 2016;16(2):161-8.

Ltd CNPIC. Analysis of key Chinese antibiotic products in the international market (中国主力抗生素产品国际市场形势分析). http://www.cnpic.com.cn/353-904-11517.aspx2015.

NBSC. China Statistical Yearbook. National Bureau of Statistics of China, Beijing: China Statistics Press; Various Years.

Trauffler M, Griesbacher A, Fuchs K, Köfer J. Antimicrobial drug use in Austrian pig farms: plausibility check of electronic on-farm records and estimation of consumption. The Veterinary Record. 2014;175(16):402-.

UK-VARSS. UK Veterinary Antibiotic Resistance and Sales Surveillance 2015. https://www.gov.uk/government/publications/veterinary-antimicrobial-resistance-and-sales-surveillance-2015 : Veterinary Medicines Directorate, UK; 2016. p. 1-133.

Van Boeckel T, Brower C, Marius Gilbert, Bryan T. Grenfella, Simon A. Levina, Timothy P. Robinsoni, et al. Global trends in antimicrobial use in food animals. PNAS. 2015;112(18):1-6.

Van Boeckel TP, Glennon EE, Chen D, Gilbert M, Robinson TP, Grenfell BT, et al. Reducing antimicrobial use in food animals. Science. 2017;357(6358):1350-2.

Wang J. 畜禽养殖中抗菌素耐药性的现状及对策调查 (AMR situation and measures to combat AMR in animal production). 浙江畜牧兽医 (Animal Production and Veterinary Medicine in Zhejiang). 2014;39(01):24-5.

Wang L, Zhang X, Liang X, Bloom G. Addressing antimicrobial resistance in China: policy implementation in a complex context. Globalization and health. 2016;12(1):30.

Wei X, Lin W, Hennessy DA. Biosecurity and disease management in China's animal agriculture sector. Food Policy. 2015;54:52-64.

World Health Organization. Antimicrobial resistance: Global report on surveillance: World Health Organisation. 2014.

Wu Z. (2018), "Antimicrobial use in food animal production: Situation analysis and contributing factors", Frontiers of Agricultural Science and Engineering, Vol. 5(3), pp. 301-311.

Wu Z. 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.

Xia J, Fang L-X, Cheng K, Xu G-H, Wang X-R, Liao X-P, et al. Clonal Spread of 16S rRNA Methyltransferase-Producing Klebsiella pneumoniae ST37 with High Prevalence of ESBLs from Companion Animals in China. Frontiers in Microbiology. 2017 2017-March-29;8(529).

Xiao Y. A National Action Plan to Contain Antimicrobial Resistance in China: Contents, Actions and Expectations. AMR Control. 2017.

Xiao Y-H, Giske CG, Wei Z-Q, Shen P, Heddini A, Li L-J. Epidemiology and characteristics of antimicrobial resistance in China. Drug Resistance Updates. 2011 2011/08/01/;14(4):236-50.

Xiao Y, Zhang J, Zheng B, Zhao L, Li S, Li L. Changes in Chinese policies to promote the rational use of antibiotics. 2013.

Xiong W, Sun Y, Zhang T, Ding X, Li Y, Wang M, et al. Antibiotics, antibiotic resistance genes, and bacterial community composition in fresh water aquaculture environment in China. Microb Ecol. 2015;70(2):425-32.

Yang H. Livestock development in China: animal production, consumption and genetic resources. J Anim Breed Genet. 2013;130(4):249-51.

Ying G-G, He L-Y, Ying AJ, Zhang Q-Q, Liu Y-S, Zhao J-L. China must reduce its antibiotic use. ACS Publications; 2017.

YUBOINFO. Antimicrobial Use in Chinese Livestock Production. http://www.chinabgao.com/report/468385.html: 2016.

Zhang W-H, Lin X-Y, Xu L, Gu X-X, Yang L, Li W, et al. CTX-M-27 Producing Salmonella enterica Serotypes Typhimurium and Indiana Are Prevalent among Food-Producing Animals in China. Frontiers in Microbiology. 2016 2016-March-31;7(436).

Zhang Q-Q, Ying G-G, Pan C-G, Liu Y-S, Zhao J-L. 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.

Zhang X, Li Y, Liu B, Wang J, Feng C, Gao M, et al. Prevalence of veterinary antibiotics and antibiotic-resistant Escherichia coli in the surface water of a livestock production region in northern China. PloS one. 2014;9(11):e111026.

Zhao X, Ye C, Chang W, Sun S. Serotype Distribution, Antimicrobial Resistance, and Class 1 Integrons Profiles of Salmonella from Animals in Slaughterhouses in Shandong Province, China. Frontiers in Microbiology. 2017 2017-June-21;8(1049).

Zhu Y-G, Johnson TA, Su J-Q, Qiao M, Guo G-X, Stedtfeld RD, et al. Diverse and abundant antibiotic resistance genes in Chinese swine farms. Proceedings of the National Academy of Sciences. 2013;110(9):3435-40.