Antibiotic use in animals and humans in Australia

Developing strategies to reduce both the transmission of important pathogens and antimicrobial resistance is of paramount importance

Freya Langham[1]

Allen C Cheng[2]

1 Alfred Health, Melbourne, VIC.

2 Monash University, Melbourne, VIC.

f.langham@alfred.org.au

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Since the 1960s, there has been concern about the use of antibiotics in food animals and its contribution to antibiotic resistance in humans. The increasing intensification of modern food animal production has resulted in an increase in antimicrobial use in livestock, for both therapeutic and non-therapeutic purposes. There are a number of mechanisms by which antimicrobial use in animals affects resistance in human pathogens, such as transmission by direct contact and, indirectly, through food consumption and environmental contamination.[1] Moreover, there is emerging literature stating that limiting antimicrobial use in animals leads to reduced resistance in humans.[2]

However, in Australia, there are limited data on the extent of antibiotic use in animals and how it compares with the use in humans. The only comprehensive data on veterinary antibiotic sales in Australia cover the period 2005–2010 and were published in 2014. We thus estimated the relative volume of key antimicrobial classes in animals and humans in Australia.

We extracted data from three sources on antibacterial agents of importance to human health.[3] Data on veterinary use were derived from the Australian Pesticides and Veterinary Medicines Authority (APVMA).[4] In food animals, antibiotic use is broadly divided into therapeutic, prophylactic, metaphylactic (ie, treatment of a herd of animals when some in the group have infection) and growth promotion purposes. In the APVMA report, the use of antibiotics for prophylaxis and metaphylaxis is incorporated within the therapeutic category, and only growth promotion is considered non-therapeutic use.

Data on human use in primary care were calculated from Pharmaceutical Benefits Scheme (PBS) statistics,[5] which are reported by number of prescriptions. These data were converted to total volume by class and agent by multiplying by the pack size and strength. Data on human use in patients admitted to hospital were estimated from the National Antimicrobial Utilisation Surveillance Program (NAUSP),[6] which reports on the rate of antibiotics use per occupied bed day. National usage by weight was estimated by multiplying the rate of use by the defined daily dose for each antibiotic and the total number of hospital bed days in Australia. Because hospital usage data were reported by calendar year, usage by financial year was estimated by averaging the reported usage for each consecutive year to enable comparison with data from other sources.

Across all antimicrobials of importance to human health, an average of 182 138 kg were sold for use each year in animals between 2005 and 2010, and 121 076 kg per year were used in humans.[4–6] Most antibiotic classes were predominantly used in either humans or animals; the only antibiotic classes with near equal use between animals and humans were β-lactamase sensitive penicillins and extended-spectrum penicillins (Box).

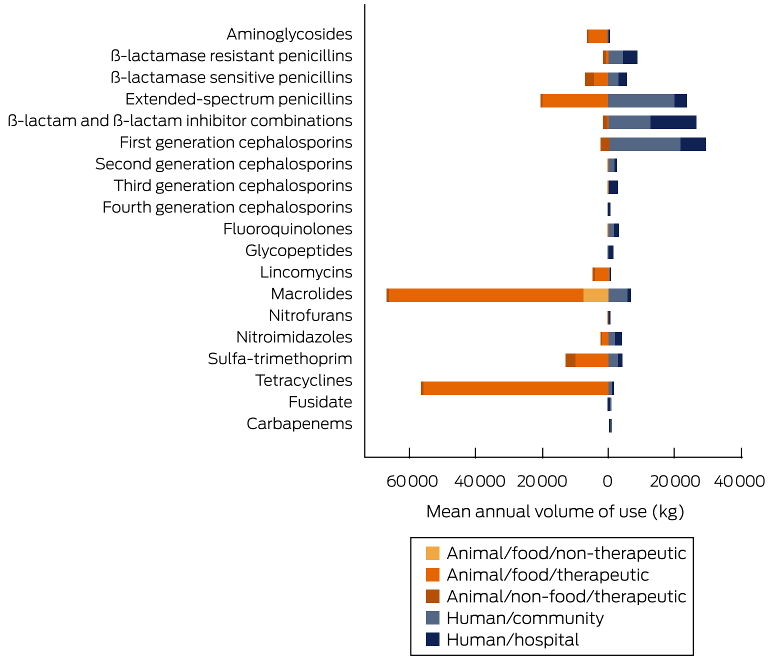
In humans (both in community and hospital settings), penicillins made up the majority of antibiotic use, representing 52.9% of all use (mean, 64 004 kg/year; standard deviation [SD], 4045 kg/year), with extended-spectrum penicillins accounting for 23 540 kg/year, followed by cephalosporins (28%; mean, 34 461 kg/year; SD, 2017 kg/year). A similar pattern was also seen in non-food animals.[4–6]

Macrolides (mean, 66 666 kg/year; SD, 8389 kg/year) and tetracyclines (mean, 56 490 kg/year; SD, 8141 kg/year) were used in much greater volumes in animals compared with humans (macrolides mean, 6702 kg/year [SD, 423 kg/year]; tetracyclines mean, 1212 kg/year [SD, 42 kg/year]).[4–6] This use is predominantly in food animals for therapeutic purposes (88.2% of mean animal macrolide use); however, during this period, macrolides were the only antibiotic class used in food animals for growth promotion purposes, accounting for 11.5% of mean animal macrolide use.[4]

Antimicrobial use in animals is dominated by two classes: macrolides and tetracyclines, with smaller volumes of amoxicillin, aminoglycosides and folic acid inhibitors used. This largely reflects the major therapeutic indications for antibiotics in food animals, especially in pigs and chickens.[1] Of the most commonly used antimicrobial classes in animals, only amoxicillin and aminoglycosides are rated of high or medium importance by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance.[3] However, macrolides are becoming increasingly important in human medicine for the treatment of foodborne enteric pathogens, and are classified by the World Health Organization as a critically important antimicrobial class.[7] We found that macrolides are the main class of antibiotic used in animals, for both therapeutic and non-therapeutic purposes. Following an extensive review by the APVMA initiated in 2001, the use of macrolides in growth promotion of food animals is now being phased out in Australia.[8]

It is notable that several important classes of antimicrobials, including glycopeptides and quinolones, are not registered for use in food-producing animals in Australia, in contrast to many countries internationally. While the volume of use is difficult to compare with other countries due to

Volume of antibiotics use in Australia, by indication and setting*



* Excludes ionophore coccidiostats agents, which are used extensively in animals (300 tonnes per year) but are not believed to contribute to resistance in human pathogens.[1,2] ◆

population differences in both humans and animals, the pattern of use appears to be quite distinct to data from other countries where macrolide use in animals is much less common.[9–11] Some of this difference may be due to the use of macrolides in livestock feed in Australia for growth promotion purposes, which is not authorised in the European Union[12] and is being phased out in North America.[10,13] In the United States, over 70% of antibiotics sold (by weight) are used in animals — a greater proportion compared with our data (approximately 60%).[9]

In humans, antimicrobial use is dominated by β-lactams, particularly the extended-spectrum β-lactams (amoxicillin, especially in community settings), β-lactam inhibitor combinations (amoxicillin/clavulanic acid and piperacillin/tazobactam), and first generation cephalosporins (cephalexin and cephazolin).[14] The Australian Atlas of Healthcare Variation report noted a large variation in antibiotic use between different areas in Australia (of more than tenfold between the areas with the highest and lowest usage).[15] Similarly, the Australian report on antimicrobial use and resistance in human health found that antibiotics were prescribed for a higher than expected proportion of patients with respiratory tract infections. Hospital surveys have estimated that 38% of patients are receiving at least one antimicrobial at any single point in time, and 23% of these antibiotics were inappropriate.[16]

Antimicrobial use is only one factor that leads to prevalence of antibiotic resistance in human pathogens. Antimicrobial use in animals is likely to be a major determinant of some foodborne pathogens, particularly *Salmonella* and *Campylobacter* and, to a lesser degree, other enteric bacteria such as *Escherichia coli*. In contrast, resistance in bacteria that are restricted to humans, such as *Streptococcus pneumoniae* and *Neisseria gonorrhoea*, is likely to relate only to human antibiotic use. Different settings, such as aged care facilities or intensive food production facilities, vary in the potential for cross-transmission and amplification of resistance. In addition, the external or environmental exposures required to produce resistance vary depending on the mechanism. The relationship between use and resistance is also complicated by coselection of antibiotic resistance, such as ceftriaxone exposure increasing the risk of infection with vancomycin-resistant enterococci.[17]

In analysing these data, there are limitations. Antibiotics vary in potency and the appropriate metric to assess selective pressure on bacteria, whether total weight, exposure per person or animal or some other measurement, is not well defined. A population correction unit that adjusts for the population and standardises weights of animals has been used to facilitate comparisons, but still does not account for differences in dosage, potency, formulation and lengths of treatment.[11] Our estimates of community use may be underestimated by use of PBS data only, although previous work has established that more than 95% of antibiotics are subsidised by the PBS.[14] Our calculations of hospital antibiotic use assume that hospitals participating in NAUSP during the study period were representative of all Australian hospitals. Finally, APVMA data are based on sales data; therefore, documented indication for use and the animal species for which antibiotics were used cannot be verified. In particular, off-label use in some industries, such as aquaculture, is not captured.

In summary, a large volume of antibiotics is used in food-producing animals in Australia. A reduction in this volume may be possible by reducing non-therapeutic use of antibiotics and limiting the use of antibiotics of critical importance to human health. Reducing transmission of important pathogens is also a key area to address through the development of alternative strategies, such as vaccination and improved design of production facilities. There is a need for ongoing volume- and quality-based surveillance of antimicrobial use in animals, particularly in food-producing animals. Moreover, the available evidence suggests that a significant proportion of antibiotic use in humans is inappropriate, and this needs to be addressed in both hospital and community settings.

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