Antimicrobial stewardship through a one health lens

Observations from Washington State

Marisa Anne D’Angeli, Joe B. Baker, Douglas R. Call, Margaret A. Davis, Kelly J. Kauber, Uma Malhotra, Gregory T. Matsuura, Dale A. Moore, Chris Porter, Paul Pottinger, Virginia Stockwell, Carol Wagner, Ron Wohrle, Jonathan Yoder, Leah Hampson Yoke and Peter Rabinowitz

(Information about the authors can be found at the end of this article.)

Abstract

Purpose – Antibiotic resistance (AR) is a global health crisis that is attracting focussed attention from healthcare, public health, governmental agencies, the public, and food producers. The purpose of this paper is to describe the work in Washington State to combat resistance and promote antimicrobial stewardship from a one health perspective.

Design/methodology/approach – In 2014, the Washington State Department of Health convened a One Health Steering Committee and two workgroups to focus on AR, the One Health Antimicrobial Stewardship work group and the One Health Antimicrobial Resistance Surveillance work group. The group organized educational sessions to establish a basic understanding of epidemiological factors that contribute to resistance, including antibiotic use, transmission of resistant bacteria, and environmental contamination with resistant bacteria and antibiotic residues.

Findings – The authors describe the varied uses of antibiotics; efforts to promote stewardship in human, and animal health, including examples from the USA and Europe; economic factors that promote use of antibiotics in animal agriculture; and efforts, products and next steps of the workgroups.

Originality/value – In Washington, human, animal and environmental health experts are working collaboratively to address resistance from a one health perspective. The authors are establishing a multi-species resistance database that will allow tracking resistance trends in the region. Gaps include measurement of antibiotic use in humans and animals; integrated resistance surveillance information; and funding for AR and animal health research.

Keywords One health, Antibiotic resistance, Antibiotic stewardship, Washington State

Paper type Viewpoint

Antibiotic resistance (AR) is a global health crisis (World Health Organization, 2012) that threatens patient care, public health, agriculture, economic growth, and national security (King, 2014). It has recently attracted increasing attention from healthcare professionals, public health officials, federal governments, international agencies, the public, and food producers. Despite seven decades of warnings, AR continues to increase (Centers for Disease Control and Prevention, 2013). It is clear that AR is a threat to all – healthy and vulnerable humans in high- and low-income nations, pets and animals raised for food – and that cooperative, collaborative global action is essential to mitigate this threat. The purpose of this paper is to describe Washington’s statewide effort to combat antibiotic resistant bacteria from a one health perspective, and to present our findings and observations about the challenges we face.
In 2014, the Washington State Department of Health established a statewide One Health Steering Committee with representation from State Departments of Agriculture, Fish and Wildlife, and Health; academic researchers from University of Washington Center for One Health Research and Washington State University Paul G. Allen School for Global Animal Health; human and animal health experts; the Washington State Veterinary Medical Association; and the Governor’s office. The committee’s goal is to improve knowledge, communication, cooperation, and coordination in responding to health issues that cross the human and animal health sectors. Many zoonoses and emerging infections are worthy of attention using a one health lens. However, in response to President Obama’s National Strategy for Combating AR that calls for a one health approach, the Washington One Health committee chose to focus first on AR.

The complex epidemiology of AR guides our work in Washington. Figure 1 illustrates the principal transfer pathways for antibiotics and AR genes between humans, animals, food, and the environment. We believe a one health approach to combating AR should be based on a comprehensive understanding of how, where and why antibiotics are used, how previously susceptible bacteria acquire new resistance traits, and what factors favor amplification and transmission of resistant bacteria. The main factors promoting resistance have been well documented in the literature and will receive only a cursory review here.

Antibiotic use – Most antibiotics are derived from naturally produced compounds that can be found in association with existing AR traits (Cox and Wright, 2013), but the prevalence of acquired resistance has dramatically increased due to selection pressure imposed through large-scale use in human medicine. Clinically important AR is often identified within a relatively short time after introduction of new antibiotics (Levy et al., 1976). In some cases, withdrawal of antibiotics results in reduced AR (Dutil et al., 2010), but not always (Enne, 2010). Resistance mechanisms include mutations, such as spontaneous point mutations (Hooper and Jacoby, 2015), or acquisition of entire functional genes coding for resistance traits via conjugation, transduction, or transformation processes (Huddleston, 2014). Occurrence of
mutations and horizontal gene transfer events are considered stochastic processes, but evidence suggests that exposure to some antibiotics may increase mutation and horizontal gene transfer rates via the SOS response (an inducible DNA repair system), phage induction, and by influencing gene expression (Andersson and Hughes, 2014; Blazquez et al., 2001).

Transmission of antibiotic resistant bacteria – the primary transmission routes for resistant bacteria are between people in healthcare settings (Magill et al., 2014) and in the community (Rafee et al., 2012); between people and animals, such as to and from household pets (van Duijkeren et al., 2004; Harrison et al., 2014) and farm animals (Fey et al., 2000; Harrison et al., 2013; Price et al., 2012); between livestock (Le Devendec et al., 2011); between environmental systems such as soil and water; and between the environment and living creatures (Blanco et al., 2009; Vieira et al., 2011), either directly, or indirectly through food. The most significant routes of transmission likely vary by setting, for example, in low resource settings with poor sanitation, contaminated water could be a more significant route than in high-income countries.

De novo resistance generated in ecosystems – bacteria in water, soil, and sewage may be acted upon by antibiotic residues and metabolites that result from industry, runoff from agricultural uses, improper disposal of antibiotics, excreta from humans and animals, and household uses. Improperly treated wastewater containing antibiotics from pharmaceutical manufacturing has been documented in India (Fick et al., 2009). The risk from antibiotic contamination generating resistance depends on the environmental conditions, and concentration and bioavailability of antibiotics (Youngquist et al., 2014, Subbiah et al., 2011).

Horizontal gene transfer – horizontal gene transfer between bacteria may result in increased prevalence of a new resistance characteristic, particularly in the context of antimicrobial selection pressure. This process of genetic mixing may occur between different species of bacteria, such as between Klebsiella, E. coli, and Enterobacter. These genera in the family Enterobacteriaceae are normally found in the stool of mammals and birds and are common causes of healthcare- and community-associated infections. Plasmid-mediated gene transfer is thought to be responsible for the rapid and alarming spread of carbapenemase-producing Enterobacteriaceae around the world (Nordmann et al., 2011). There is also concern that resistance genes from food sources may be transferred intra-intestinally via whole bacterium transmission or mobile genetic elements and ultimately cause extra-intestinal disease (Lazarus et al., 2015; Manges, 2016; Singer, 2015).

Our goal is to identify the most important causes of AR and interventions that are low cost and high impact in order to maximize the effectiveness of our limited resources. Toward this goal, Washington State’s Combating Antibiotic Resistant Bacteria initiative identified the following 5 strategies for addressing AR: detect; protect; prevent; innovate; and collaborate.

(1) detect includes surveillance and laboratory capacity to identify important mechanisms of resistance;

(2) protect refers to reporting, notification, and communication about epidemiologically important organisms, and promoting best practices in infection control and biosecurity;

(3) prevent encompasses antibiotic stewardship, immunization, health enhancement, and other novel interventions to prevent infections from occurring;
innovate denotes development of new, better diagnostics and therapeutics, and improvements in health management; and

(5) collaborate represents local, regional, national, international and cross-disciplinary work to comprehensively address resistance.

One-Health antimicrobial stewardship workgroup
The One Health Antimicrobial Stewardship workgroup convened in early 2015 and meets quarterly. In addition to those represented on the steering committee, the workgroup includes representatives of local health departments; Washington State University College of Veterinary Medicine and Cooperative Extension; Centers for Medicare and Medicaid-designated quality improvement organization for Washington; Washington State Hospital Association, academic and practicing physicians and veterinarians; physician assistants; nurse practitioners; pharmacists; microbiologists; horticultural experts; and economists.

Working together
Human and veterinary health care communities do not routinely work together on AR and sometimes view each other with suspicion. An early one health goal was for our human and animal health representatives to become more familiar with each other’s “culture.” Members developed a vision and mission statement to define the group’s purpose and goals in the first list below and, subsequently, defined common principles for collaboration and communication which include showing mutual respect, seeking win-win solutions, avoiding blame, and focussing on science (second list below).

Vision and Mission of the Washington One Health Antimicrobial Stewardship Workgroup:

(1) Vision:
- Judicious use of antimicrobials in all species to maximize health, minimize harm, and preserve effectiveness.

(2) Mission:
- represent key partners and stakeholders in human, animal, and plant health;
- work collaboratively to promote judicious use of antimicrobials across all sectors;
- identify gaps, strategize solutions, and mobilize resources to advance antimicrobial stewardship;
- promote education and shared learning; and
- evaluate outcomes with a one health perspective.

Washington One Health Principles of Collaboration and Communication
The members of the Washington State One Health Steering Committee and its subcommittees and workgroups acknowledge that the process of working across the sectors of human health, animal health, and environmental health requires unique processes of collaboration and communication. The principles underlying these processes include the following:
- mutual respect for the perspectives and needs of the different disciplines;
agreement to work on solutions to complex problems that are “win-win” in terms of
simultaneously maximizing human, animal, and environmental health;

• agreeing that we will work whenever possible in a collaborative manner to develop
standards for best professional practices across sectors and not single out particular sectors for “blame” or attribution regarding particular health issues;

• agreeing that we will focus on evidence based, scientific approaches for best
practices and conclusions regarding root causes of problems; and

• agreeing that when sharing data between sectors, integrated data will be
analyzed in a responsible manner based on science and not politics.

Members therefore agree to follow these principles in their professional involvement
and activities with the Steering Committee and workgroups.

The group’s early accomplishments served to publicize our collaborative effort and
recruit others to work in a similar manner to improve antibiotic use in all sectors.
Members authored a position statement for the Council of State and Territorial
Epidemiologists promoting antimicrobial stewardship in veterinary medicine and
animal agriculture (Council of State and Territorial Epidemiologists, 2015). We also
collected and disseminated a “call to action” to improve antibiotic stewardship in
human and animal healthcare and in food animal production, citing specific actions for
consumers, prescribers, and food animal producers to improve antibiotic use. This
letter was signed by 18 state agencies and organizations in Washington, a novel
element of human and animal sectors working in common cause to combat AR

Increasing basic knowledge
To provide a basic working knowledge for workgroup members with different areas of
expertise, we coordinated a series of speakers on antibiotic use in human health care,
companion animal care, animal agriculture, fisheries, horticulture, and apiculture. We
learned that antibiotic use in human and companion animal medicine is surprisingly
similar, primarily for disease treatment and, less frequently, for infection prevention.
Most antibiotic applications in human and veterinary medicine in the USA require a
prescription. In high-income countries, companion animals may receive specialized
medical care similar to human medicine, such as chemotherapy and complex surgeries,
with a similar need for antibiotics to ensure success and prevent complications. In both
human and companion animal care, pharmaceutical advertising and detailing may
contribute to higher healthcare costs and inappropriate prescriptions through
promotion of newer, more expensive, broad-spectrum antibiotic agents. In human
healthcare, there is concern that certain elements of pharmaceutical promotion, such as
gifts, free meals, and speakers’ fees, may result in a conflict of interest for prescribers
(Ornstein et al., 2011). Unique to companion animal care, veterinarians often prescribe
and dispense medications generating almost 30 percent of their income from pharmacy
services (Arp, 2012) which may incentivize over-prescription.

Antibiotic use in food animals may be divided into three categories: therapeutic; sub-
therapeutic (preventive); and non-therapeutic (growth promotion). Non-therapeutic, or
growth-promoting antibiotics, are administered in low concentrations and generally
during early life. However, new Federal Drug Administration (FDA) rules require that
after December 2016, no antibiotics be used for growth promotion, and any in-feed or
water use of any antimicrobial for treatment will require a veterinary feed directive
(VFD), changes that should substantially reduce growth promotion uses (Food and Drug Administration (FDA), 2013). Therapeutic uses in food animals, as in humans and companion animals, encompass treatment of infectious and control of infectious disease. Prescriptions may be for a single animal (treatment) or for an entire group when one or several are ill (control). Preventive antibiotics are administered in low doses when animals are known to be vulnerable to infectious diseases, for example, in times of physiologic stress such as during transportation, exposure to environmental contamination, crowding, and weaning.

Other agricultural applications of antibiotics include aquaculture, although compared to other countries, the USA is a relatively small producer (Food and Agriculture Organization of the United Nations, 2015). The few antibiotics registered for use in USA aquaculture are typically administered via feed and therefore will also fall under the new FDA rules; thus oversight of antibiotics used in aquaculture will increase as of January 2017. It is important to note that antibiotic use in food animals requires a mandated wash-out period (withholding period) to allow complete metabolism and excretion of antibiotics. As a consequence, even if food animals are treated with antibiotics, adherence to defined withdrawal periods ensures the absence of antibiotic residues in the food supply. These practices, unfortunately, are not consistently applied in developing countries (Dipeolu and Alonge, 2002).

Other less commonly known uses of antibiotics occur in horticulture and apiculture. Overall, plant uses of antibiotics account for only 0.1 percent of the total agricultural use of antibiotics in the USA (McManus, 2014). Three antibiotics are registered for use on tree fruits in the USA (pear, apple, peach, and nectarine), and less than half the acreage is treated with antibiotics within a single year (Stockwell and Duffy, 2012). Generally, antibiotics are not registered for field applications on annual crops (e.g. grains or vegetables), conifers, or small fruits and berries. Similar to the “withholding period” described for animal and aquaculture systems, there is a mandated “pre-harvest interval” ensuring that antibiotics are not applied to fruit trees at least a month before harvest. Consequently, antibiotic residues on harvested fruit are not detected or, in rare cases, are detected at levels well below the tolerances set by government agencies (Stockwell and Duffy, 2012). Numerous studies have not detected a significant impact of antibiotic use on plants on the prevalence of AR genes in bacteria residing on plants or in soils (McManus, 2014). Antibiotics are also fed to honey bees to treat and prevent foulbrood disease. It is recommended that the treatment be given in the early spring or late fall before the main honey flow begins to avoid contamination of production honey. Antibiotic contamination of honey has been documented, particularly Chinese honey, which was banned from importation by the European Union (EU) (European Commission, 2013a).

Future educational topics for our group will include information about quantity and sources of antibiotic residues in water and soil, environmental contamination with antibiotic resistant bacteria from food animal operations, human solid waste, and wastewater treatment facilities. The current practices regarding treatment of these sources of bacterial contamination (e.g. composting) and the economics of stewardship, particularly in food animal production will be additional foci for education.

Cross-pollination between sectors
The workgroup catalogued currently known stewardship activities in Washington. This effort provided an opportunity to learn from counterparts and identify efforts that might be adapted for use in another sector. A product of this cross-pollination was an
educational brochure for veterinarians on AR and stewardship (Washington State Veterinary Medical Association, 2015). A second activity was a survey of Washington State veterinarian practitioners on knowledge and practices regarding resistance and stewardship. The survey results will guide future training and education for veterinarians in Washington and has been submitted for publication (Heather Fowler, personal communication, April 29, 2016). This accounting of activities also allowed a comparison of the organizational structure and resources for antibiotic stewardship in different sectors.

Antibiotic stewardship in human healthcare

Antimicrobial stewardship is a coordinated effort to promote appropriate use of antibiotics resulting in improved patient outcomes and reduced bacterial resistance. Antibiotic stewardship was originally described as the “4 Ds” – the right drug, dose, duration, and de-escalation (Joseph and Rodvold, 2008). In human healthcare, implementing stewardship may be more straightforward than in food animal production because antibiotics are primarily used therapeutically, and fewer economic pressures encourage antibiotic use. Multiple sources suggest that antibiotics in human healthcare are overprescribed (Fleming-Dutra et al., 2016; Hecker et al., 2003) and that judicious antibiotic use can improve patient outcomes, reduce resistance and Clostridium difficile infections, and lower healthcare costs (Davey et al., 2006; Fridkin et al., 2014). Factors that promote over- and inappropriate antibiotic use include the sometimes mistaken perception that patient satisfaction depends on receiving an antibiotic; weighing the potential for a dangerous infection more heavily than potential harms from antibiotic use; and inadequate knowledge of prescription guidelines. A stewardship program devoted to supporting best practices has been shown to be vital for sustained improvements in prescribing practices (Barlam et al., 2016). The core elements of antimicrobial stewardship, which include leadership commitment, accountability, expertise, action, tracking, reporting, and education, provide a framework for implementing and evaluating an antibiotic stewardship program that is adaptable to different care settings (Pollack and Srinivasan, 2014). Antimicrobial stewardship programs in hospitals are usually more developed than in outpatient settings due to increased oversight by administration on hospital-wide practices, and ease of collecting key outcome metrics, but there are examples of successful stewardship interventions in ambulatory settings (Meeker et al., 2014; Pittenger et al., 2015). Tracking process measures, such as adherence to guidelines for appropriate antibiotic use and including indication for all prescriptions, and outcomes of interest, such as C. difficile infections and antibiotic costs or days of therapy, are useful for assessing the success of the program.

Measurement of antibiotic use with feedback to prescribers comparing them to their peers is an effective approach for improving prescribing, but requires electronic infrastructure not available in many settings. Various systems to measure human antibiotic use exist but are fragmented and incomplete, such as CDC’s National Healthcare Safety Network (NHSN) Antibiotic Use module, Intercontinental Marketing Services (IMS) Health’s Xponent database, “all-payer-claims” databases, and electronic health record data mining programs. None of these is currently able to provide a comprehensive measurement of human antibiotic use in the US. In Washington, the Department of Health has promoted CDC’s NHSN Antibiotic Use module, a system to allow hospitals to electronically measure and report antibiotic use, but since this program requires costly technological upgrades and expertise, state progress has been
limited to date. A statewide Washington all-payer-claims database is in development that will be useful for assessing outpatient antibiotic prescribing. Proprietary systems such as IMP Xponent can provide prescribing data for a fee. Any widespread antibiotic use measurement requires a high level of financial and human resources, therefore state and federal mandates with financial support may be necessary in order to achieve broad measurement.

**Antimicrobial stewardship in companion animal practice**

Surveys indicate that small animal veterinarians are increasingly concerned about AR. (American Veterinary Medical Association Task Force for Antimicrobial Stewardship in Companion Animal Practice, 2015) yet in companion animal practice, as in outpatient human health care, there is little infrastructure to support antibiotic stewardship. In the EU, 37 percent of pharmaceuticals sold are for use in companion animals (Guardabassi et al., 2004), but in the USA there is no system for accurately measuring the proportion of antibiotics sold for use in companion animals. FDA estimates 80 percent of antibiotics sold in the USA are for use in animals, but this proportion includes both companion animals as well as animals raised for food (Food and Drug Administration (FDA), 2015). At Washington State University Veterinary Teaching Hospital, an antimicrobial policy and oversight group performs stewardship for the teaching hospital, but there is limited communication between academic and community veterinarians. Available education and training resources for stewardship include US Department of Agriculture (USDA) Veterinary Accreditation Training Modules and the Antimicrobial Resistance Learning Site for Veterinarians. A structured guide for implementing a stewardship program in a veterinary practice or hospital similar to “core elements” for stewardship for human medicine has not been developed or promulgated, however, the American Veterinary Medicine Association has produced educational guidance on judicious therapeutic use of antibiotics to educate veterinarians about appropriate use of antibiotics (www.avma.org/KB/Policies/Pages/Judicious-Therapeutic-Use-of-Antimicrobials.aspx), and has convened a task force to develop practice guidelines for implementing antimicrobial stewardship in companion animal practice. Our Washington One Health group will be using results of the veterinarian survey described earlier to guide educational outreach on stewardship for veterinarians that, if well received, can be shared nationally.

**Antimicrobial stewardship in livestock and animal agriculture**

In animal agriculture, antibiotic treatment and control uses are most amenable to stewardship interventions, similar to human and companion animal practices that focus on the “4 Ds.” However, stewardship in food-animal agriculture presents three special challenges not seen in human and companion animal sectors: antibiotics can frequently be purchased and dispensed without a prescription; antibiotics are often used sub-therapeutically for prevention and non-therapeutically for growth promotion; and some food animal producers and veterinarians view efforts to reduce antibiotic use as a potential threat to timely attention to animal welfare, affordability of meat, reliability of the supply chain, and profits. Concern about widespread use of antibiotics in animal agriculture and associated risk of resistance has prompted actions at the federal level. In 2007, USDA recommended certain farm management practices that can reduce the need for antibiotics such as use of vaccines, probiotics, immune enhancers, proper nutrition, and diet with adequate trace minerals, and improved operation procedures, such as
buying animals from herds with higher health status, pre-arrival testing of animals, use of quarantine facilities, and elimination of contaminated feed and water (US Department of Agriculture, 2007). In Washington, veterinarians associated with the Washington State University work through the Cooperative Extension service to advise farmers about the use of antibiotics but uptake by farms is voluntary.

In the past few years, the FDA issued new rules to increase veterinary oversight of medically important antibiotics used in animal agriculture and promote judicious use of these drugs by limiting use to treatment, control, and prevention of disease through FDA Guidance for Industry No. 209 and No. 213, and changes to the VFD (FDA, 2013). These mandates were structured with voluntary phase-in periods, allowing time for pharmaceutical companies to change label indications and for industry to adjust animal husbandry practices. Although antibiotics are currently available over-the-counter for administration in animal feed products and water, mandatory changes in 2017 will require a veterinary directive for any antibiotics administered in food and water. There is hope that these new requirements will result in increased veterinary oversight for use of therapeutic antibiotics. Some proponents of strict regulation on antibiotic use in animal agriculture, however, are concerned that antibiotics previously used for growth promotion may subsequently be used, under veterinarian prescription, for prevention purposes (Pew Charitable Trusts, 2014). Continued tracking of antibiotic sales for use in food animals (FDA, 2015) will provide estimates as to whether guidance No. 213 is successful in reducing the total mass of antibiotics used in animals. In 2016, FDA is also providing new research funding to track antibiotic use in animal agriculture after the mandatory changes are implemented.

Several states have undertaken assessments of knowledge, attitudes, and practices about antibiotic use in food animal production. Larger food animal operations more frequently followed written antibiotic use protocols, sought veterinarian consultation, maintained better record keeping, and demonstrated a greater understanding of biosecurity risks (Hoe and Ruegg, 2006; Raymond et al., 2006). In Washington, veterinarians associated with the Washington State University provide educational programs for veterinarians, farmers and farm workers on the development and risks of AMR and alternatives to antibiotics, but participation by farms is voluntary.

Examples from other regions
Examining other state and international examples of restrictions on antibiotic use in animal agriculture provide case studies that may inform future actions. A 2015 California law, Senate Bill 27, bans all growth promotion uses of antibiotics and requires all medically important antibiotics (as defined by FDA) be given only with a veterinary prescription (California Legislative Information, 2015). The law also mandates monitoring antibiotic use and resistance, and requires development and provision of guidance to farmers on optimal use of antibiotics for food animal production. Denmark and Europe provide opportunities to compare antibiotic use in food animals in comparable high-income countries. Denmark halved antibiotic use in the pork industry between 1992 and 2008 by banning antibiotic growth promoters yet increased swine production by 47 percent, while remaining competitive with neighboring countries that did not restrict antibiotic use in pigs (Cogliani et al., 2011). However, the Danish annual report on use of antimicrobial agents and occurrence of resistance in food animals, food and humans, indicates that in recent years therapeutic use of antibiotics has increased more rapidly than herd size, suggesting a need to increase therapeutic use as non-therapeutic use decreases (Danish Integrated Antimicrobial Resistance Monitoring and Research
Subsequent to Denmark’s ban on antibiotic growth promoters, the EU dictated an EU-wide ban on these growth promoters in 2005. Despite the ban, there is still a wide range in antibiotic use in animal agriculture in the four largest pork producing countries in Europe, Denmark, France, Germany, and Spain, where overall use in animals varies from 44 mg/population control unit in Denmark to 317 mg/kg in Spain (European Medicines Agency, 2015). Longitudinal study of the California and European experiences will be instructive for tracking resistance in relation to antibiotic use.

Animal agriculture stakeholders often cite concerns about restrictions on antibiotic use potentially causing increases in meat price. The economics of antibiotic use in US livestock agriculture production was recently reviewed by USDA (Sneeringer et al., 2015). The report details two important findings. First, antibiotics for growth promotion are used widely in US livestock; in 2009, 40 percent of hogs received antibiotic growth promoters as did 75 percent of cattle in feedlots with more than 1,000 head. Second, production uses of antibiotics may occur in two different structures: vertical integration in which a single large business entity dictates and regulates production conditions over the entire course of the animal’s life, and smaller operations that focus only on one life stage. Vertical integration, with centralized oversight and fewer decision-makers, provides more opportunity for systematically controlling how antibiotics are used over the entire life course. According to USDA, use of antibiotics for purposes other than disease treatment (i.e. for control, prevention, and production) is associated with only a 1-3 percent increase in productivity, and restrictions on production uses of antibiotics would result in less than 1 percent increase in wholesale price and even smaller increases in retail prices (Sneeringer et al., 2015).

From a stewardship perspective, preventive uses may be minimized by reducing physiologic stress to animals to keep them healthier, for example, by improving animal husbandry practices, later weaning, reduced density of herds, improved hygiene, rerouting air flow, and raising disease resistant breeds (European Commission, 2013b). These interventions may be financially costly and may increase the price of meat but, to date, no one has clearly evaluated the hidden costs related to the contribution of animal agriculture to AR and thus the tradeoffs remain undefined. In 2015, only approximately $11 million was available in funding for competitive extramural funding for the 24 US veterinary colleges for research on animal health (Peter Johnson, personal communication). Greater investments in research on animal health have potential to substantially improve knowledge in this important area.

Recent announcements by McDonalds, Subway, Chicka-Fil-A, Panera, and Chipotle that they will expand use of meat raised without antibiotics important to human medicine indicate that the marketplace is responsive to consumer demands for reducing antibiotic use in animal agriculture. Time will tell how completely these companies can meet their pledges. An essential step is to clearly define and validate label claims, such as “no non-therapeutic use,” “no production use,” or “no antibiotics ever” to allow verification that actions live up to promises. Improved transparency about how and how much antibiotics are used, how blanket restrictions on use adversely affect animal welfare, and how variations in use affect animal safety, meat availability, and prices, may allow consumers to make more informed decisions about food purchases. The combination of regulation and marketplace demands may result in significant changes over the coming years. The National Institute of Animal Agriculture is acknowledging the changing environment by convening annual meetings since 2011 that address scientific and production concerns regarding antibiotic use (www.animalagriculture.org/WhitePapers).
The One Health Surveillance and Data Integration workgroup is a counterpart to the One Health Antimicrobial Stewardship workgroup. Its task is to develop an integrated database for tracking resistance data from humans, animals, and the environment in Washington State. The group is compiling antimicrobial resistance data from regional isolates, including: human and animal enteric pathogens from the National Antibiotic Resistance Monitoring System; human and animal clinical isolates from local microbiology labs; isolates from environmental sources such as soil and water; and indicator species. The goal of the Washington One Health Database of Antibiotic Resistance is to provide an ongoing local data source to detect new trends in resistance and attempt to assess the impact of antimicrobial stewardship efforts across human and animal and environmental sectors in the region. In creating and analyzing such data, the database project will explore comparability of human, animal, and environmental resistance patterns. To encourage collaboration and ensure correct interpretation of results, the Washington One Health Steering Committee will oversee data use, analyses and dissemination of results from the database.

Summary
In summary, AR is increasing due to widespread use of antibiotics, and transmission of resistant organisms in healthcare settings, in the community, via travel, and from food. International, national and state efforts are underway to combat AR. In this paper, we have described progress to date in Washington State to address this challenge from a one health perspective. Our One Health committee and workgroups have succeeded in convening key subject matter experts from the human, animal and environmental health sectors to learn, strategize, and act to combat AR. We have chosen to focus initially on increasing understanding of the current state of AR in Washington and trends over time; minimizing transmission of resistant organisms; and improving use of antibiotics in all sectors. Engaging food animal producers to learn and work with us is an important next step.

As Lord Kelvin said, “If you cannot measure it, you cannot improve it.” In all sectors, accurate measurement of antibiotic use is important to allow evaluation of the effectiveness of stewardship interventions and to assess correlation between antibiotic use and resistance surveillance data. In animal agriculture, more granular measurement of antibiotic administration than that provided by the FDA antibiotic sales data may allow increased understanding of how changing antibiotic use affects animal health and production costs. Current US capabilities to measure antibiotic use are deficient, especially when compared to continent-wide surveillance of antibiotic use and bacterial resistance by the European Centre for Disease Prevention and Control. With new funding for combating AR efforts in the USA, there is potential for improving measurement of antibiotic use in human medicine (both acute care and ambulatory settings), veterinary medicine and agriculture. Additional federal support for implementing national antibiotic use measurement in both acute care and ambulatory settings would be extremely helpful since there is a need to both develop and sustain such tracking systems.

Additional funding for research on resistance is needed to address other knowledge gaps and identify how to best focus limited resources. Critical research opportunities
include: animal management strategies and their effect on animal health; source and quantity of environmental transmission of resistant strains; and quantification of type and duration of antibiotics and AR genes in the environment, among others. We hope that a description of our efforts can offer a model to other states that choose to engage in similar work and may provide stimulus for national and international collaboration to improve antibiotic use and minimize AR.

References


Danish Integrated Antimicrobial Resistance Monitoring and Research Programme (2014), “Use of antimicrobial agents and occurrence of antimicrobial resistance in bacteria from food animals, food and humans in Denmark”, Statens Serum Institut National Veterinary Institute, Technical University of Denmark National Food Institute, Kongens Lyngby, September 2015.


Author Affiliations
Marisa Anne D’Angeli, Department of Communicable Disease Epidemiology, Washington State Department of Health, Shoreline, Washington, USA
Joe B. Baker, Animal Services Division, Washington State Department of Health, Olympia, Washington, USA
Douglas R. Call and Margaret A. Davis, Paul G. Allen School for Global Animal Health, Washington State University, Pullman, Washington, USA
Kelly J. Kauber, Department of Communicable Disease Epidemiology, Washington State Department of Health, Shoreline, Washington, USA
Uma Malhotra, Department of Infectious Diseases, Virginia Mason Hospital and Seattle Medical Center, Seattle, Washington, USA
Gregory T. Matsuura, Department of Infection Prevention/Antibiotic Stewardship, Yakima Valley Memorial Hospital, Yakima, USA
Dale A. Moore, Department of Veterinary Clinical Sciences, College of Veterinary Medicine, Washington State University, Pullman, Washington, USA
Chris Porter, United Advanced Registered Nurse Practitioners of Washington, Seattle, Washington, USA
Paul Pottinger, Allergy and Infectious Disease Division, University of Washington Medical Center, Seattle, Washington, USA
Virginia Stockwell, Agricultural Research Service, Horticultural Crops Research Unit, United States Department of Agriculture, Corvallis, Oregon, USA
Carol Wagner, Patient Safety Program, Washington State Hospital Association, Seattle, Washington, USA
Ron Wohrle, Zoonotic Disease Program, Office of Environmental Public Health Sciences, Washington State Department of Health, Olympia, Washington, USA

Leah Hampson Yoke, Vaccine and Infectious Disease Division, Fred Hutchinson Cancer Research Center, Seattle, Washington, USA and Allergy and Infectious Disease Division, School of Medicine, University of Washington, Seattle, Washington, USA, and

Peter Rabinowitz, Center for One Health Research, Department of Environmental and Occupational Health, University of Washington, Seattle, Washington, USA

Corresponding author
Marisa Anne D'Angeli can be contacted at: marisa.dangeli@DOH.wa.gov
This article has been cited by:

1. David Birnbaum Applied Epidemiology, North Saanich, Canada Michael Decker Department of Health Policy, Vanderbilt University, Baxter, Tennessee, USA. 2016. Halfway to salvation, or halfway to hell?. *International Journal of Health Governance* **21**:3, 106-113. [Abstract] [Full Text] [PDF]

2. Fiona MacVane Phipps University of Salford, Salford, UK. 2016. IJHG review. *International Journal of Health Governance* **21**:3, 194-199. [Abstract] [Full Text] [PDF]