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Antimicrobial Resistance Futures:

Five critical uncertainties threaten policy and response plans of the livestock sector in low- and middle-income countries

by Dr. Kevin Bardosh

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Introduction

"Antimicrobial resistance is a global crisis that risks reversing a century of progress in global health."

Interagency Coordination Group on Antimicrobial Resistance, 2019

We live in an increasingly complex world where the speed of change is unprecedented and the risks, forces, feedback loops and scales are perplexing to the public and decision-makers (Leach et al. 2010). To avoid being blinded by surprise, planning and policymaking need to move beyond rigid, reactive and disciplinary *modus operandi* grounded in reasoning based solely on the present. But what does this mean, and how can this be done? Foresight and futures thinking offer a rich repertoire of creative tools to help reorient problems and policy pathways, and these tools are starting to be used in global social, development, environmental and health problems.

One immensely complicated challenge where futures thinking may be useful is in the prevention and control of antimicrobial resistance (AMR) in the livestock sector. Like climate change, AMR is often presented in near-apocalyptic terms (Torjesen, 2013). The problem in animals is multi-scalar and linked to the structure of industrial economies, and it will require concerted global policy responses across a wide range of stakeholders and systems. Global antimicrobial use in animals is three times that of humans, contributing to the spread of resistant genes and zoonotic drug-resistant pathogens (Van Boeckel et al. 2019). Current trends suggest that livestock intensification will increase dramatically over the next few decades in low- and middle-income countries to meet rising consumer demand for animal protein, and this growth will dramatically increase animal antimicrobial use (FAO, 2013).

Global policy documents focus heavily on the need to limit or ban animal growth promoters as well the use of critically important human antibiotics in the veterinary sector. The World Health Organization (WHO) recently published new guidelines for how member states can reduce veterinary antimicrobials; it developed a high-level Global Action Plan on AMR endorsed by the UN General Assembly, and it supported 133 national AMR action plans (WHO, 2015; 2017; IACG, 2019). To move these global plans forward into national policies and mechanisms for action, multi-sectoral national AMR taskforces have been established in many countries. To be effective, these will need to address uncertainties, political conflicts and difficult decision-making trade-offs. In many countries, however, only a rough roadmap currently exists for the livestock sector, with very little commitment and a lack of clarity on how to move far-reaching "wish-lists" forward into implementation. Successful AMR mitigation is far from certain.

As low- and middle-income countries undergo 21st century transformations, AMR emergence in the livestock sector will be intimately connected to complex forces of social, cultural, political, economic, technological, climatic, and ecological change. A few initiatives have attempted to integrate strategic thinking and planning into AMR. The FAO Africa Sustainable Livestock 2050 project used scenario planning to guide futures thinking in the livestock sector with activities in six countries, and this included some work on AMR. In this case, scenarios were developed based on large-scale economic and political forces that described broad changes to all aspects of the livestock sector. Another approach, taken by the WHO South East Asia Regional Office

(SEARO), was more linked to monitoring and evaluation. SEARO developed a system-wide analysis tool for all aspects of AMR, with the goal of using multisectoral reviews to identify country vulnerabilities, implementation stages and to evaluate progress (Kakkar et al. 2017).

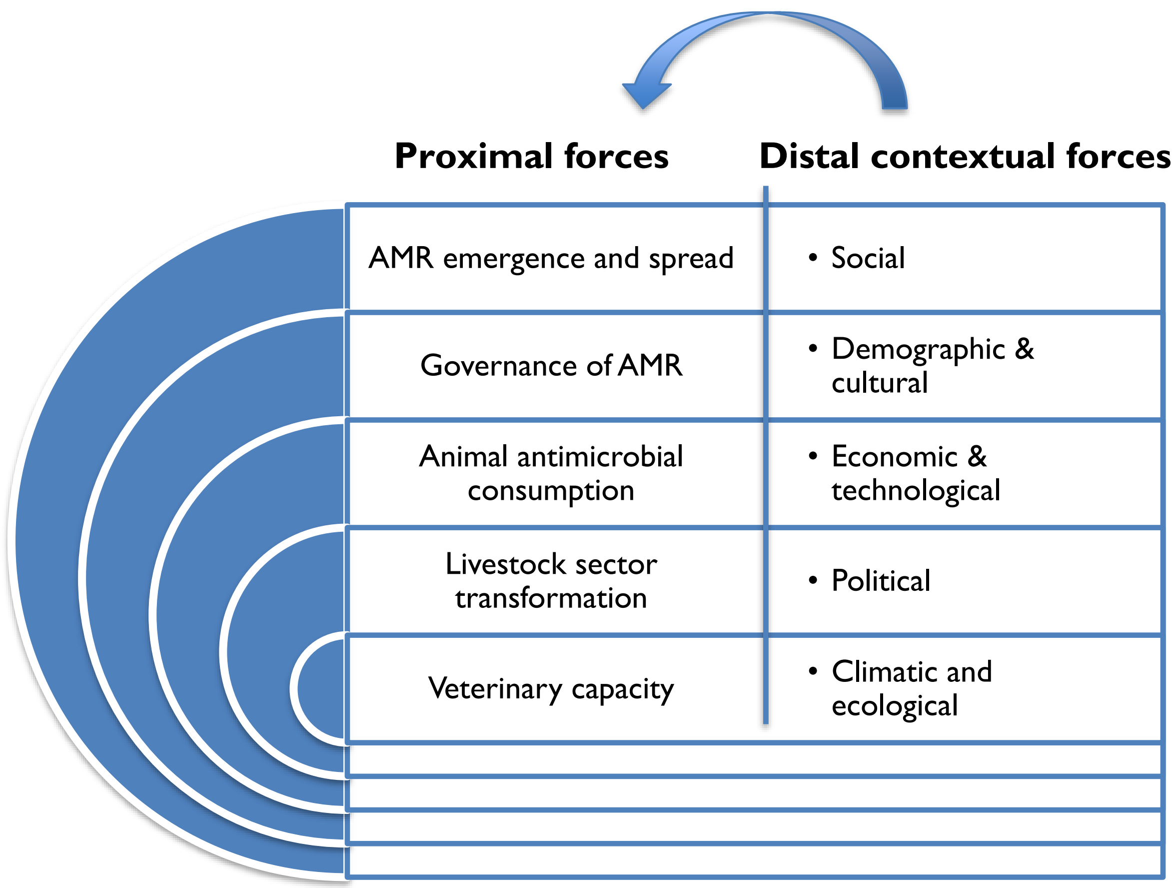

Figure 1: Future uncertainties for the livestock policy-AMR interface

We propose a slightly different approach that aims to integrate scenario planning with pragmatic policy review and strategy development. As part of this approach, outlined in a forthcoming manual, we have identified five proximal, thematic uncertainties that will be influenced by distal forces to shape antimicrobial resistance policy and response in the livestock sector in low- and middle-income countries in the coming decades (see Figure 1). We argue that integrating aspects of foresight and futures techniques into livestock and public health policymaking can contribute to strengthening strategic planning. Awareness about these uncertainties should serve as anchors for contemporary debate and decision-making, balancing the need to protect human health, access to animal proteins, livelihoods, and ecosystems. Such an approach could be integrated with ongoing activities of national multi-sectoral AMR task forces and contribute to National Action Plans.

Foresight and futures: a brief introduction

Foresight is an umbrella term for future exploring, predicting and visioning methods. These approaches often take uncertainty as a starting point in order to challenge our preconceptions about the future, current trends and accepted mental models or dogma (Gidley, 2017; Peterson, 2003). Futurists use the plural term “futures” to denote the potential for many alternative futures: some possible, plausible, probable or preferred (Inayatullah, 2008; Voros, 2001).

Although the roots of foresight are grounded in the business and military use of scenario planning (Schwartz, 2012; Schoemaker, 1995), it has increasingly been adapted to the field of global public goods (trans-national problems of immense complexity and scale), including science and research for development and health. There are many foresight frameworks, methods and techniques (Popper, 2008), including practical toolkits developed by the Government Office for Science (GO-Science) Futures Toolkit UK[1] and a guide from UNDP.[2] An overview of common methods is provided in Box 1.

In general, these approaches recognize five interdependent phases to foresight activities: 1) gathering and analyzing intelligence, 2) exploring change dynamics, 3) describing possible futures, 4) testing policy and strategy against those futures to evaluate levels of resilience, and 5) applying the results to strategic planning.

Many foresight methods are built around imaginative thinking in a creative group process that explores different possibilities and negotiates values and interests, with the goal of creating more resilient policy and planning. However, systematic facilitation, design and support (both financial and professional) is incredibly important to avoid poorly defined recommendations that achieve very limited practical impact and are summarily dismissed as a “cute” abstraction (Bowman et al. 2013; Lame et al. 2019). Cultural context and bureaucratic structure and processes are essential considerations, and the quality of the foresight process can be greatly improved by considering these while ensuring ownership and buy-in among key stakeholders. The foresight approach should be linked to policy cycles and longer-term strategic decision-making processes in a country or region. It needs to be taken seriously to contribute thoughtfully to the policy landscape. Note, however, that if well done then even short workshops can be incredibly fruitful and impactful, depending on the organization and network involved.

Scenario planning is the most widely known and emblematic technique of the foresight repertoire. A scenario is a story illustrating visions of a possible future. Scenario planning typically takes place with a small group of actors in a series of workshops, where participants develop four distinct futures, each with a name and compelling narrative (Peterson, 2003). Early on, this involves mapping basic trends and driving forces of the policy problem and identifying key

[1] The Futures Toolkit: Tools for Futures Thinking and Foresight Across UK Government. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/674209/futures-toolkit-edition-1.pdf

[2] Foresight Manual: Empowered Futures for the 2030 Agenda. www.undp.org/content/dam/undp/library/capacity-development/English/Singapore%20Centre/UNDP_ForesightManual_2018.pdf

uncertainties (Inayatullah, 2008). Driving forces help us look past the everyday mental models that frame the contours of our thoughts so that we may examine long-term, hidden and powerful forces through what is called "the axis of uncertainty."

BOX 1: Repertoire of common foresight methods [3]

Tools for gathering intelligence about the future:

- **Horizon Scanning** involves looking for early warning signs of change.
- **7 Questions** is an interview technique for gathering insights from a range of stakeholders.

Tools for exploring the dynamics of change:

- **Driver Mapping** is used to explore political, economic, societal, technological, legislative and environmental drivers that will shape the future policy ecosystem.
- **Axes of Uncertainty** are used to define critical uncertainties, used in scenarios.

Tools that describe what the future may look like:

- **Scenarios** are stories that describe alternative futures, used to explore the resilience of policy and strategy under these different conditions.
- **Visioning** is used to describe what the future will be like if specific project aims and objectives are met.
- **SWOT Analysis** explores strengths, weaknesses, opportunities and threats.
- **Causal Layered Analysis** identifies driving forces and worldviews underpinning diverse perspectives about the future.

Tools for testing policy and strategy

- **Policy Stress-Testing** tests policy, strategy or project objectives against a set of scenarios.
- **Back Casting** is a method for determining the steps that need to be taken to deliver a preferred future.
- **Road Mapping** shows how different inputs will combine to shape future development of policy or strategy.

To develop the scenarios, these forces are reduced to two of the most important. Once this is complete, the driving forces should be displayed on two (x,y) axes to assess each force. These can include alternating control/absence of control, certain/uncertain and/or high/low impact polarities. The four axis are used so that four very different, but plausible, uncertainty quadrants can be defined. This is shown in **Figure 2.**

[3] This has been adapted from *Foresight Manual: Empowering Futures for the 2030 Agenda*, available at: www.undp.org/content/dam/undp/library/capacity-development/English/Singapore%20Centre/UNDP_ForesightManual_2018.pdf

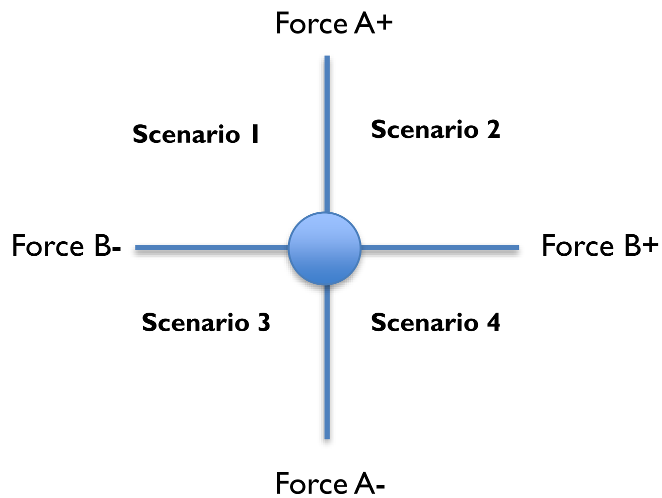

Figure 2: Schematic of an axis of uncertainty used in scenario planning

Coons (2019) outlined a framework of four essential components of powerful scenarios: they draw people into the story, and are enjoyable, realistic and challenge conventional thinking. They should illustrate dynamic stories that capture the uncertainties of a system, its conflicts and interactions while challenging our beliefs, our perspectives and our normative values about the world and our place in it. The narratives behind these scenarios tend to be very similar, with winners and losers, cycles, revolution and evolution, and archetypes, often written in a mythological style and narrative (Schwartz, 1991; Coons, 2019). With beginnings, middles and ends, this makes the scenario stories more digestible and easier to believe. Scenarios are often considered to be most effective when they engage issues with high uncertainty, low controllability and for periods of at least 10 years (or more) into the future.

According to Chermack (2011), scenario planning as a process to change organizational strategy should involve a series of steps that include dialogue, learning, decision-making, challenging mental models and supporting leadership. In this sense, each driver, uncertainty and change in the system should be explored from the perspective of actors within these systems. Scenarios should inspire us to prepare for future challenges. They represent "scaffolding" for sense-making, dialogue and innovation (van der Heijden, 2011).

In the sections below, we outline five critical uncertainties that AMR policymakers will need to contend with as they adapt to stresses and drivers that will impact AMR emergence and policy in the livestock sector in the coming decades. Instead of focusing on broader contextual drivers, such as economic growth, climate change and political change, we focus on these more proximal and specific thematic uncertainties and orientate the analysis to low- and middle-income countries. In each case, we provide a short sample of what these uncertainties may look like, which could serve as the x or y axis in a scenario. These can be used in subsequent scenario planning and foresight exercises as a way to link futures thinking with pragmatic policymaking and activities.

Uncertainty 1: Scale of the AMR problem

Although antimicrobial resistance was documented as far back as the 1940s, the 1990s saw a dramatic change in scope. Today, an estimated 700,000 people die annually from resistant organisms, including 35,000 (from nearly 3 million infections) in the United States alone (CDC, 2019). According to a high-level UK report released in 2014, upwards of 10 million people globally may die annually from AMR by 2050 (O'Neil, 2014). The World Bank has called AMR a "tragedy of the commons" and a "grave threat to our future" (World Bank, 2017). Common diseases may once again become bearers of early mortality and severe morbidity, straining vulnerable health systems and generating new risks for routine medical procedures, such as surgery. Resistance affects nearly all pathogens where antimicrobial treatment exists (including HIV/AIDS, TB, malaria, gonorrhea, etc.), including foodborne and zoonotic diseases such as *Salmonella*, *Campylobacter* and *E. coli*.

Most discussions about AMR predict that the problem is going to rapidly get worse, although others point to the large variability in model estimates and the compounding challenges of generating accurate data (de Kraker et al. 2016).[4] So this is the first critical uncertainty: how bad is the AMR problem going to get?

Critical uncertainty 1: The scale of the AMR crisis

<u>Future 1:</u> AMR emergence leads to new global pandemics with high numbers of human deaths that are linked directly to animal antimicrobial consumption.

<u>Future 2:</u> AMR emergence is slow, and the role of animals is not seen as a major problem compared to the challenges of hospital-acquired infections.

The future of AMR is intimately linked to scientific research that makes the invisible visible. The link between antibiotic use in food animals and the development of AMR in humans is somewhat controversial and the science is complex (Kahn 2016). Antibiotics are poorly adsorbed in the gut of most people and livestock (pig, chickens, cattle, etc.) and are excreted in feces and urine in large quantities (Landers et al. 2012). This waste contaminates nearby water and soil with residues and genes that are spread in the environment (Davis et al. 2011; Sarmah et al. 2006). Meat processing in slaughterhouses and unhygienic food preparation can also spread resistant microbes to people. Wildlife, especially birds, carry resistant genes around the world during their migrations. And poor hygiene, overcrowding, food safety and structural conditions of poverty are

[4] de Kraker et al. (2016), however, questioned these estimates, arguing that they were based on questionable data and variable assumptions, which highlights the challenges with ascribing AMR to specific mortality and morbidity events in the face of limited surveillance systems. Much of the literature focuses on gonorrhea, *E. coli,* MRSA and *K pneumonia* (Laxminarayan et al. 2013).

also important factors in the global "resistome", which encompasses a huge variety of socio-ecological drivers.

The assumption that reducing antibiotic use in farm animals will reduce antibiotic resistance in humans has been well documented in a number of cases, including with the development of resistance to streptothricins and glycopeptides in Europe and colistin in China (Webb et al. 2017). A meta-analysis of > 900 prevalence studies over the last 20 years found that the rates of resistance (of *Escherichia coli*, *Campylobacter* spp., nontyphoidal *Salmonella spp*., and *Staphylococcus aureus*) found in livestock were increasing globally (Van Boeckel et al. 2019). There are simultaneous increases in resistance among many medically important antibiotics, including ciprofloxacin and erythromycin and third- and fourth-generation cephalosporins. Innes et al. (2020) calculated the external societal costs of AMR in humans attributed to use in livestock as US$1,500 per kilogram of fluoroquinolones administered in broiler chicken production in the United States. However, for many pathogens and drugs, these human and environmental links are poorly understood, and it is not clear what proportion of the AMR burden in humans can be attributed to agriculture (Woolhouse et al. 2015). Future AMR burden and emergence as well as our ability to track the causal connections between AMR in humans and animals will play an important role in determining future policy and social response.

Uncertainty 2: Governance of AMR

The AMR crisis involves a series of conflicting societal tensions and interests that present distinct challenges to global and national governance and institutions (Rochford et al. 2018). For example, policies aimed at "protecting" human antibiotics must be designed to account for the fact that millions of people die each year from a *lack* of access to essential antimicrobials (Carlet and Pittet, 2013). Many farmers in low- and middle-income countries have financial and access constraints to veterinary care that lead them to disregard (often unenforced) laws to care for their animals, which are the basis of their livelihood. As with human medicine, antibiotic usage is intrinsic to the production systems of modern animal farming, food safety and access to animal protein. During the Cold War, American and Soviet policymakers and scientists celebrated agricultural antibiotics, often given at sub-optimal dose levels, as a sound way to enhance animal productivity and ensure cheap meat, milk and eggs for their growing economies (Kirchhelle, 2018). This creates a central tension in governing AMR in the animal sector: livestock farmers and veterinarians want to avoid being blamed for AMR in humans but are also expected to ensure access to animal protein, animal welfare and food safety. The medical community is reticent to engage in the animal farming sector and believe the AMR problem in humans should focus on human consumption and hospital-acquired infections (Hinchliffe et al. 2018).

The source of the problem (across humans, animals, environments) can, at times, appear too complex and too diffuse contributing to AMR falling between the gaps and being ignored or dismissed. Because it requires a multi-sectoral approach, grounded in the idea of One Health, this too can become a policymaking roadblock (Bardosh et al. 2017). Different decision-making groups will have different priorities and emphases, even different conceptualizations, of what

AMR is, what should be done and how it should be done. Different countries also have different cultures of policymaking and ideas of what global regulations or mechanisms should be supported (Begemann et al. 2018). Strong lobbying groups, including farming associations, have an interest in delaying or questioning bans or enforceable regulatory policy frameworks. In 2017, the United States Department of Agriculture stated that WHO guidelines for restricting antibiotic use in agriculture were "not supported by sound science…erroneously conflating disease prevention with growth promotion in animals."[5] All of this has implications for trade, economic growth, sustainable development and governance.

Critical uncertainty 2: The governance of the AMR crisis

Future 1: Strong international leadership generates a global antimicrobial regulatory framework and country level multi-sectoral One Health tasks forces achieve significant domestic buy-in and traction.

Future 2: AMR has fallen off the global radar, with a patchwork of disjointed efforts with little enforceability; country efforts are completely dependent on donors.

A global plan for reducing antibiotic consumption only really emerged in 2015, with the World Health Assembly's endorsement of a WHO action plan, and support from an international tripartite (WHO, FAO, OIE). Since then, national action plans have been established in 135 countries, and monitoring and evaluation frameworks developed and R&D accelerated through public-private partnerships, such as the Global Antibiotic Research and Development (GARDP). The focus of these efforts is on appropriate use of antibiotics/antimicrobials in animals and humans and strengthening surveillance, research, public awareness, behavior change, infection prevention control (IPC) and water, sanitation and hygiene (WaSH), and developing new technologies while ensuring access to current antimicrobials for the most vulnerable (Rochford et al. 2018).

However, the current governance landscape is a patchwork of global regulation that lacks long-term institutionalization. Some argue that national regulations on antimicrobial use will have limited impact outside a globally agreement regulatory framework (Kirchhelle, 2018) and that, while it is easy to sign accords, addressing the AMR challenge will require regulating supply chains with clearly defined goals and transparent surveillance and evaluations, which should include international legal agreements, regulatory framework and/or an AMR commission (Rochford et al. 2018). On the other hand, there are calls for greater localization of AMR policy away from a donor-driven agenda, which defined many NAPs, and towards a "stepwise approach" to national plans through multisectoral national task forces that prioritize activities according to each country

[5] USDA Chief Scientist Statement on WHO Guidelines on Antibiotics. https://www.usda.gov/media/press-releases/2017/11/07/usda-chief-scientist-statement-who-guidelinesgpa-antibiotics

(Laxminarayan et al. 2013). This includes food safety regulatory bodies at the national level as well as general zoonotic disease control surveillance and prevention.

Uncertainty 3: Animal antimicrobial use

Animal antimicrobial use and policies to limit them vary greatly around the world and their change over time is a third critical uncertainty. More than two-thirds of all antimicrobial sales globally are estimated to be from the livestock sector (Van Boeckel et al. 2019; Landers et al. 2012) and usage is especially high in intensive pig and chicken production systems. Currently, most countries do not collect sales and consumption data, although the EU has now obliged member states to do so (More, 2020). Van Boeckel et al. (2015) estimated that between 2010 and 2030, the global consumption of antimicrobials would increase by 67%, rising significantly in Brazil, Russia, India, China, and South Africa. Decades of high use in the United States and Europe have plateaued or declined slightly, but they are still significantly higher than most LMICs and well-above levels observed in the 1960s. The trajectory of antimicrobial consumption patterns and the types of policies that will be put into place by different countries is highly uncertain.

There are twelve classes of antimicrobials that can be used in farm animals[6]; while some of these are not used in human medicine, others such as tetracyclines, penicillins and sulfonamides are widely used in both humans and animals (Grace, 2012). Antibiotics are used in the farm sector for therapeutic and preventive use, to improve feed efficiency and as growth promoters. Practices and doses range widely. Low-dose blanket antibiotic use for growth promotion has become indispensable for many large-scale farms, supporting early weaning, higher animal density, cheap feed and compensating for otherwise poor hygiene conditions. Sub-therapeutic doses and preventive use control specific diseases among group of animals or at times of stress, like during weaning and transport.

Critical uncertainty 3: Antimicrobial consumption

Future 1: Antimicrobial consumption in animals reduces dramatically through well-designed restrictions and bans, especially for priority human drugs on the WHO list of critically important antimicrobials (CIA) list, and antibiotic alternatives.

Future 2: Antimicrobial consumption in animals increases dramatically with livestock intensification and a lack of restrictions and bans, including with priority human drugs on the CIA list, and antibiotic alternatives do not emerge.

Research on AMR emphasizes that the majority of human and animal antimicrobial use is not necessary for a variety of reasons (Laxminarayan et al. 2013). This imbalance is because illness is

[6] This includes: arsenicals, polypeptides, glycolipids, tetracyclines, elfamycins, macrolides, lincosamides, polyethers, beta-lactams, quinoxalines, streptogramins, and sulphonamides (Landers et al. 2012).

incorrectly diagnosed and prescribed for, and for the livestock sector, it is due to the use of sub-optimal dosage animal growth promoters (AGPs). From the perspective of the medical community, a worldwide ban on AGPs is often presented as an urgent imperative, but the need to balance access to cheap protein with veterinary care makes this issue much more complicated. Globally, substandard and counterfeit drugs, including veterinary antimicrobials, are a major issue (Kingsley, 2015). All of this has made WHO's critically important antimicrobials (CIA) list controversial as countries like China and India (which manufacture most drugs) have resisted efforts at regulation.

The first ban on AGP was implemented by Sweden in 1986 and was followed by an EU-wide ban on avoparcin in 1997 (Kirchhelle, 2018). This occurred during the Mad Cow disease scare of the late 1990s that shed significant light on the ethical and health implications of industrial animal agriculture. In 2006, and relying on the precautionary principle, a full ban on AGPs was instigated in the EU and laws requiring a prescription for all veterinary antimicrobials (More, 2020). Other countries have followed suit; Vietnam is planning to ban AGPs in 2020, Russia has restricted all AGPs that are used in humans, and Brazil and China have banned colistin (Kirchhelle, 2018). The US has been more concerned about milk residuals and, instead of outright restrictions and bans, has initiated a voluntary industry-driven phase-out of medically important AGPs (Kahn, 2016).

In general, restrictions on AGPs in developed countries have not shown long-term detrimental effects on livestock industries (Maron et al. 2013). Evidence from Scandinavia shows these effects have been short-term and mitigated by adapted farm practices such as later weaning, improved diet and reduced stock densities, which have also dramatically reduced *Salmonella* rates in poultry (Maron et al. 2013). In some contexts, bans have been easy to circumnavigate. In Sweden, initial restrictions on AGPs led some producers to replace them with higher-dose prophylactics as they struggled to adapt, at least in the short-term. In China, the domestic colistin ban resulted in thousands of tons being exported to other Asian countries.

Studies on stewardship interventions aimed at reducing antibiotic usage in animals are relatively few. Wilkinson et al. (2019) could not find any animal health intervention studies that evaluated changes in antibiotic prescriptions in low- and middle-income countries. A study in Denmark, Portugal, and Switzerland found that veterinarians appeared to favor mandatory and regulatory interventions to limit antimicrobial usage (Carmo et al. 2018). Moran (2019) argued for the need to develop a prioritization framework to evaluate cost-effectiveness of interventions. A meta-analysis by Tang et al. (2017) on AMR interventions in animals focused largely on high-income countries and found that restricted antibiotic use caused a 10-15% reduction in absolute risk of AMR in humans, depending on antibiotic class, bacteria and social group. In high-income countries, such as France, some have questioned whether the initial antimicrobial reductions will be sustainable (Fortane, 2019). A final consideration is the possible development of new technologies (such as bacteriophages, non-microbial growth promoters and pro/pre-biotics) that may reduce the need for antimicrobials in animal faming.

Uncertainty 4: livestock sector transformations

Future trajectories and policy responses to AMR will be influenced by changes in the livestock sector and food systems. Currently, the 7.7 billion people on this planet consume an estimated 80 billion animals each year and 800 million tons of milk; at any given moment, an estimated 24 billion chickens, 700 million swine and 1.5 billion cows are alive.[7] Over the past 20 years, meat consumption has remained relatively consistent in high-income countries but increased by 68%, 64% and 40% in Asia, Africa and South America, according to FAO (2017) (cited in Van Boeckel et al. 2019). FAO's (2013) livestock report estimated that from 2010 to 2050, global meat consumption would increase by 73%. Van Boeckel et al. (2019) called the increasing demand for animal protein from low- and middle-income countries to be one of the defining features of the 21st century.

The expansion of livestock farming is intimately linked with various forces of the Anthropocene Epoch: urbanization, industrialization, capital accumulation, global supply chains, pollution, etc. (Whitmee et al. 2015). With decreasing biodiversity in animals and plants, the world is increasingly dominated by humans, their pets and food animals, and ecosystems are fragmenting, stressed and under threat of collapse. Climate change projections show a disproportionate effect in Africa by 2050 due to heat stress, drought and flooding (Jones and Thornton, 2009). Human population is expected to rise to 10 billion by 2050, with more people living in cities and towns than ever before. A recent spatial analysis of AMR studies in animals found that travel time to cities was the leading factor for resistance, likely due to the proximity to veterinary drug suppliers (Van Boeckel et al. 2019).

Critical uncertainty 4: Livestock sector transformations

Future 1: Increasing consumer demand for animal protein drives substantial consolidation of animal farming into intensive, large-scale industrial factory farms.

Future 2: Increases in consumer demand for animal protein are not as drastic as predicted, allowing for pro-poor policies to support a wide-range of agricultural changes that benefit small and medium-sized livestock-keepers.

While efforts are made to diversify protein sources to insects and protein substitutes, it is highly likely that this growing demand will be met by expanding intensification of livestock, with the goal of cheap meat, dairy and eggs. The cost of livestock sector inputs (feed, housing, breeds, drugs) will be critical for producers and consumers. Public awareness of AMR and increasing demand for antibiotic-free meat could play a mitigating role, albeit this niche market took decades to develop in the United States and Europe. Beef and poultry raised in intensive systems cost significantly less than free-ranging grass-fed animals currently being sold mostly in high-end grocery shops (Kahn,

[7] https://ourworldindata.org/meat-production

2016). The structure of consumer demand and animal farming will be shaped by shifting geopolitical, ideological and macroeconomic forces, as they did in earlier transformations of livestock industries in the 1950s in both the United States and the Soviet Union (Kirchhelle, 2018).

Intensification may shift livestock farming and rural economies away from indigenous practices. Groot and Hooft (2016) noted that focusing only on production of milk per cow per year (sometimes called the "holsteinization" of dairy farming) can have serious effects on animal health, increase agro-chemicals and environmental impacts, and reduce milk quality for consumption. Intensification will have an impact on pasture management, biodiversity, animal genetic diversity, animal disease prevalence and the level of demand for inputs and drugs (Groot and van't Hooft, 2016). Expansion of extension services, income and education are likely to increase antibiotic usage in animals. Low- and middle-income countries may see an exponential growth in concentrated animal feeding operations (CAFOs). These already number hundreds of thousands in the United States and China, where millions of tons of animal feces are produced each year, contaminating nearby air and water and contributing to the spread of AMR and other health problems. On the other hand, focusing on improving livestock production can also reduce antimicrobial use. Pro-poor policies focused on protecting and strengthening rural livelihoods, supporting local veterinary services, revitalization of ethno-veterinary knowledge and husbandry practices, supporting farmer awareness and learning, and wide-ranging vaccination and parasite control would all have positive benefits in reducing overconsumption of antimicrobials. In some EU countries, antibiotics in animals have dropped by 30-40%, with biosecurity measures playing an important role (More, 2020). However, AMR control may also have unintended financial consequences for smaller farms, which may struggle to adapt. The future may involve substantial consolidation of livestock industry conglomerates with an assortment of changes to the culture of the countryside, pastoralist systems, ecosystem health and rural life.

Uncertainty 5: Veterinary service capacity reform

Veterinary service capacity, including animal surveillance, is a final overarching development to consider in thinking about the future of AMR. In many low- and middle-income countries, surveillance and extension services are extremely limited. Whereas surveillance systems exist in many countries for AMR in humans, including the WHO's Global Antimicrobial Resistance Surveillance System (GLASS), there are limited reporting frameworks for AMR in animals—at least outside Europe and North America. The EU has outlined a harmonized surveillance program focused on collecting samples from poultry and cattle for *E. coli*, *Salmonella* and ESBL/AmpC beta-lactamase/carbapenemase testing (More, 2020). In Vietnam, Mitchell et al. (2020) found a near complete lack of surveillance in the animal health sector for One Health and AMR issues (Mitchell et al. 2020). Diagnostic infrastructure, training and supply networks are all important to building lab capacities.

In many countries, veterinary services are an under-funded cousin of the health sector and an overlooked component of the agricultural sector. An amorphous mixture of public, private and paraprofessional providers exist. Disjointed and only partially enacted regulations oversee the distribution and use of animal antimicrobials and livestock extension services (Leonard, 2000; Chauhan et al. 2018). Disease outbreaks are regularly addressed by central governments, but most services are decentralized, creating challenges in planning, funding and implementation. Veterinary public health systems and risk-based management, for milk and abattoir quality control and movement control of infected animals and quarantine, are important components to these systems.

Critical uncertainty 5: Veterinary service capacity reform

Future 1: The capacity for veterinary services increases significantly in low- and middle-income countries, including professional standards, regulation, training and national surveillance capacity.

Future 2: The capacity for veterinary services decreases in low- and middle-income countries and current standards of professionalism stagnant or decline with negative results on regulation, training and national surveillance.

In many cases, AGP bans in Europe and North America have been integrated with efforts to reform veterinary services, animal welfare laws, movement controls, farmer cooperatives, food safety, regulation and microbiological lab surveillance. Groot et al. (2016) and others have called for an integrated national livestock farming approach to reduce antimicrobial use in the farming sector, with a focus on leadership, commitment and funding (Laxminarayan et al. 2013). In most low- and middle-income countries, however, there are no current laws, standards or guidelines to control the use of animal antimicrobials (Phares et al. 2020). How feasible will comprehensive and integrated veterinary service reform be in the coming decades and how will this influence AMR?

Outside towns and cities, access to veterinary inputs and market chains are often weak. Where they exist, veterinary prescription practices are embedded within conflicting pressures and forces: professional obligation, therapeutic expectations, financial dependency, risk avoidance, advisory and diagnostic skills, financial barriers, legal guidelines, farmer compliance to recommendations, public health interests, personal beliefs, etc. (Fortane, 2019; Speksnijder et al. 2015). Veterinarians need incentives and payment structures to change unnecessary prescriptions, including monetary caps on veterinary sales, dividing prescription and dispensing and an accountability system (public disclosure) to limit farm antimicrobial usage, as done in Scandinavia.

Discussion and conclusion

We have identified five proximal critical uncertainties that will be influenced by contextual forces to shape antimicrobial resistance policy and response in the livestock sector in low- and middle-income countries in the coming decades. Using these five uncertainties to guide foresight and futures exercises may be helpful to livestock, veterinary and public health policymaking and contribute to improving strategic planning for AMR. This approach does not exclude brainstorming and engagement with distal contextual forces, such as economic growth, climate change and political change, but aims to ground them to these AMR-specific issues and themes. We outline this approach in a forthcoming manual.

While scenarios are increasingly popular management techniques, theoretical and methodological case studies that evaluate their effectiveness are surprisingly few (Bowman et al. 2013; Lame et al. 2019). Are scenarios the most appropriate method for achieving the goals of foresight for AMR policymaking in the livestock sector in low- and middle-income countries? To choose an old adage: when you have a hammer, everything looks like a nail. This is an important methodological and practical question. The repertoire of foresight methods beyond scenarios is rich (Popper, 2008; Box 1) and there are many ways these techniques could be modified. There are also ways that these critical AMR uncertainties could be discussed and integrated with existing AMR monitoring and evaluation tools (Kakkar et al. 2017) and the activities of multi-sectoral AMR task forces.

The future of AMR as a global health crisis is emergent and yet to be decided. Predictions and trends present a worrisome picture, however, and historical examples and current realities from Europe and North America offer mixed guidance and hope, at best. Growing demand for meat, dairy and eggs is a result of expanding socio-economic change and reductions in poverty and should be celebrated. Future trajectories are highly uncertain, however, and the weak signals of war, automation/artificial intelligence or catastrophic climate change cannot be ignored in any futurist analysis.

Our discussion of five critical uncertainties in AMR has been focused on proximal rather than the more common emphasis on distal forces. This has allowed us to raise a series of pertinent questions for strategic planning today: how will changes in livestock intensification and rural livelihoods impact antimicrobial consumption? How will veterinary drug markets and regulations change? Will the emergence of resistant pathogens in humans put greater pressure on the livestock sector to ban certain antimicrobials? How will countries balance the need for cheap meat, dairy and milk with AMR policy decisions and interventions? Will comprehensive global governance frameworks be introduced, or will countries be left largely on their own? And what will happen to veterinary surveillance and food safety systems? These are questions that need to be asked in the present. Engaging with them, in acts of creative and imaginative group thinking, should help expand the mental models we use to think about the AMR problem. This could have far-reaching consequences, given the dire warnings of an impending post-antibiotic era.

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