Antibiotic resistance and One Health: A mapping project in KwaZulu-Natal, South Africa

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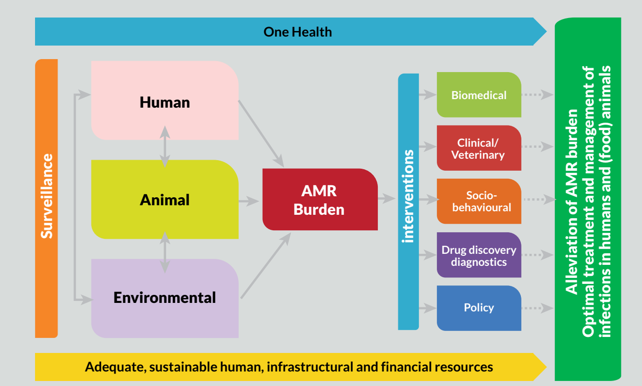
Since their introduction into clinical practice in the 1930s and 1940s, antibiotics have revolutionized global public health by substantially decreasing the morbidity and mortality associated with bacterial infections in humans and animals *(1)*. Antibiotics have saved innumerable lives and made possible major surgery, organ transplantation, treatment of pre-term babies and cancer chemotherapy *(2)*. Antibiotics have further advanced food security and food safety. However, infectious diseases remain the leading cause of death, particularly in low- and middle-income countries and increasingly as a result of antibiotic resistance (ABR).

ABR is a direct consequence of the selection pressure from warranted and indiscriminate antibiotic use in humans, (food) animals and the environment. ABR has been described as the "quintessential One Health issue" as it exists in each sector, but the relative roles of the three sectors in the development, transmission and persistence of ABR genes is yet to be elaborated *(3)*. Antibiotics used in humans and animals are frequently analogues which potentially drives transmission of resistance between people and animals and there is a growing body of evidence that links antibiotic consumption in livestock to ABR in the clinic *(3, 4)*. The burden of ABR is least well understood in environmental health. Environmental bacteria which are quantitatively the most prevalent bacteria serve as sources of resistance genes that can become incorporated into human and animal pathogens over time. This natural phenomenon is exacerbated by the influx of resistance genes from livestock and human waste into the environment as well as the entry of antibiotic residues from pharmaceutical industries, intensive livestock farming and hospitals that disrupt the soil and water microflora in addition to exerting selection pressure for the development of resistance. It is thus important to understand the relative importance of each sector in the evolution of resistant bacteria and the genetic determinants of resistance, their interactions and transmission routes *(3)*.

The aim of the ABR and One Health project is to delineate the molecular epidemiology, nature and extent of ABR in human, animal and environmental health to map the fluidity of antibiotic resistant bacterial clones, antibiotic resistance genes and their associated mobile genetic elements (MGEs) within and between the human, animal and environmental

Figure 1: Illustrates the conceptual framework



hospital, one tertiary hospital, two specialized TB hospitals and three specialized psychiatric hospitals . The human health study sites consist of the four non-specialized hospitals and three community health centres (CHCs). A pig and a poultry farm, with their associated abattoirs, form the food animal study sites. The influent and effluent from a waste water treatment plant receiving waste water from the healthcare facilities and farms together with surface water upstream and downstream from the plant constitute the environmental water samples. Soil fertilized with chicken litter serves as the environmental soil samples.

Using the WHO Surveillance standards for antimicrobial resistance *(5)* and the "Global Antimicrobial Surveillance System (GLASS)" *(6)*, passive, sentinel and comprehensive surveillance of specific pathogens was implemented for three months each at community and hospital levels in blood stream infections (BSIs), urinary tract infections (UTIs) and acute diarrhoea in order to ascertain the most cost effective and technically feasible surveillance strategy yielding reliable, representative ABR data within a financially constrained public healthcare system. The pathogens of interest for BSIs were *E. coli, K. pneumoniae, Salmonella spp., S. aureus, S. pneumonia* and *Acinetobacter spp., E coli* and *K. pneumoniae* were investigated in UTIs and *Salmonella spp.* and *Shigella spp.* in diarrhoea. Preliminary results show statistically significant differences in antibiotic resistance in descending order of passive, sentinel and comprehensive surveillance highlighting the need for CHC/hospital-specific antibiograms from comprehensive surveillance to inform treatment decisions. It was further evident that the existing nationally-determined standard treatment guidelines and associated essential medicines lists for infections would not be consistently effective because of the diverse case mix and burden of infectious diseases in different districts and indeed different healthcare facilities in the districts.

ABR surveillance in intensively farmed food animals took the form of the WHO Integrated surveillance of antimicrobial resistance: Application of a One Health approach *(7)* where an ABR surveillance programme was instituted in indicator bacteria across the food production chain, from "farm-to-fork". This encompassed litter and faecal samples from animals on the farm, crate and transport vehicle swabs from holding areas, caecal samples, carcass rinsates and carcass swabs post slaughter and swabs from retailed meats. Preliminary results do not indicate bacterial transmission across the food chain in the vast majority of indicator bacteria with unique clones and diverse antibiograms evident across the continuum.

ABR surveillance in water ascertained the quantity and resistance phenotypes and genotypes of *E. coli* and *Enterococci* as indicator bacteria from influent, effluent and surface water samples that were collected bi-monthly. Raw litter, raw soil and soil fertilized with litter was monitored on day 0, 1, 3, 7, 14 and bi-monthly thereafter until no growth of the indicator bacteria was evident on three consecutive sampling events. Environmental surveillance is ongoing and results from the triangulation of resistance phenotypes and genotypes in *E. coli* and *Enterococci* from the three sectors is imminent.

It is anticipated that the project will:

- launch an electronic platform that will triangulate, in real time trends in antibiotic resistance from robust, representative One Health surveillance programmes;
- allow early identification of emerging/escalating resistance within and between sectors;
- establish a database for evidence-based treatment guidelines and associated essential medicines lists for the optimal management of infections in humans and (food) animals;
- ascertain whether the surveillance of ABR in sewage and animal manure-based fertilizers could serve as suitable proxies for ABR in human, animal and environmental health;
- unambiguously give credence to the One Health approach for the containment of ABR; and
- provide "information for action" by the various sectors and their regulatory bodies.

The prevention and containment of AMR requires coordinated, multi-pronged, multi-disciplinary evidence-based One Health solutions and social compacts that suspend sectoral interests for the public good.■

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References

1. Davies J, Davies D. (2010). Origins and Evolution of Antibiotic Resistance. *Microbiology and Molecular Biology Reviews.* 74 (3): 417-433.
2. Laxminarayan R, Duse A, Wattal C, et al. (2013). Antibiotic resistance – the need for global solutions. *Lancet.* 13: 1057-1098.
3. Robinson TP, Bu DP, Carrique-Mas J, et al. (2016). Antibiotic resistance is the quintessential One Health issue. *Transactions of the Royal Society of Tropical Medicine and Hygiene.* 110: 377-380.
4. Robinson TP, Wertheim HFL, Kakkar M et al. (2016). Animal production and antimicrobial resistance in the clinic. *Lancet.* 387 (10014): e1-3.
5. World Health Organization. (2002). *Surveillance Standards for Antimicrobial Resistance.* World Health Organization, Geneva, Switzerland.
6. World Health Organization. (2014). *Global Antimicrobial Surveillance System: Manual for Early Implementation.* World Health Organization, Geneva, Switzerland.
7. World Health Organization. (2013). *Integrated Surveillance of Antimicrobial Resistance: Application of a One Health Approach.* World Health Organization, Geneva, Switzerland.