Antimicrobial Resistance (AMR) in South Asia
Addressing Current Gaps in AMR Surveillance and Monitoring

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Acronyms

AMR	Antimicrobial resistance
APUA	Alliance for the Prudent Use of Antibiotics
AST	Antibacterial susceptibility testing
DOMI	Diseases of the Most Impoverished
FAO	Food and Culture Organization of the United Nations
GARP	Global Antibiotic Resistance Partnership
INDEPTH	International Network for the Demographic Evaluation of Populations and Their Health in Under-Resourced Countries
LMICs	Low and middle-income countries
MIC	Minimal inhibitory concentration
MDR-TB	Multidrug-resistant tuberculosis
MRSA	Methicillin-resistant Staphylococcus aureus
NRLs	National Reference Laboratories
OIE	World Organisation for Animal Health (Organisation International des Epizooties)
PARN	Pakistan Antimicrobial Resistance Network
SES	Socioeconomic status
WHO	World Health Organization

Executive Summary

Antimicrobial resistance (AMR) is a global health security threat and the reliability of surveillance systems that provide accurate information is crucial. Through the use of quantitative and qualitative methodologies, the surveillance and monitoring process can provide a diagnosis of AMR within under-resourced settings in South Asia. A literature review within a scoping/narrative structure was conducted for this capstone in order to illustrate current deficiencies in AMR surveillance and monitoring for select countries in the South Asian region. This capstone project embraces the perspective that AMR surveillance is the first and most crucial step in illustrating the current burden and impact of this issue and informing change-inducing policies and interventions. The project is a global call to action on AMR surveillance in the developing world.

It was found that there is a general lack of systematic data collection regarding AMR in the region, rendering it a neglected problem within many countries. The emergence of AMR in developing nations in South Asia is a symptom of substandard surveillance practices. Pathogens that are problematic in terms of resistance are not well represented through surveillance information. Resource-related constraints and sociocultural attitudes are also problematic in terms of antibiotic use. Antibiotic misuse/overuse are important determinants as they can create environmental pressure that causes resistant strains to emerge in both humans and animals. It is often difficult to measure AMR burden in developing countries, due to biases in reporting, testing methodologies, defective legislative practices, etc.

The development of a global surveillance system that overarches local systems and increases coordination, cohesion, and comprehensiveness is recommended. The ultimate goal is to supplement the creation of a global strategy to mitigate AMR through the development of stronger surveillance systems and collaborative networks around the world. These approaches should aid with the creation of time-oriented, realistic, and visible change. The WHO report, in conjunction with this capstone project, is an important first step in highlighting the magnitude of the problem and moving towards addressing the visible gaps in AMR surveillance in South Asia and other resource-limited settings. The lack of evidence should fuel further examination of this issue and increased discussion within global health policy and practice.

1.0 Introduction

1.1 Background – What is Antimicrobial Resistance (AMR)?

Antimicrobial resistance (AMR) can be defined as the process whereby microbes become less sensitive to drugs (i.e. antibiotics); resistance occurs when an antibiotic is no longer effective against infections caused by a particular microorganism (WHO, 2015a). Infections that become resistant have negative effects on mortality, treatment costs, spread of diseases, duration of illness and society at large (Okeke et al., 2005a; Yalcin, 2003). These effects are intensified when resources are constrained in developing settings (WHO, 2014a). Although resistance is a natural phenomenon, it is exacerbated by a variety of external factors, including antibiotic misuse/overuse (Drlica and Perlin, 2011). Patient/provider ignorance, cultural biases, health system failures, lack of knowledge/education, and a lack of resources are among factors that can contribute to antibiotic misuse and AMR (Byarugaba et al., 2010). Not adhering to prescription instructions, self-medicating with antibiotics, and sharing are examples of antibiotic misuse (Radyowijati, 2014). In addition to personal attitudes/behaviours, antibiotic use in the food supply chain and interest-based marketing by the pharmaceutical industry can dictate AMR progression (Byarugaba et al., 2010). AMR can affect anyone but the following groups are especially susceptible: young children, the elderly, and those with weakened immune systems (PHAC, 2014). These findings have important implications for susceptible populations in resource-limited settings.

Due to the dynamic nature of AMR and its dependence on a range of geographically and contextually varied factors, surveillance and monitoring of the issue becomes extremely important. Without adequate surveillance to monitor AMR levels and trends, treatment for resistance can become deficient. Without immediate

intervention, the spread of AMR can prove disastrous to the realm of infection treatment

and modern medicine at large (WHO, 2014a). Slow progress of new antibiotic

development, and limited resistance data also render it imperative to preserve current

methods of treating infections and enhance understanding of AMR (Reardon, 2014;

Appendix A; Fig. 4). Strong surveillance and monitoring systems can aid with these

components and serve as a foundation for AMR-related public health practice. In an

increasingly globalized world, the emergence and spread of resistance thus presents a

major challenge. Of particular concern for this project is AMR surveillance in select

developing countries in South Asia.

1.2   Surveillance and Monitoring of AMR

   1.2.1   The Surveillance and Monitoring Process

       Surveillance and monitoring of diseases is defined as the systematic collection,

analysis, and interpretation of health-related data; dissemination to policy-makers and

other decision-makers is an important component of this process (WHO, 2015b).

Surveillance ensures that health information is high in quality and is a useful tool for

offering timely data that can be utilized to aid with disease prevention and treatment.

Definitions of surveillance can vary at the local, national, regional, and/or international

levels (Byarugaba et al., 2010). Surveillance systems can be narrow or broad-based,

focusing on specific diseases/organisms or a broad range, respectively (Bax et al.,

2001). Due to the multidimensional nature of the surveillance process, variations within

practices can be observed across the globe.

       Understanding the organization of public health systems is essential for

effectively analyzing and monitoring health outcomes. Surveillance and monitoring, as

an applied method for assessing health, can aid with evaluating the extent of AMR.

Local, national, regional, and global surveillance strategies rely on laboratory-based

technical measurements (e.g. minimal inhibitory concentration – MIC) of resistance

through the use of patient pathogenic isolates (Drlica and Perlin, 2011). These are

important indicators for streamlining scientifically-based and targeted treatment

strategies. Thus, Drlica and Perlin (2011) term surveillance the 'first line of defense' in

preventing AMR. Surveillance results are reported back to the various stakeholders

(physicians, infection-control experts, governmental agencies, academic sector, etc.) in

order to provide a forewarning and direct future action (Drlica and Perlin, 2011).

Surveillance covers a range of purposes, including identification of resistance

outbreaks and their burden, informing public health interventions, and educating the

medical/general community (Drlica and Perlin, 2011; WHO, 2014a). Surveillance is

advantageous for preventing increased costs due to the emergence of AMR, reduced

chance of resorting to new and expensive drug development, and avoiding longer

rehabilitation for patients (Byarugaba et al., 2010). Surveillance data is also useful for

monitoring medical drug regimens and antibiotic sales, directing drug supplies, and

producing context-appropriate infection control strategies (Byarugaba et al., 2010).

Strong surveillance systems are accurate, reliable, flexible, and timely; they

should be able to efficiently pinpoint and report changes in antimicrobial susceptibility

(Bax et al., 2001). They would also be able to recognize the various factors (e.g. social,

political, scientific, economic, etc.) that inherently affect AMR data. Adaptability to the

changing AMR landscape is beneficial if surveillance systems are specifically tailored to

the environments in which they operate. In relation to this, Drlica and Perlin (2011)

outline several key questions to ask of any surveillance system: 1) Are the patient

samples representative in terms of disease severity and resistance prevalence? 2) Are

definitions of patient populations and methods within diagnostic laboratories

standardized? 3) Is the data comparable across regions? 4) Are surveillance results

relevant for community (in addition to hospital) settings? 5) Is the surveillance biased

due to the source of funding? These are significant points of inquiry as poor surveillance

can have numerous negative consequences. The WHO global report on AMR

surveillance as well as other literature cited in this capstone highlight these gaps within

South Asia and other developing settings.

1.2.2   2014 WHO Antimicrobial Resistance Global Report on Surveillance

The 2014 WHO Antimicrobial Resistance Global Report on Surveillance stems

from the need for more advanced surveillance of AMR patterns and trends. Some

current observations on the fundamental gaps in surveillance include unstandardized

methodologies/data sharing and an absence of coordination/harmonization (WHO,

2014a). Specifically, underreporting of data and a lack of a global strategy leads to

biases in data collection that tend to over-represent outbreaks and severe hospital-

based infection cases, for example (WHO, 2014a). The report places emphasis on the

need for greater surveillance of community-acquired infections as well as the

development of robust national databases. Issues of timely dissemination and

comparability of information, as well as the capacity of existing surveillance structures

(e.g. precision of pathogenic testing) are also brought to the forefront (WHO, 2014a).

These findings prioritize the need for enhancement of country-level AMR surveillance

data from regions such as South Asia.

As the WHO (2014a) states, resource-related constraints such as cost barriers

can prevent the use of expensive last-resort antimicrobial agents (i.e. carbapenems). The cycle of resistance continues whereby AMR levels increase and strategies to contain the issue become limited. The lack of data on AMR impact and high levels of antibiotic misuse accelerate the problem. Poor quality surveillance in settings with high infection rates is a major barrier to defining AMR burden (WHO, 2014a). For example, global data on gonorrhea resistance is lacking in reliability and antimalarial drug efficacy needs to be increasingly monitored (WHO, 2014a). Stronger surveillance will give heed to better estimation of the wider societal impact of such challenges.

In this report, the WHO proposes the development of a global surveillance system that would improve AMR data availability and quality. A supplementary strategy is the development of an AMR global action plan (WHO, 2014b). In order to effectively identify and classify global burdens, standardized tools and increased collaboration are necessary. The WHO (2014a) asserts the need for multisectoral/integrated surveillance as well as an enhancement of strategies to assess the socioeconomic impacts of AMR. Okeke et al. (2005b) summarize some of the WHO's key strategies for the containment of AMR, including a strengthening of global surveillance (Appendix B; Table 4). With regards to the data presented in this report, the WHO (2014a) emphasizes caution in interpreting the results, as various national/regional biases (e.g. lack of quality assurance/representativeness) may affect the quality of AMR data. Nonetheless, the report should be utilized as a tool for further development in this area (WHO, 2014a).

1.2.3 AMR, Animal Health, and Surveillance

In comparison to medical use, antibiotic use for the industrial production of food animals is disproportionately high (Drlica and Perlin, 2011). As such, increased

therapeutic guiding practices within health and agricultural sectors are essential for promoting sustainable antibiotic treatments, reduced AMR rates and improved human and animal health. A general lack of data availability for antimicrobial use in food animals hinders surveillance capacities for classifying resistance associations (Angulo et al., 2004). Assessing the development of resistance in the food chain is a beneficial multisectoral approach that allows for data sharing and comparability. Global surveillance systems that assess animal health, antibiotic use, and AMR rates and aid with appropriate interventions are necessary for pinpointing current trends.

The WHO (2014a) suggests an integrated surveillance approach that incorporates tools/standards for cohesive analysis of AMR in food-producing animals and the supply chain to humans. In line with this, WHO has formed an alliance with the Food and Agriculture Organization of the United Nations (FAO) and the World Organisation for Animal Health (OIE) that promotes collaboration, coordination, capacity-building, advocacy, and policy development between the various sectors (WHO, 2014a). As part of managing non-human antimicrobial use, inconsistencies in surveillance methodologies and gaps in system design have been observed (WHO, 2004). Weak legislations have also been ineffective at exercising control over the appropriate use of antibiotics within the animal sector in many countries (WHO, 2014c).

The OIE is involved in numerous efforts that involve the development and enhancement of global standards/guidelines for animal health/veterinary services/laboratories, training for national systems, and assisted surveillance/data collection (WHO, 2014c). While surveillance of animal health can be complicated by differing species, priorities, and contexts, collaboration with the human health sector is emphasized in order to identify common pathogens of concern (WHO, 2014c). Clinical

management of animal infections should be appropriated through enhanced mechanisms for antibiotic approval and use (Simonsen et al., 2004). Rapid data sharing and interoperability between international surveillance systems is an important element of success for preventing AMR in animals and humans in South Asia and globally.

1.3   The Situation in South Asia

South Asia, or the Indian subcontinent, is comprised of several developing countries that present tremendous health and economic burden in terms of AMR. Laxminarayan et al. (2013) point out the recent increase in sales of last-resort antibiotics in India and Pakistan. Consequentially, resistance to last-resort carbapenems can be seen in as many as ninety five percent of adults in India and Pakistan (Reardon, 2014). Some primary developing world infections in humans that are the most influenced by AMR include tuberculosis, malaria, severe acute respiratory infections, and gram-negative bacteria induced sepsis (Vernet et al., 2014). As Byarugaba et al. (2010) point out, the burden of combined/multi-drug resistance is high in developing countries; these regions are also lacking in authentic and reliable surveillance data. Currently, case studies or point-prevalence assessments provide a large portion of resistance data in these settings; systematic surveillance systems are generally not in place (Okeke et al., 2005a). The lack of surveillance has made it difficult to retrieve comparable and quantifiable baseline data that can be used to develop and monitor AMR-related interventions (Okeke et al., 2005; Falagas & Karveli, 2006).

Antibiotic usage in hospitals is high and community-acquired infections are one of the primary causes of mortality in these settings (Okeke et al., 2005a; Rosenthal et al., 2006). Ashley et al. (2011) analyzed the antibiotic susceptibility of various

pathogens from community-acquired infections in South Asian countries, finding high rates of antibiotic consumption and resistance in such areas. However, resistance reports from developing countries have variations in methods and quality of testing, which complicates the process of analysis (Ashley et al., 2011). Furthermore, poor laboratory diagnoses negatively affect the availability and reliability of AMR data (Ashley et al., 2011). In response to this, the authors emphasize the urgent need for improved laboratory methods and surveillance systems, in combination with increased centralization of information resources to improve documentation of community-acquired infections in LMICs (Ashley et al., 2011).

Selective pressure on certain antibiotics and abundant dissemination channels encourage the spread of resistance in developing areas (Okeke et al., 2005a). In addition to haphazard antibiotic use by patients and providers, a lack of human and financial resources is of concern in South Asia (Byarugaba et al., 2010). Deficiencies in isolate testing and the fact that treatment regimens are often based on clinical diagnoses instead of broader indications of resistance promote antibiotic overuse (Byarugaba et al., 2010; Reardon, 2014). Furthermore, surveillance is often not longitudinal in these regions; there is a lack of routine analysis of resistance patterns (Byarugaba et al., 2010). In South Asia, challenges in surveillance are due to many factors such as biases in reporting tactics, variations in study designs, variations in global bacterial strains, variations in patient populations and usage patterns, etc. (Byarugaba et al., 2010). These problems are often visible in developing countries and are exacerbated by an array of challenges linked to the scarcity of resources.

2.0 Project Purpose and Objectives

As Drlica and Perlin (2011, p. xv) warn,

"Our failure to adequately address resistance problems may ultimately push the control of infectious disease back to the pre-penicillin era."

This capstone serves as a key point of discussion for current limitations in understanding and addressing AMR in developing settings. The primary purpose of this project is to examine the broad range of factors that influence AMR and analyze the role of surveillance and monitoring in recognizing these elements. The objective is to demonstrate how appropriate surveillance and monitoring systems can navigate AMR data and aid with reductions in prevalence and incidence. This will be primarily achieved through analysis of ground-level data from various countries in the Indian subcontinent, including India, Pakistan, Bangladesh, and Sri Lanka. These case studies will provide a point of comparison (as per WHO recommendations) that will shed light on the potential link between resource scarcity and increased negative effects of AMR. The primary aim is to identify and assess existing needs in the health and surveillance systems of these countries in order to promote improvement in performance. An evidence-based approach will be utilized to answer the following question: What are the current gaps that exist in AMR surveillance in South Asia and how can these inform future practice-based recommendations for AMR mitigation?

3.0 Methods

The primary method for this project was a literature review that was conducted within a scoping/narrative structure in order to assess the magnitude of AMR and associated challenges in surveillance for the South Asia region. This review is an

attempt to scope/map out key concepts in the area of South Asian AMR surveillance and monitoring, while identifying gaps in the associated research. The final result is a summary of current literature on the topic that provides a narrative for understanding the complexities of AMR surveillance and monitoring. As part of these methods, a variety of data sources were consulted, mostly discovered through extensive searches on Google Scholar as well as specific electronic databases such as MEDLINE, PubMed Central, Web of Knowledge, Global Health (Ovid), and Web of Science. Through this systematic method, peer-reviewed journal articles were navigated by utilizing various combinations of the following indicators: resistance, antimicrobial resistance, AMR, antimicrobial drug resistance, antibacterial resistance, antibiotic resistance, antibiotic (use), (global) surveillance, monitoring, South Asia, India, Pakistan, Bangladesh, Sri Lanka, resource-constrained, resource-limited, under-resourced, low and middle income, developing countr(ies), challenge(s), health, etc. The search strategy was comprised of selective input of indicators into database search functions in order to produce relevant results.

The aim of the review was to find literature that encompassed surveillance of AMR in developing regions as a whole and areas of South Asia, specifically. Current status of South Asian surveillance was the key area of interest and determinant for data selection. Primary search results from several databases yielded broad-based clinical studies of specific pathogens and associated resistance. Literature on surveillance-specific challenges and/or recommendations was limited. Overall, selection of journal articles was based on inclusion of discussion on AMR surveillance as the focal point. Information on South Asian surveillance systems was extracted from these articles for case-by-case analysis as well as for cross-country comparisons. Narrowing of search results to more specific research was also done through scanning of article reference

lists. In general, the majority of results covered AMR prevalence/incidence with notable gaps in information with regards to resource scarcity and AMR surveillance.

4.0   Findings

4.1   Overview of Search Results

Overall, has been found that increased use of certain antimicrobial agents has led to increased levels of resistance in some parts of South Asia (Byarugaba et al., 2010). This has placed immense burdens on disease-specific control programs that are in place within these countries (Byarugaba et al., 2010). AMR has greater consequences for developing countries and further weakens their health systems, leading to increased underdevelopment (Sirinavin & Dowell, 2004). Furthermore, the presence of resistance deteriorates health outcomes in these countries for previously treatable infections such as tuberculosis and malaria (Okeke et al., 2005a). Laxminarayan (2004) also points out the general inaccessibility of effective antimalarial drugs (e.g. artemisinin) in resource-constrained settings, which enlarges the issue. It is therefore evident that AMR presents a great concern for the region, highlighting the importance of starting with a top-down approach to resolve these problems.

In the South Asian region and for developing countries as a whole, there is a substantial lack of specific literature on AMR surveillance. Literature searches yielded primarily clinical studies that examined the scientific nature of AMR in this region; country-specific data was also not readily available. From these findings, one can make the assumption that AMR surveillance is not prioritized in these countries. For developing settings, there are a variety of other issues internal and external to the health sector that can take precedence. For example, developing countries often lack a

cohesive framework for collecting/interpreting data for surveillance purposes, which puts the success of infection control at risk. Often, passive surveillance techniques are utilized, which may result in biased populations and/or samples (Byarugaba et al., 2010). Methodological difficulties such as a lack of international reporting (due to unpublished work) and differing testing methods/quality assurance protocols can lead to serious deficits in AMR data (Byarugaba et al., 2010). Furthermore, noncompliance with study design guidelines is also problematic in these regions (Byarugaba et al., 2010).

National resistance data is generally unavailable in South Asia for bacteria of public health importance, as evidenced by the WHO (2014a; Appendix B; Table 2). In India, for example, requested national resistance data for select bacteria-antibacterial drug combinations was not available (WHO, 2014a). Systematic multi-centre collaboration is not present in these countries; microbiological cultures that are valuable tools for strong surveillance are not high in quality (Byarugaba et al., 2010). External factors such as a lack of resources/funding, as well as the political climate, play a role in determining these challenges (Byarugaba et al., 2010). Governmental bodies are often focused on providing quick and short-term solutions to health problems in developing countries; long-term data collection and surveillance planning are not prioritized (Byarugaba et al., 2010). Koplan (2001) points out that the lack of surveillance system presence in developing countries is also related to increased expenditure of resources on other new diseases and related potential threats of bioterrorism.

Limited funding for conducting surveillance studies has negative impacts on the extent and quality of pathogenic testing in the developing world (Byarugaba et al., 2010). Antibacterial susceptibility testing (AST) tests the susceptibility of infectious microbes to various antibiotics (Drlica and Perlin, 2011). This is achieved through

collecting isolates, exposing them to a variety of antibacterial agents, and analyzing the results through the use of commercial microbial analysis systems (Drlica and Perlin, 2011). A lack of resources often means that optimal testing methods are not utilized; limited budgets influence the use of traditional methodologies (e.g. disk diffusion tests) rather than testing for MICs (Byarugaba et al., 2010). In line with this, the health sector is often not prioritized in terms of resource allocation, which ultimately affects the development of national surveillance programs (Vaughan & Walt, 1984). Weak infrastructure and fractured health care capacities provide further detriment. As a result, quality assurance and the availability of comparable data are hindered.

Byarugaba et al. (2010) utilize the term 'microbiological gap' to refer to local laboratories within developing countries that are not exhibiting optimal functioning and/or training with regards to AMR. Archibald and Reller (2001) attribute these challenges to widely held perceptions that encourage the idea that AMR is not a major health problem. Furthermore, a lack of communication between laboratory technicians and physicians adds to the issue in these countries (Archibald & Reller, 2001). With reference to the microbiological gap, Byarugaba et al. (2010) point to the need for increased quality assurance and resource management for appropriate analysis of patient samples and surveillance reporting. Use of expensive technologies for bacteriological analysis presents a challenge for resource-constrained settings, where skewed priorities and costly AST limits the amount of surveillance reporting (WHO, 2014a). Furthermore, incomplete reporting that is fueled by flawed data storage practices contributes to the observed challenges (Byarugaba et al., 2010). Deficiencies in laboratory capacities such as supply-chain issues, inadequate culture preparations, and insufficient harmonization of methods are other contributors (Vernet et al., 2014).

Regulatory practices are often less than substantial and increase the use of antibiotics and thus resistance in developing countries (Byarugaba et al., 2010). Although legislations surrounding antibiotic use may exist, enforcement is weak and is further complicated by social factors such as poverty, war, and other types of human conflicts (Byarugaba et al., 2010; Mitema, 2010). A lack of regulatory bodies in developing countries highlights the need for appropriate leadership/governance and collaboration with regards to the control of prescription practices as well (WHO, 2001). Developing settings often serve as 'breeding grounds' for AMR development, which is further disturbed by the absence of appropriate guidelines (Byarugaba et al., 2010).

A lack of structure that promotes appropriate infection control guidelines results in an environment that is not cohesive in terms of public health action. Sirinavin and Dowell (2004) relay that unstructured and under-resourced settings are often prone to ineffective infection control strategies (e.g. insufficient hand washing) and/or leadership with regards to AMR. As Byarugaba et al. (2010) note, weak health systems in developing countries (due to lack of staff, training, resources, etc.) lead to weaker infection control practices and thus increased rates of AMR in hospitals. It is also possible for the resistance to spread to the larger community through these means (Okeke et al., 2005a; 2005b). Although highly skilled workers and planners are present in most of these countries, medium-skilled workers that are needed in order to conduct relevant work are facing shortages (Byarugaba et al., 2010). Furthermore, rural to urban migration in most developing countries is a cause for concern; it is difficult to attract workers to rural communities where there is a high need for surveillance studies (Byarugaba et al., 2010). In line with this, worker motivation is often low, primarily due to the vertical hierarchy that results in limited opportunities (Byarugaba et al., 2010).

In LMICs, a lack of resources, combined with various markers of social location (e.g. age, gender, race, SES, etc.), can negatively affect health outcomes such as AMR. DiazGranados et al. (2008) effectively illustrate the impact of AMR according to various levels of resources, along with possible solutions to relevant problems (Appendix B; Table 6). For settings with moderate resource limitation, incomplete or inconsistent information/practices are of main concern (DiazGranados et al., 2008). It is a challenging feat to set up surveillance systems in resource-constrained settings, where there are major limitations in laboratory capacity, quality control, availability of reliable reagents, supervision, and staff training (Byarugaba et al., 2010). Other deficits include limited availability of demographic data, informational databases, and information dissemination channels (Byarugaba et al., 2010).

Comparatively, it is evident that resistance data sourcing from developing countries is not on par with strong surveillance system requirements. Unavailability, non-representativeness, and inaccuracy of data are some current challenges that affect the quality of AMR surveillance in South Asia (Byarugaba et al., 2010). Inadequate diagnostics can also lead to delayed detection of AMR as health care providers assume their duties without appropriate knowledge of susceptibility patterns (due to weak surveillance) (Byarugaba et al., 2010). Prescribers often base clinical diagnoses on solely the strength of the patients' symptoms, often disregarding important diagnostic tools (Okeke et al., 2005b). In line with this, laboratories in resource-constrained settings will often change protocols and/or create their own, which poses a serious problem (Okeke et al., 2005b). These resource-dependent capacities form the basis of strong surveillance and are essential targets for intervention in these countries.

On an individual level, the data reveals that the 'diversity in readership' of

antibiotics across geographic settings is a challenge (Drlica and Perlin, 2011). This means that varying interpretations of appropriate antibiotic use and their potential effects are hindering efforts to reduce AMR in regions such as South Asia. In order to change attitudes and practices, interventions in South Asia must be targeted to the relevant contributors (e.g. lack of knowledge, personal behaviours, misconceptions, traditional practices, etc.). Potentially harmful practices such as self-medication are enabled through ease of antibiotic accessibility through non-prescription means and a lack of enforcement (Drlica and Perlin, 2011). This creates a 'culture of nonchalance' towards antibiotic use (Drlica and Perlin, 2011), which has important implications for controlling misuse/overuse. High availability of counterfeit drugs (which is a common symptom of drug development in under-resourced countries) may further increase AMR through treatment failures (Hadi et al., 2006). Financial gain through sale of counterfeits is often prioritized over drug quality in such areas (Byarugaba et al., 2010).

Tupasi (1999) notes the emergence of resistance to quinolone-based antibiotics in the developing world, alluding to sociocultural attitudes and deficient economic policies as the causes. Sirinavin and Dowell (2004) point out that individual perceptions of antibiotics in developing countries deem them to be the stronger or more 'powerful' drugs, which inhibit rational use. Attitudes also revolve around the idea that antimicrobial agents should be able to 'fix' most problems, even if they may not be infection-related conditions (WHO, 2001; Sirinavin & Dowell, 2004). Another perspective-driven issue that poses a problem is the commonly held notion that new and costly drugs are more effective than pre-existing ones (WHO, 2001). Ideas such as these tend to affect prescription, dispensing, and utilization rates (increased use of new types) of antibiotics (Hadi et al., 2006). The cost of antibiotic use seems small on an

individual level but has wider consequences on a community level in South Asia.

The behaviours of health care providers are influenced by financial gains (e.g. through antibiotic prescription sales/pharmaceutical referrals), which increase rates of irrational antibiotic prescription in South Asia (WHO, 2001; Sirinavin & Dowell, 2004). The same can be said for pharmaceutical companies, where the use of newer and costlier antibiotics results in profit (WHO, 2001). The current lack of training among health providers with regards to appropriate treatment methods only magnifies the issue (WHO, 2001). These systems-oriented factors within developing countries need to be more carefully scrutinized and monitored. In relation to this, Finch et al. (2004) point to the need for educational interventions for health care providers that currently use outdated information in these countries; a lack of continuing education directly affects antibiotic use. These factors, in confluence with weak surveillance systems, deem the management of AMR a challenging task in developing countries.

A lack of resources can reduce the capacity of health systems. In this case, gaps in data availability can point to issues in national health system functionality. These factors may lay evidence to additional constraints within LMIC health systems, including patient sampling difficulties (e.g. low sample sizes) and deficiencies in national accumulation and summation of laboratory data (WHO, 2014a). Data on resistance to third-generation cephalosporins in the Escherichia coli pathogen, for example, indicates that limited sampling is an issue in South Asian countries (WHO, 2014a). Considering the high burden of these infections, there also are gaps in South Asia for surveillance knowledge of Streptococcus pneumoniae and its susceptibility, pointing to the need for increased laboratory capacity and AST (WHO, 2014a). In relation to this, Sirinavin and Dowell (2004) found that there is often a lack of diagnostic testing that accompanies

health service delivery in resource-constrained settings. As such, the lack of a clinical base for medical practice often leads to overprescription and overuse of antibiotics (Sirinavin and Dowell, 2004). Therefore, potential gaps in knowledge and/or operational systems have serious implications for the quality of surveillance in these regions.

Informational gaps, including pathogen definitions, also need to be more clearly addressed so that disease burden can be appropriately estimated. For example, it was found by the WHO (2014a) that nontyphoidal Salmonella disease burden is high in South Asia but the largest information gaps with regards to its resistance occur in the same region. Byarugaba et al. (2010) also assert that resource-constrained settings often lack patient and public-friendly informational resources on heath-related issues. In general, it is evident that large gaps in knowledge and high disease burdens occur simultaneously in developing countries. Critical evaluation of such aspects can strengthen surveillance capabilities and overall effectiveness. With this information in mind, public health professionals and stakeholders from other sectors should be wary of the fine balance that will be required to address the visible gaps.

4.2   Case Study: India

With regards to AMR, multidrug-resistant tuberculosis (MDR-TB) rates are high in India (especially among those who were previously treated) and treatment for the disease is generally limited (WHO, 2014a; Prasad, 2005). There are several factors that contribute to this shortfall, including insufficient training of staff, limited facilities for treatment/monitoring, and overall lack of coordination in programming (WHO, 2014a). Salmonella infections are also prevalent in India (Parry, 2003). Mathai et al. (2008) point out that there is also major multi-drug resistance amongst E. coli strains in rural and

urban areas of Southern India. Prevalence rates are often higher for urban areas due to the availability of antibiotics and poor sanitary conditions that harbor pathogens (Hart & Kariuki, 1998). Similarly, Ochiai et al. (2008) found that annual incidence of typhoid in India is relatively high (approximately 493.5 per 100,000 population) and there is visible multi-drug resistance amongst these isolates. Uneven methodologies, differences in health-seeking behaviours, and inappropriate use of antibiotics (e.g. fluoroquinolones) could be potentially contributing factors (Ochiai et al., 2008; Kumar et al., 2007). Although the emergence of typhoid-related resistance has been well characterized (Nath et al., 2000; Mirza et al., 1996; Okeke et al., 2005a) in the Indian subcontinent, surveillance-oriented interventions to combat these infections must be prioritized.

Holloway et al. (2011) conducted several pilot projects in India, finding high AMR rates for various pathogens. The authors also found methodological issues with obtaining isolates and thus difficulties with data comparability. Logistical challenges for long-term surveillance activities were highlighted through this study; challenges with testing, sample size, data standardization, and data collection/management were echoed in the results (Holloway et al., 2011). The authors recommend enhancements in multidisciplinary capacity to produce more uniform AMR data in India (Holloway et al., 2011). Similarly, a high prevalence of gram-negative bacterial infections and associated resistance has been found among travelers to India (Vernet et al., 2014). Use of fluoroquinolones in poultry is another contributing factor for antimicrobial resistance that is acquired through the food supply chain in South Asia and other continents (WHO, 1998). These findings have important implications for AMR surveillance and potentially controlled use of antibiotics in these regions.

Within South Asia, India has been estimated to have the highest rates of HIV-

infected individuals, but results vary according to different studies and areas (Byarugaba et al., 2010; Kumarasamy et al., 2005). Greater surveillance of HIV drug resistance is urgently needed in developing settings (Walensky et al., 2007; WHO, 2014a). Overall, patterns of resistance in India are varied. For example, some studies have found antiretroviral resistance among certain populations in India (Deshpande et al., 2004; Hira et al., 2004) while others have not (Balakrishnan et al., 2005; Eshleman et al., 2005). Uniformity in data collection, as part of the development of broader surveillance systems, is therefore encouraged in such countries to promote clearer data. The nature of antibiotic use also affects the type of data that is available in developing countries such as India. For instance, Morris et al. (2008) noted that influenza vaccine use is low in India, despite the prevalence of influenza (IBIS, 2002).

Candida species fungal infections are also abundant in India (Xess et al., 2007; Girish Kumar et al., 2006). Several global surveillance programs have targeted these types of infections but continued surveillance support is needed (Pfaller et al., 2007). Cholera is another prominent disease in several South Asian countries and outbreaks have been observed in India, Pakistan, and Bangladesh (Sack et al., 2004; Krishna et al., 2006; Okuda et al., 2007; Narang et al., 2008). Underreporting of cases is a cause for concern in these regions; enhanced surveillance can aid with addressing such challenges. India also exhibits high rates of resistant infections within its hospitals, which creates a high socioeconomic burden (Rosenthal et al., 2006; Yalcin, 2003).

Within the context of antibiotic misuse and/or overuse, Ray et al. (2000) found that use of fluoroquinolones against N. gonorrhoeae pathogens produced resistance in New Delhi, India. Prevalence of penicillin-resistant N. gonorrhoeae infections is high in India (Bala et al., 2003); inability to afford expensive cephalosporins could be worsening

these conditions for patients. It has also been found that oral treatments for gonorrhea have not been effective in India and should be monitored through increased surveillance (Byarugaba et al., 2010). Intensive care units in several Indian hospitals also displayed very high rates of methicillin-resistant Staphylococcus aureus (MRSA) infections; potential contributing factors include the vulnerability of intensive care units as well as inappropriate antibiotic use (Mehta et al., 2007).

Shukla et al. (2004) reported high rates of resistant pneumoniae infections in Indian tertiary care hospitals. Song et al. (2004) found similar results among penicillin-resistant pneumoniae infections. Duttaroy and Mehta (2005) also provide evidence for resistance to these infections in Gujarat. There is also a high prevalence of shigellosis infections in Kolkata (Sur et al., 2004). Moreover, resistance to various Shigellae strains is prominent in Indian pediatric patients (Dutta et al., 2002). Furthermore, Manchanda and Bhalla (2006) reported resistance amongst antimicrobial agents used to treat bacterial meningitis. Although rates are high, anecdotal evidence of such patterns and questionable testing methodologies decrease the uniformity/accuracy of data, calling for increased epidemiological surveillance of resistance levels and trends in India.

With regards to the social determinants of AMR, Vajpayee at al. (2007) found that patient expectations and satisfaction are key determinants for physicians' prescribing behaviours in India (Vajpayee et al., 2007). Moreover, Dua et al. (1994) found that more than three thirds of patients rely on their prescriptions when determining which antibiotics to use, suggesting a strong influence. On a similar note, Singh and Raje (1996) discuss the influence of patient demands in relation to traditional healers in India and their antimicrobial dispensing practices. A lack of training, technology, and supervision, combined with patients' perceptions about antibiotics,

results in inappropriate use of these agents (Singh and Raje, 1996). In essence, patient

benefits outweigh population benefits in terms of antibiotic use in such regions, which is

often detrimental for mitigating AMR rates.

The vast availability of counterfeit drugs in India also deems it necessary to

enforce stricter drug regulations (Raufu, 2003). In line with this, Dua et al. (1994) found

that in Nagpur, lay networks have a large influence on patterns of antibiotic use.

Individuals often rely on advice from friends and/or family in terms of infection treatment;

traditions and cultures affect these practices. Often, antibiotics are acquired through

non-prescribed means and the abundance of drug stores in India with varying practices

makes it difficult to enforce legislations (Dua et al., 1994). Furthermore, it is not

uncommon for pharmacy attendants to change prescriptions so that they are more

affordable for the patients (Dua et al., 1994). Kotwani et al. (2012) note that there is a

general lack of data on the behaviours of community attendants with regards to

antibiotic use, making it difficult to implement relevant interventions. Some key

determinants of antibiotic misuse by pharmacy attendants in New Delhi included

commercial interests, overstock, and near-expiry of drugs (Kotwani et al., 2012).

In India, the rise of the corporate healthcare industry has also jeopardized

surveillance planning and implementation (Byarugaba et al., 2010). This has had

serious consequences for potential resources that the Indian government could have

utilized for conducting broad-scale surveillance studies (Byarugaba et al., 2010).

Environmental concerns such as the release of antibiotics into wastewater are also

prudent in terms of dissecting the pharmaceutical industry in India (Reardon, 2014).

Insufficient use of public reporting methods, in addition to the general lack of national

interventions and regulations, produce the observe effects (Byarugaba et al., 2010). In

line with this, electronic and print media coverage of AMR issues in India should align with the larger goal of increased antimicrobial stewardship (Byarugaba et al., 2010).

Ghafur et al. (2013) outline the multi-stakeholder meeting in Chennai that aims to develop a road map for India with regards to addressing the challenge of AMR. This is an important first step in creating a consensus on the issue and developing action plans that are based on the Indian perspective. The lack of a national AMR policy in India, in addition to non-compliance with recommendations, deems it necessary. In addition to a broader multisectoral approach, policies on rational drug use and curriculum changes in medical training are some of the proposed road map action items (Ghafur et al., 2013). Infection control teams, task forces, hospital accreditations, and microbiological enhancements are some other highlights (Ghafur et al., 2013; Appendix A; Fig. 5). Dissemination of information and supervision of usage remain key concerns for India (Sharma et al., 2005). The road map for tackling AMR in India should also address domains of practice such as over-the-counter antibiotic sales, in-hospital antibiotic use, and auditing of pharmaceutical services. Currently, working groups in India under the Global Antibiotic Resistance Partnership (GARP) promote actionable policy for LMICS that includes improved surveillance and rationalization of antibiotic use (GARP, 2011).

4.3   Case Study: Pakistan

Dispensing practices in Pakistan are leading to vast amounts of antibiotic overuse and misuse. For example, Bhutta and Balchin (1996) noted that despite the presence of some regulations on pharmacies, antibiotic dispensing is very high, usually based on demand. Attitudes towards antibiotics can be highly blasé in Pakistan. In addition, Sturm et al. (1997) attribute over-the-counter availability of antibiotics to high

rates of self-medication in Karachi. They also highlight note-worthy sociocultural attitudes in Pakistan such as the misplaced belief that any antimicrobial agent can treat respiratory tract infections. An additional community-based trigger for irrational use is the reliance of the population on drug dispensers for medical advice. As Byarugaba et al. (2010) state, drug dispensers are often not formally trained in these settings. Additionally, drug dispensers try to accommodate the patients' resources and often bargain in order to make the sale (Byarugaba et al., 2010).

Parry (2003) notes that resistance to Salmonella infections is common in Pakistan. AMR associated with cholera infections is also prominent (Sack et al., 2004). Javaid et al. (2008) also illustrate the high prevalence of MDR-TB in Pakistan. Sabir et al. (2004) analyzed the relationship between antibiotic use and E. coli infections, finding that fluoroquinolone use could lead to resistance. Similarly, Jabeen et al. (2006) reported resistance to N. gonorrhoeae resulting from inappropriate treatments. Okeke et al. (2005a) reference a study that demonstrated gradual decreases in antibiotic sales in Karachi, paired with reductions in multidrug-resistant S. typhi isolates, suggesting a possible link. AMR levels can be attributed to a variety of patient, provider, and governmental factors; social, cultural, and economic factors also play a role (Byarugaba et al., 2010; Appendix A; Fig. 2/3). Sabir et al. (2004) suggest increased surveillance of AMR for community-acquired infections, coupled with educational programs and the development of guidelines to address these factors in Pakistan.

Resources that combat selective pressures due to hospital use, the lack of preventative practices, and drug supply issues are urgently needed (Safdar & Maki, 2002). Rates of methicillin-resistant S. aureus infections are also prevalent and increasing in Pakistani hospitals (Perwaiz et al., 2007; Shabir et al., 2010); contributing

factors include defective infection control measures and hospital conditions that induce overcrowding. Similarly, Byarugaba et al. (2010) discuss an audit of a public sector hospital in Karachi that revealed substandard AMR containment strategies (e.g. poor hand washing), a lack of occupational safety measures, insufficient sanitary practices, and absent policies/training. Overall, Naeem et al. (2006) found high rates of hospital-based antimicrobial resistant infections in Pakistan. In line with this, overprescribing of antibiotics was a direct result of limited laboratory facilities and/or a lack of funds to utilize these services (Nizami et al., 1996). Moreover, physicians' antibiotic prescribing rates in hospitals were high for the treatment of childhood diarrhea, even when these antimicrobial agents may not have been needed (Nizami et al., 1996).

The Pakistan Antimicrobial Resistance Network (PARN) is an example of collaboration and knowledge sharing in action. The network serves as a common medium for information collection/dissemination by health professionals (Byarugaba et al., 2010). Technicians/clinicians can utilize the network to improve surveillance practices and technological operations through standardized techniques (Byarugaba et al., 2010). Public-private partnerships and increased consultation with global experts can further the cause. Vernet et al. (2014) also suggest increased monitoring of neonatal infections and related health outcomes in Pakistan and other South Asian countries, as part of a broader strategy to contain AMR in the developing world.

4.4   Case Study: Bangladesh

Cholera is of concern in Bangladesh, where antibiotic use/misuse contribute to a large portion of such epidemics (Sack et al., 2004). Resistant shigellosis infections (Talukder et al., 2004) and resistant Salmonella and pneumonia infections (Parry, 2003;

Granat et al., 2007) remain causes of concern. Rahman et al. (2002) and Bhuiyan et al.

(1999) also found intensifying gonorrhea resistance in Bangladesh. Currently, antibiotic

use that stems from local pharmacies is quite abundant in developing countries. One

study in Bangladesh found that ninety five percent of drugs that were utilized by

participants over one month were supplied from local pharmacies (Okeke et al., 1999).

In Bangladesh, Istúriz and Carbon (2000) estimate that approximately ninety

percent of drugs can be sold without a prescription. Hadi et al. (2006) point out that

developing countries such as Bangladesh can be notorious for non-prescribed antibiotic

use. It was found through a survey conducted in a rural district that antibiotics were

prescribed by medical practitioners to sixty percent of their patients (Hadi et al., 2006;

Sirinavin & Dowell, 2004). Additionally, over one hundred thousand doses of antibiotics

were dispensed by pharmacies in this region; an additional one hundred thousand

doses were dispensed without prescriptions (Hadi et al., 2006; Sirinavin & Dowell,

2004). In line with this, Guyon et al. (1994) highlight the knowledge gaps that exist with

regards to drug prescribing practices in Bangladesh. For example, it was found that

prescribing rates for metrozinadole, a drug that is often not recommended, were the

same between medical doctors and their assistants (Guyon et al., 1994). Not only are

suboptimal drugs being prescribed in developing countries, qualifications of prescribers

and differences in levels of knowledge and/or training are not clear. This can create

serious problems for rational drug use and thus complicate epidemiological surveillance.

Chowdhury et al. (2004) found that out of ten brands of pediatric drugs that were

sold in pharmacies in Bangladesh, seven were substandard. As Hanif et al. (1995)

describe, counterfeit medicine has had serious health consequences for some

populations in the past. Islam and Farah (2007) note the lack of adherence with regards

to medicinal drug promotion; up to thirty five percent of promotional drug pamphlets that were distributed to health care physicians contained inaccurate information (Islam & Farah, 2007). Uppal et al. (1993) found that primary care settings in Bangladesh and other South Asian countries prescribed antibiotics based primarily on their availability. The practice of overlooking the medical needs of patients in favour of antimicrobial availability is alarming. Increased surveillance would give way to better regulatory and legislative policies that could improve accessibility and prescribing practices.

4.5   Case Study: Sri Lanka

Chaung et al. (2008) noted high rates of resistance to pathogens that cause typhoid fever in Sri Lanka. Corea et al. (2003) examined the extent of methicillin-resistant Staphylococcus aureus infections in Sri Lanka. Their findings imply the need for comprehensive surveillance of AMR that incorporates the various determinants of health. Shigellosis epidemics have also occurred in Sri Lanka and other countries in the Indian subcontinent (Byarugaba et al., 2010). Song et al. (2004) report the high prevalence of penicillin-resistant S. pneumonia infections in the country. AMR is evidently prevalent in Sri Lanka, pointing to the need for increased surveillance.

Wolffers (1987) studied dispensing practices within several pharmacies in Colombo. One of the deficiencies noted by the author included the dispensers' general lack of knowledge about antimicrobial agents. It was noted that attendants paid more attention to pricing and sales instead of the medical effects of these drugs (Wolffers, 1987). Furthermore, dispensers were highly reliant on physicians' prescriptions to dictate their practices, suggesting possible knowledge gaps. In line with this, Wolffers (1987) discusses the heavy influence of the pharmaceutical industry on pharmacy

attendants; dispensers relied on pharmaceutical sales representatives for most of their knowledge about drugs. Observations such as these have important consequences for larger policy-making that covers appropriate antibiotic use and training.

5.0   Discussion

5.1   Current Gaps in AMR Surveillance and Monitoring

AMR is competing with an array of issues within the global health agenda (WHO, 2013). Prevalent gaps in AMR knowledge are the main concern in terms of regional and national sources for surveillance in the developing world (Appendix B; Table 1 provides summary data for each South Asian country analyzed in this project). Through the literature review, it was also found that a large portion of the data on this topic is outdated and it was generally difficult to obtain relevant literature that focused on AMR surveillance in developing settings. Furthermore, most approaches provide recommendations but not actionable items. It was found that despite discussions of possible areas of interventions, specific strategies were often not part of the analyses. Moreover, case studies generally focus on the clinical aspects of AMR; surveillance is not at the forefront within most literature. The key action for moving forward would be to refine proposed recommendations and provide practicable strategies for intervention.

Lackluster regulation and enforcement of legislative laws are key issues for developing countries. Governmental and regulatory issues are contributing to the spread of AMR. Due to prevailing attitudes and tendencies that foster an environment in which antibiotics are frequently and inappropriately utilized, resistance is becoming an increasingly serious concern for this region. Use of antibiotics without prescriptions and demand-related pressures on physicians are some contributing factors. Once again,

appropriate surveillance of AMR and antibiotic use trends can provide ground for analysis of these deeper issues regarding patient-provider reliance and cultural biases.

As Okeke et al. (2005b) note, health systems within developing countries are extremely varied in terms of structure, making the need for specific and context-appropriate surveillance very apparent. Kunin et al. (1987) assert similar views, suggesting that the characteristics of medical systems need to be carefully dissected for each country, as patterns of antibiotic use vary so widely. Allegranzi et al. (2011) conducted a systematic review and meta-analysis of healthcare-associated infection data in developing countries, finding visible surveillance constraints. Sampling methods, susceptibility methodologies, and study design are also vastly varied among surveillance structures (Bax et al., 2001). Furthermore, deficits in testing protocols, quality assurance, and capacity-building are leading to fragmented data (WHO, 2012). Underreporting and resulting non-representativeness of data in the developing world are other prominent AMR surveillance issues (Allegranzi et al., 2011).

As Bax et al. (2001) point out, appropriate funding for supporting surveillance systems is of concern. Despite growing and documented interest in improving surveillance, studies lack support (Bax et al., 2001). Masterton (2008) emphasizes the unaffordability of surveillance system development in resource-constrained countries; a lack of data fuels further uncertainties about AMR and an inability to take action on the issue. Selgelid et al. (2008) point out that deficits in health systems increase difficulties in combatting resistant strains such as MDR-TB if appropriate resources for diagnosis, treatment, and follow-up are limited. Furthermore, a lack of MDR-TB surveillance in South Asia limits data availability for these infections (Vernet et al., 2014). Globally, systems are often funded by sectors (e.g. pharmaceutical industries) that may not have

interests that fully align with reduced resistance. Greater utilization of international expertise, clinical evidence, and infection control practices are some strategies for multi-faceted improvement (Allegranzi et al., 2011; Appendix B; Table 5).

Furthermore, a 'lack of stewardship' for AMR prevention/treatment means that there has been no coherence or leadership that promotes collective action on the issue (Drlica and Perlin, 2011). Only until very recently did the WHO collaborate on a draft global action plan for AMR. The action plan emphasizes shared ownership and engagement through outlining priorities for action and guiding principles (WHO, 2014b). Technical consultation, multinational commitment, and interagency/cross-sectoral discussions are other components (WHO, 2014b). A strategic objective of the plan is to strengthen the evidence base through rapid generation of knowledge that can rationalize intervention strategies. Ensuring that surveillance systems and diagnostic tools remain current is an importance objective (WHO, 2014). Greater investment in research for developing settings should also aid surveillance practices therein. Although progress is being made in the right direction, there are still serious deficiencies in the global health agenda in terms of AMR. Moreover, uncontrolled use of antibiotics within community and agricultural practices has yet to be cohesively regulated (Drlica and Perlin, 2011). These are all potential areas of intervention that are not only applicable on a regional level in South Asia but also on a global scale.

5.2 Alignment with the WHO Global Report

As Okeke et al. (2005b) point out, AMR-related recommendations by the WHO present a complex challenge when applied to developing countries and the intersection of such a multitude of contributing factors. Navigating drug resistance in resource-

limited settings is a complex feat. Overall, findings from this capstone resonate with the WHO report. In terms of policy implications, more coordinated and timely surveillance systems would prove highly beneficial for targeting the issue of AMR. In addition, increased health policy surrounding health delivery (specifically antibiotic prescription) and rational antibiotic use would ensure relatively uniform, regulated, and cohesive practices. Legislations that enforce regular reporting of AMR rates should be increasingly mandated within developing countries, so as to ensure timely data collection and enhanced quality control. Additionally, enforcements surrounding the sale of antibiotics through non-prescription means can tackle some of the observable community-based challenges with regards to AMR.

As Drlica and Perlin (2011) indicate, a shift in the current 'antibiotic philosophy' is needed in order to ensure appropriate dosage and treatment regimens in hospital settings. There is also no standardization of surveillance systems in these settings. In terms of the WHO (2014a) recommendation of increased multisectoral integration among surveillance networks, there is an evident gap in South Asia. Increased national and regional efforts that imitate the WHO's approaches of intersectoral collaboration (e.g. alignment with agricultural organizations) should be applied (WHO, 2014a). Furthermore, greater connection with the pharmaceutical industry in promoting AMR reduction would promote inclusive practice. Overall, the observed challenges in South Asia provide support for the WHO's discussion of current surveillance gaps and the proposed recommendations should be followed. The primary lesson from South Asia is that ground-level action should be modified to suit the needs of relevant populations.

6.0   Conclusion and Recommendations

Global improvements in surveillance and monitoring have been stressed as one of the principle strategies to contain AMR, as seen in a number of WHO documents and the wider literature. More specifically, regular surveillance and monitoring of the use of antibiotics, general resistance patterns, and antibiotic sales are key aspects of examining the extent of the problem. In line with this, Byarugaba et al. (2010) assert that surveillance data should serve as an educational (rather than a marketing) tool for the introduction and utilization of new antibiotics. In other words, surveillance reports often influence physicians to utilize stronger drugs to combat increasing resistance (Byarugaba et al., 2010). The findings should instead promote discriminate antibiotic use as a way of addressing elevated AMR rates. Byarugaba et al. (2010) also suggest increased surveillance of pharmaceutical activities, specifically industry marketing tactics that may promote indiscriminate drug use (Appendix B; Table 3).

Strengthened surveillance should be accompanied by the development of guidelines and educational programs for rational antibiotic use (Tupasi, 1999). The WHO (2001) strategy for containing antimicrobial resistance outlines key areas of intervention, including: community education on infection transmission modes, prescriber education on antibiotic use, guidelines for antibiotic use, development of infection control programs, monitoring hospital antibiotic use, support for microbiology laboratories, development of governmental task force projects for special concerns, and international collaboration. For example, the Alliance for the Prudent Use of Antibiotics (APUA) is a collaborative initiative that creates a common platform for international surveillance practices. The APUA performs several functions, some of which include: raising awareness, knowledge sharing, promoting research and multidisciplinary

interventions, providing comprehensive solutions, incorporating feedback for global planning purposes, and encouraging international networking (Byarugaba et al., 2010).

Future goals must build on current successes in terms of AMR surveillance and management. For example, Dineshkumar et al. (1995) illustrate the success of several institutions in India that have improved awareness and practice with regards to defining and measuring AMR burden. Working groups that aid with scientific/technical advancements, as well as broader analysis of the socioeconomic determinants of AMR, will also be beneficial (WHO, 2013). Overall, it is clear from the evidence presented in this capstone that although the issue of AMR is widespread, strategies to contain it are not. There is an unequal balance of emphasis on the issue, depending on geographic regions and context-dependent factors. In order to harmonize public health practices in South Asia and on a global scale, AMR needs to be a central public health priority. This can be addressed through the development of robust, comprehensive, and uniform surveillance systems that can detect AMR burden and increase understanding of the issue, especially within LMICs. Recommendations for the future should fall within the following broad domains: knowledge, support, and collective action.

Knowledge

On a broader systems level, detailed analysis and evaluation of prescription practices, treatment regimens (e.g. determining antibiotic dosage), and dispensing behaviours within developing nations, in combination with meticulous vigilance to other contributing factors, will prove useful for mitigating AMR. As an example, Kotwani et al. (2012) suggest the inclusion of pharmacists as partners with the community to raise awareness and promote rational antibiotic use. A multidisciplinary framework that targets a multitude of sectors, as well as the recruitment of motivated stakeholders, are

also key for improving knowledge on AMR (Kotwani et al., 2012). Improved surveillance would provide the data needed to conduct such analyses. In line with this, advancement of research and development on a global scale through increased funding can unlock valuable knowledge and provide innovative and practicable solutions.

It is clear from the evidence that antibiotic use is closely linked to the development of AMR. In addition to promoting increased knowledge on a systems level, individual knowledge is crucial for changing consumption patterns and contextual behaviours. In terms of both local and global considerations, one future measure that can be taken is to prevent antibiotic misuse through increased training of healthcare professionals, especially within resource-limited settings. Through increased knowledge and awareness about the nature of antibiotics and drug-resistant bacteria, providers can take more precautionary measures when prescribing antibiotics to the general population. In line with this, medical curriculum in these countries should include education on pharmacotherapy and the promotion of evidence-based prescribing practices (De Vries et al., 1995; Vollebbregt et al., 2006). Bhutta and Vitry (1997) have asserted that pharmaceutical motives often fuel irrational use of antibiotics in medical settings; continuing education programs can serve as a buffer to combat these negative effects. Drlica and Perlin (2011) suggest that education for medical professionals should occur early on during their training.

Knowledge in the form of educational programs for the public can also have a positive effect on changing common misconceptions about antibiotics and inducing subsequent behaviour change. The principles for antibiotic use need to be better taught (Sharma et al., 2005). Additionally, the harmful consequences of noncompliance with prescription regimens and other forms of improper use can be enforced through these

educational programs (Drlica and Perlin, 2011). They can also promote a change in perspective about antibiotic use as a method to treat all types of infections, which is a visible challenge in developing settings. Public education is an affordable strategy that can be achieved through greater use of the media and literature. Other strategies include focus groups, workshops, large-scale seminars, and the use of informational pamphlets in order to reduce unreasonable use. Radyowijati and Haak (2003) suggest exploring the 'socio-cultural rationality' of antibiotic use through these interventions. Similarly, Laxminarayan et al. (2013) emphasize the importance of addressing social norms in order to ensure future success. Alliances with civil society organizations are also crucial for improving the situation (Nweneka et al., 2009).

Educational programs should also be targeted towards drug dispensers and those in pharmaceutical positions. In terms of health care provision, Wilkins et al. (2008) assert the usefulness of performance analysis through enhanced health information systems; this would aid with tracking and managing antibiotic use. Surveillance systems should function as a guide for antibiotic use in developing countries so that AMR can be mitigated and the effectiveness of current drugs maintained. Brusaferro et al. (2006) point to the benefits of focused inflection control programs in developing country hospitals. Patient indicators that give the most useful and relevant information should be selected to paint a picture of local conditions and inform interventions, from the perspective of surveillance studies (Brusaferro et al., 2006). These strategies at large will be useful downstream supplements to improved surveillance systems in developing countries. In line with this, Okeke et al. (2005b) suggest the implementation of pilot programs in advance of large-scale intervention to ensure the success of such efforts.

Support

A lack of support, whether financial, supervisory, or scientific, has rendered it difficult to analyze the precise causes of AMR in developing countries. Through a community-based approach to facing the issue of antimicrobial resistance, it can be ensured that multiple contributing factors are addressed. Competence of healthcare providers, within the larger goal of health systems strengthening, is a key component of change in relation to this issue. These actions can be performed with the help of aid (e.g. monetary funding, other resources) from relevant stakeholders. Utilizing increased funding for enforcement of laws pertaining to antibiotic sales will also prove beneficial.

Support in the form of the sustainable provision of resources can have many positive consequences in terms of AMR surveillance. Simply, an increase in resources can lead to an increase in AMR information that is usable for informative interventions. Resources must be used in the most cost-effective way to combat the issue of AMR in developing countries. With increased capacity for conducting more appropriate and effective monitoring of AMR in laboratory settings, for example, countries can adequately equip themselves with the knowledge required to develop and implement strong surveillance systems. As Planta (2007) discusses, socioeconomic factors such as poverty affect the emergence and spread of AMR in developing countries; improved conditions would provide the necessary resources for effective surveillance systems. These changes can serve as mechanisms for augmenting local research capabilities.

Increased funding on a global scale can ensure that applicable technologies and personnel are available to conduct the extensive surveillance work. This would also alleviate the issue of bias in the results due to limited agencies providing the funding for surveillance work. A key recommendation in this regard would be for countries to

develop national-level surveillance systems that align with the WHO global-level data repositories. On a national level, AMR-specific surveillance systems would aid with overall standardization, comparability, coordination, and harmonization. Accessibility and usability of these surveillance systems is crucial for developing world contexts.

With regards to the need for technological advancement, the WHONET software is a free electronic tool for AMR surveillance that is already being utilized in many parts of the world (Stelling & O'Brien, 1997). WHONET exemplifies a robust surveillance system as it has built-in quality control functions that can identify laboratory errors and can be customized for specific purposes (clinical, epidemiological, veterinary, molecular, pharmacological, infection control, etc.) (Byarugaba et al., 2010). Furthermore, WHONET can utilize an array of graphic representations to analyze susceptibility patterns and has guidelines for interpretation of various methodologies for testing (Byarugaba et al., 2010). Other prominent features include its compatibility with global software systems (e.g. through provision of common codes/universal file formats for data storage) and its flexibility with data representation (Byarugaba et al., 2010; Sharma & Grover, 2004; Stelling & O'Brien, 1997). WHONET serves as an important and unified platform for decision-making (e.g. guiding empiric treatment of infections) in order to enhance AMR surveillance and mitigate resistance. Countries can analyze their own data for more consistent monitoring of AMR and are able to comparatively share the information to support national and global surveillance (Stelling & O'Brien, 1997).

If considering the South Asian region, WHONET is currently being utilized as a surveillance support mostly in India. Sharma and Grover (2004) emphasize expanded and continued use of WHONET within hospitals, for example, in order to assist with the formation of control measures (e.g. restrictive drug policies) through web-based data

sharing between networks. Additionally, Agarwal et al. (2009) analyze the benefits of

utilizing WHONET within military hospitals as a more efficient way of accumulating data

and collectively analyzing it to promote health policies and control measures. A potential

limitation of applying this software would be that WHONET does not function as a

comprehensive patient management system and thus susceptibility data may have to

be separately/manually entered (e.g. if a patient management system already exists)

(Agarwal et al., 2009). As such, Agarwal et al. (2009) suggest that surveillance systems

be integrated with patient management systems in hospitals/laboratories in order to

ensure future success and sustain manpower in developing countries. From the

perspective of health systems strengthening as a tool for enhancing public health

surveillance, increasing funding from global partners can aid progress (Nsubuga et al.,

2010). The Global Fund Against Tuberculosis, AIDS, and Malaria, for example, can

increase its focus towards building sustainable surveillance systems (incorporating

health systems strengthening) within developing countries (Nsubuga et al., 2010).

     In Nepal, Ghosh et al. (2013) recently documented the effects of initial WHONET

use in the country to monitor and assess resistance among uropathogens. The study

was conducted in order to promote the development of a surveillance network that

would assist with AMR policy-making in Nepal and interact with the national public

health laboratory in the country (Ghosh et al., 2013). Increased communication of

resistance data at various levels of functioning is also considered by the authors;

hospitals, communities, and clinicians are some stakeholders that would benefit from

information sharing at the local level (Ghosh et al., 2013). Increased international use of

WHONET will promote uniformity in data storage, ease of data sharing/comparability,

and collaboration for establishing surveillance networks in other developing countries

(Ghosh et al., 2013).

There are several countries in South Asia that are utilizing WHONET (over one hundred laboratories) but there is always room for improvement (Grundmann et al., 2011). Currently, Pakistan and Sri Lanka each have singular laboratories that utilize WHONET, and Bangladesh is currently not utilizing it. Increased efforts to promote WHONET use in these countries should be an integral component of future interventions. Development of national systems in South Asia can be achieved through increased partnerships with international agencies and non-profit organizations. AMR surveillance on a regional level should also be more greatly prioritized for South Asia, as it remains the most under-addressed WHO region in this regard; regional activities have been proposed but hardly conducted (Grundmann et al., 2011). As such, future progress towards the establishment of regional surveillance networks is crucial.

Grundmann et al. (2011) report that WHONET as a surveillance system is being applied in over one hundred countries on a global scale in order to support local and national surveillance; close to two thousand clinical, public health, food, and veterinary laboratories are utilizing the program. WHONET plays a central role in the national surveillance systems of most of these countries (Grundmann et al., 2011). In relation to this, pathogen-specific WHO-affiliated surveillance networks are currently operating in South Asia and on a global scale for disease-control programs that address malaria, tuberculosis, and gonorrhea, to name a few (Grundmann et al., 2011). Grundmann et al. (2011) also outline the existence of external quality assessments of these initiatives; assessments are occurring in all WHO regions and should be increasingly supported and incorporated within regional surveillance processes. As part of regional surveillance, greater focus on community-acquired infections is also necessary;

application of the WHONET software is mostly visible for hospital settings in India, for example (Ahmed et al., 2014).

Collective Action

With respect to a broader scale of analysis, increased communication and collaboration in terms of understanding and addressing AMR in developing countries is greatly needed. Strengthened surveillance and monitoring responses can ensure that the development of AMR in a specific community and/or population is accurately, efficiently, and effectively detected. This, in turn, can ensure timeliness of appropriate prevention and treatment methods. Addressing informational gaps within local and national surveillance systems can improve the development of treatment guidelines and result in enhanced and informed decision-making. From a global perspective, this can result in positive implications for timely policy-making, programming planning, and other intervention initiatives for high levels of AMR. It has been stated that strong policies surrounding AMR surveillance would require effective antibiotic stewardship by relevant stakeholders, regular screening/auditing of the process, and continual changes that pertain to observable and time-oriented AMR trends (Byarugaba et al., 2010). Ensuring that the balance between access and excess in relation to antibiotic use is maintained will require effective feedback loops within LMIC health systems (Laxminarayan et al., 2013). As such, resistance-driven policy changes must be accompanied by and result in practical and substantial changes in drug production, supply, and usage.

Pertaining to the evidence presented in this capstone, health systems strengthening is crucial for ensuring that communities and countries are prepared with regards to AMR. With well-equipped and more knowledgeable health workers, AMR can play a prominent role in the practice of health professionals. Adopting a broader

systems thinking approach for this issue would further illuminate the gaps that exist with regards to AMR surveillance and monitoring. Through highlighting the numerous factors that inform the organization of health systems, complex relationships between the individual and society become more visible. This would be a key incentive to action in targeting the contributors to AMR within developing settings. Increased communication between institutional and community partners, as well as other varied stakeholders, would ensure that surveillance and monitoring of AMR is prioritized in South Asian countries. Specifically, profits attained through antibiotic sales/prescriptions need to be addressed and the motives and/or interests of patients, physicians, pharmacists, and the agricultural industry need to better aligned in order to produce change.

Vernet et al. (2014) suggest the creation of a global road map that serves to enhance AMR surveillance in resource-constrained countries; development of a research agenda that focuses on existing surveillance networks and recommendations to unite them are also suggested (Appendix B: Table 7). In line with this, Grundmann (2014) provides a primer for the road map that would aid with the development of a global AMR surveillance system. Through prioritization of AMR surveillance on a global scale, the primer can aid with identifying/defining specific objectives, as well as the scale, scope, and structure of surveillance efforts (Grundmann, 2014). Common demands of relevant stakeholders, focused on future global surveillance, are grouped into three main subject areas by the author. More specifically, patient-, population-, and pathogen-centred surveillance objectives are outlined in relation to clinical, policy, and infection control demands, respectively (Grundmann, 2014). Improving clinical treatments and reducing indiscriminate prescribing are some objectives relevant to patients while raising awareness and advocating for more informed allocation of health

resources are important population-relevant objectives (Grundmann, 2014). Similarly,

understanding transmission routes is a pathogen-centred surveillance objective, as

outlined by Grundmann (2014). Some other important aspects to consider include the

type of surveillance (population- or laboratory-based), funding sources (public, private,

public-private partnerships), and the organizational structure (i.e. increased

centralization of surveillance systems) (Grundmann, 2014).

With regards to type of surveillance, the WHO (2002) asserts that sentinel

surveillance which limits data collection to certain areas may be more beneficial for

LMICs, as opposed to comprehensive surveillance that covers data on all cases of an

infection. A general lack of longitudinal surveillance in these countries may favour such

systems but national coordination is still the key measure for success. In such cases,

quality can outweigh quantity through targeted approaches that ensure the reliability of

surveillance data. Proper sample definitions and consistency between participating

sentinel sites is crucial (WHO, 2002). As Chandrasekaran et al. (2006) illustrate, the

Indian sentinel surveillance system in terms of HIV prevalence data consists mostly of

unlinked and anonymous testing sites. Although sentinel surveillance is expanding in

the area, large sample population-based studies of HIV prevalence have highlighted

potential problems with sentinel estimation (Dandona et al., 2006), suggesting

increased evaluation and coordination for these sites. Overall, a step-wise approach

that incorporates international agreement will be useful in the development of targeted

national strategies as well as a global surveillance system that operates on an

international scale (Laxminarayan et al., 2013; Grundmann, 2014). The WHO (2002)

also echoes the importance of analyzing existing surveillance systems in order to build

upon available resources to conduct these types of surveillance activities in South Asia.

In essence, local surveillance programs should inform global AMR surveillance infrastructure. For example, the International Network for the Demographic Evaluation of Populations and Their Health in Under-Resourced Countries (INDEPTH) initiative currently utilizes surveillance sites in India and Bangladesh to monitor consumer-level drug use (Grundmann et al., 2011). These efforts can be expanded to other regions. Similar to the WHO, Vernet et al. (2004) also recommend the creation of a communication plan such that organizations and funding agencies can collaboratively operate on national, regional, and international levels. Action items must take precedence within policy proposals in order to implement direct and timely measures. A global monitoring system would warrant the inclusion of all aspects of AMR, relaying 'SMART' objectives through specific targets and indicators, measurable progress, and the attainment of goals that are achievable, realistic, and time-oriented. Similarly, it is hoped that countries will adopt national action plans for AMR that are in tune with the WHO's draft global action plan.

O'Brien and Stelling (2011) propose a deeper examination of limitations in data availability and/or integration within AMR surveillance. In response to this, a multilevel and integrated system is required on a global scale; improvements in informatics and genomics (e.g. improved phenotypic discrimination) can enhance microbiological functions and reporting of AMR trends (O'Brien & Stelling, 2011). Increased participation, as part of multicenter networks, can integrate the diverse range of surveillance levels that globally exist. As part of this strategy, some other factors to consider when assessing surveillance systems include the type/extent of laboratory testing, inclusivity of reports, and sources of funding (O'Brien & Stelling, 2011). In line with this, Teodoro et al. (2011) propose the implementation of a transnational

surveillance network that promotes integration between databases and provides real-time and source-independent monitoring of AMR. Efforts such as these can be applied to the South Asian context as modes of assistance for addressing current gaps.

From the perspective of public health practice, this review has provided key insights into current limitations in AMR-related research. The findings can form the basis for better data navigation and informational practice within public health. As a public health practitioner, this review has aided with the realization that there is still a lot of progress to be made within certain aspects of this field of practice. Agencies such as the WHO that are currently addressing these issues are providing good recommendations but there is always room for improvement. The bureaucratic nature of many public health organizations deems it challenging to translate recommendations into foreseeable interventions. For example, the WHO proposes a global surveillance system but sources of funding for such a project are not clearly stated (Reardon, 2014). These challenges faced by the public health domain have provided valuable lessons in terms of professional practice and ways to move forward. A balance of knowledge and practice, in addition to the necessity for critical research, are key aspects of learning that can be attributed to this literature review.

Considering surveillance and monitoring through a professional practice lens, it remains evident that critical exploration of this process is necessary in order to produce fitting responses on both local and global scales. Greater transparency and more appropriate management of data is crucial for stronger surveillance systems that can better target and respond to AMR within vulnerable populations and settings. Needs-driven research and international cooperation would also aid these processes. Increased homogeneity of surveillance practices is required for the developing world. As

part of this strategy, more detailed examination of the 'social landscapes' of LMICs and how they interact with AMR can inform future decisions regarding surveillance system performance/sustainability. The gaps in knowledge for AMR surveillance that are outlined in this capstone should inform local and global population-based strategies and program planning on behalf of policy-makers. The use of knowledge, support, and collective action strategies can provide an effective framework for changes in attitudes, practices, and policies for AMR surveillance in South Asia and beyond (Appendix A; Fig. 1). Broader recognition of AMR as a public health emergency will underlie successful public health action. The solution lies in institutional change on a global scale.

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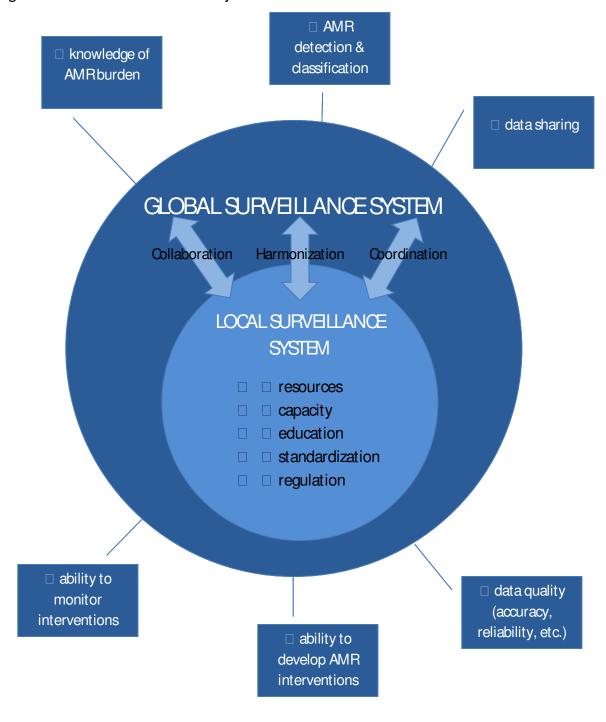Tupasi, T. E. (1999). Quinolone use in the developing world. Drugs, 58(2), 55-59.

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Appendices

Appendix A

Figure 1. AMR Surveillance Systems: Framework for Action & Effect

AMR detection & classification

knowledge of AMR burden

data sharing

GLOBAL SURVEILLANCE SYSTEM

Collaboration   Harmonization   Coordination

LOCAL SURVEILLANCE SYSTEM

- resources
- capacity
- education
- standardization
- regulation

ability to monitor interventions

ability to develop AMR interventions

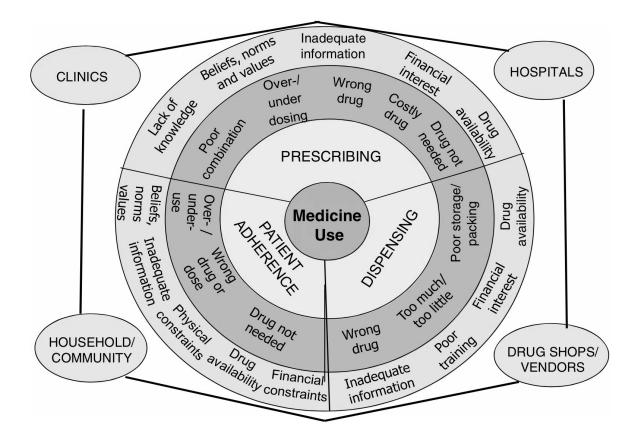data quality (accuracy, reliability, etc.)

Figure 2. Factors Affecting Antibiotic Use

Source: Byarugaba, D. K., Amabile-Cuevas, C. F., Hsueh, P. R., Kariuki, S., & Okeke, I. N.
        (2010). Antimicrobial resistance in developing countries. Springer.

Figure 3. Determinants of Antimicrobial Resistance
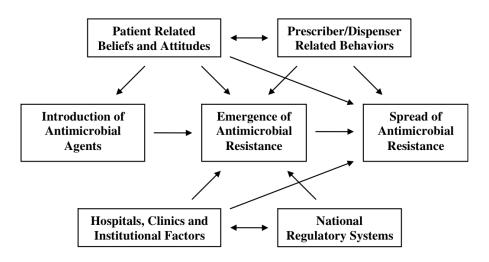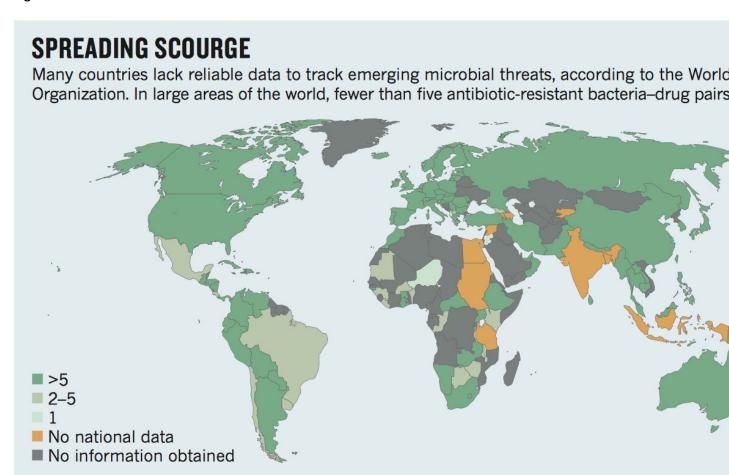

Source: Byarugaba, D. K., Amabile-Cuevas, C. F., Hsueh, P. R., Kariuki, S., & Okeke, I. N.
        (2010). Antimicrobial resistance in developing countries. Springer.

Figure 4.   Global Data Levels – Antimicrobial Resistance

SPREADING SCOURGE

Many countries lack reliable data to track emerging microbial threats, according to the World
Organization. In large areas of the world, fewer than five antibiotic-resistant bacteria–drug pairs

>5
2–5
1
No national data
No information obtained

Source: Reardon, S. (2014). Antibiotic resistance sweeping developing world. Nature, 509(7499), 141.

Figure 5. Potential Infection Control Strategies in Hospital Settings

Central Task Force

Representatives of all medical societies

DOH,DCGI,MCI,NABH,ICMR,WHO representatives

Infection Control nurses

Can have meetings over teleconferencing

Task force must have a communication/media plan so that all its decisions are conveyed to media.

Regional (District) and State Infection Control Committees

To monitor infection control standards To conduct awareness activities

To audit hospital higher end antibiotic usage .

Members from all relevant fields,Drugs controller/representative, Representatives from Government hospitals

Representatives from private hospitals,Physicians,Microbiologists, Intensivist,Gynaecologist,Surgeons ,Oncologist etc

Infection control nurses,Pharmacists,Hospital administrators.

Composition of Hospital ICT

Infection control consultant

Infectious diseases consultant /Microbiologist/Physician interested in infection control

Infection control nurse, Hospital Medical superintendent,Chief Executive Officer, and Medical director

Housekeeping supervisor, Operation theatre in charge

Representatives of all major departments [Minimum 3 clinicians- a surgeon,a physician and at least one other]

To meet at predefined intervals(Eg.3monthly) and evaluate infection control practices

Source: Ghafur, A., Mathai, D., Muruganathan, A., Jayalal, J. A., Kant, R., Chaudhary, D., ... & Parikh, P. (2013). The Chennai Declaration: a roadmap to tackle the challenge of antimicrobial resistance. Indian journal of cancer, 50(1), 71.

Table 1. Summary of Findings for Select South Asian Countries

Country	Key Findings Relevant to AMR Surveillance & Monitoring
India	□ High MDR-TB and MRSA rates □ difficulties in treatment include limited tr... infrastructure and a lack of coordination
	□ High prevalence of cholera, E. coli, and Salmonella infections □ poor sani... a general lack of intervention
	□ High annual incidence of typhoid □ contributing factors include uneven me... differences in health-seeking behaviours, and inappropriate antibiotic use
	□ Greater surveillance of HIV drug resistance is urgently needed
	□ Surveillance challenges □ obtaining pathogen isolates, varying pathogen ... sample size, non-representativeness, study design, data standardization, ... quality control, underreporting, a lack of a cohesive framework for data int...
	□ Antibiotic misuse and overuse are major concerns □ lack of knowledge an... perceptions, expectations, and satisfaction influence physicians' prescribin...
	□ Vast availability of counterfeit drugs demands stricter regulations □ abun... with varying dispensing practices and a lack of data on the behaviours of ... attendants negatively affect usage and AMR rates
	□ Rise of corporate healthcare industry has affected resource allocation for s... insufficient use of public reporting methods and a lack of national interven...
	□ Some areas of intervention include addressing over-the-counter antibiotic ... antibiotic use, auditing of pharmaceutical services, medical training of phys... development of a national AMR policy
Pakistan	□ High rates of antibiotic dispensing, usually based on demand
	□ Over-the-counter availability of drugs + sociocultural attitudes = self-medic...

	☐ Lack of training and the possible reliance of the population on drug dispens advice leads to misuse/overuse
	☐ Antibiotic sales affect AMR rates in Pakistan
	☐ Similar infection profile as India (MDR-TB, E. coli, etc.) and similar surveilla
	☐ Hospital use of antibiotics creates selective pressure ☐ inadequate diagno infection control practices, a lack of policies, limited laboratory capacities (gap'), and a lack of funds hinder AMR surveillance and containment
Bangladesh	☐ A variety of prominent infections (e.g. cholera, shigellosis, pneumonia, gor
	☐ Antibiotic use stemming from local pharmacies is high ☐ approximately 90 sold without a prescription in Bangladesh
	☐ Knowledge gaps exist within drug prescribing practices ☐ qualifications of dispensers are often unclear
	☐ Substandard antibiotics can lead to serious health consequences
	☐ Lack of adherence in medicinal drug promotion (e.g. inaccurate informatio are distributed to physicians) ☐ promote indiscriminate antibiotic use
	☐ Antibiotics are often prescribed/dispensed based on availability, raising co accessibility and weak regulations
	☐ Similar surveillance challenges as other South Asian countries ☐ a lack of negatively affects availability of quantifiable and comparable baseline AMF
Sri Lanka	☐ High rates of resistant typhoid, MRSA, shigellosis, and pneumonia infectio
	☐ Dispensers within pharmacies are often limited in knowledge on antimicrob pricing and sales often affect dispensing practices in favour of the medical
	☐ Pharmaceutical industry exerts a heavy influence on pharmacy attendants sales representatives provide most of the knowledge to dispensers, creatir antibiotic dispensing/use
	☐ A general lack of guidelines and/or policies for appropriate antibiotic use a professionals, similar to other South Asian countries

Table 2. Gaps in Resistance Data for Common Pathogens

Bacteria commonly causing infections in hospitals and in the community

Name of bacterium/ resistance	Examples of typical diseases	No. out of 194 Member States providing data	No. of WHO with nationa 50% resistar
Escherichia coli/ - vs 3rd gen. cephalosporins - vs fluoroquinolones	Urinary tract infections, blood stream infections 	 86 92	 5/6 5/6
Klebsiella pneumoniae/ - vs 3rd gen. cephalosporins - vs 3rd carbapenems	Pneumonia, blood stream infections, urinary tract infections 	 87 71	 6/6 2/6
Staphylococcus aureus/ - vs methicillin "MRSA"	Wound infections, blood stream infections 	 85	 5/6

Source: World Health Organization. (2014a). Antimicrobial resistance: Global report on surveillance 2014. Retrieved from
     http://www.who.int/drugresistance/documents/surveillancereport/en/.

Table 3. Challenges and Solutions for AMR in Developing Countries

Challenge	Possible solutions	Challenges and prospects
Enhancing microbiologic diagnostic capabilities	Increase laboratory capacity in developing countries. Increase point-of-care diagnostics using rapid testing. Reduce cost of point-of-care diagnostics	Traditional laboratory diagnostic facilities are resource intensive and require substantial management capacity. Even with increasing urbanization in developing countries, it is unlikely that the majority of patients will be treated at facilities with access to traditional diagnostic microbiologic facilities.
Improving algorithmic management of infectious diseases	Refining algorithms to be location specific, as pattern of disease differs extensively by region	The development of guidelines for the diagnosis and treatment of adult and pediatric illnesses has received considerable attention in recent years. These have been region specific to reflect the major endemic illnesses of the area – i.e., malaria endemic, HIV hyperendemic. There can be considerable variation within regions and these needs to be explored in greater depth. The most difficult regions to develop guidelines for will be the areas with the least infrastructure – where the least is known about disease endemicity
Improving knowledge of changes in patterns of infections and resistance	Improve ongoing surveillance	Recent efforts addressed at new and emerging diseases and bioterrorism have provided an impetus for developing surveillance in developing countries. Challenges are to ensure that resistance surveillance is included as part of these initiatives; to sustain surveillance systems after the initial enthusiasm for their use

Challenge	Possible solutions	Challenges and prospects
		has subsided, and after high-profile diseases such as avian influenza are no longer in the headlines; to ensure that surveillance reaches the most difficult to reach areas; and to ensure that information is acted upon
Improving information flow to health providers	Make use of newer communication systems such as text messaging and easily accessible web sites, to assure that practitioners are informed of current policies, and any changes to policies.	Assuring that Departments of Health maintain up to date lists of contact numbers of health providers is a major challenge. Assuring Internet connectivity if terrestrial lines are used remains a challenge in both urban and rural areas of developing countries. Reducing cost of Internet access remains a hurdle in many developing countries. Disseminating standard paper-based policy instruments remains erratic. Agreeing upon new diagnostic and treatment guidelines, even if current information on which to develop guidelines is available, has proved an arduous and often insurmountable task for many national Departments of Health, and hence guidelines are often out of date
Improving information flow to consumers	Use of mass media and local community groups to ensure that messages about the need to use antimicrobials judiciously is provided to consumers.	Battling long-ingrained assumptions among both providers and consumers on the need to treat many common illnesses with antimicrobials. Pharmaceutical company promotional budgets can overwhelm most public efforts and messages of pharmaceutical companies in developing

Challenge	Possible solutions	Challenges and prospects
		countries (both national and multinational) are often poorly regulated
Controlling distribution and provision of antimicrobials by the private sector and assuring the quality of pharmaceuticals	Increased regulation and control over the distribution of antimicrobials by pharmaceutical companies, their sale by pharmacies without a prescription, and the prescribing practices of private physicians. Eliminate non-approved manufacturers and assure quality of products of licensed manufacturers	Governments of many developing countries lack the capacity to enforce regulations, there remains a generally anti-regulatory environment, there are perverse financial incentives for inappropriate prescribing by private physicians and private pharmacies that would need to be changed. Assuring quality of pharmaceuticals would take greater laboratory, enforcement, and regulatory capacity
Ensuring appropriate proscribing by the public sector	Establishing and auditing adherence to guidelines; ensuring effective distribution and availability of pharmaceuticals; minimizing corruption and loss of pharmaceuticals	All of these solutions require enhanced management capacity. Increased commitment to global health, even if on specific vertical programs (HIV, TB, malaria) may result in improvement of overall management and performance of the health sector
Improving management capacity	Develop clearly defined management systems that can be implemented and sustained in the developing country context	Improved management capacity is central to achieving many of the challenges to controlling resistance in the coming years. Management capacity needs most critically to be improved in the public sector. Need systems to focus on outcome rather than process, have clear lines of responsibility and accountability, assure competitive payment of civil servants, and improve motivation and morale

Challenge	Possible solutions	Challenges and prospects
Reducing infectious disease burden	Improve living conditions, increase use of current vaccines, and develop new vaccines	Substantial investments are being made in vaccine development for an array of infections common in developing countries. Assuring affordability has still proven problematic. Improvement in living conditions has accompanied the rising income levels in many countries, especially in Asia and Latin American, and has reduced infectious disease burden in the young in those regions. This increase in wealth may have the paradoxical effect of increasing demand (and purchasing power) for antimicrobials by a new middle class that associates the use of antimicrobials with affluent status despite the decrease in infectious disease burden, and increasing antimicrobial use in hospitals as chronic diseases become more common
Alternatives to current antimicrobial therapy	Develop and test new antimicrobial compounds or new uses of current compounds. Develop alternatives to traditional antimicrobial therapy	Public–private partnerships have been developed to develop new antimicrobials, or adapt current antimicrobials, for the treatment of resistant infections in developing countries. Funding is still sparse for these initiatives and major funding for development of new classes of antimicrobial agents will still come from the private industry. Alternatives to antibiotics – such as immune therapies – have not achieved widespread success for common infections

Adapted from: Byarugaba, D. K., Amabile-Cuevas, C. F., Hsueh, P. R., Kariuki, S., & Okeke, I. N. (2010). Antimicrobial resistance in developing countries. Springer.

Table 4. WHO Strategies for AMR Containment

Target group	Recommended interventions
Patients and the public	Education to promote appropriate use and discourage self-medication
	Education on hygiene and disease transmission
Prescribers and dispensers	Education on appropriate use
	Education on promotion
	Professional regulation
	Monitoring and supervision
	Decision support tools (guidelines and formularies)
Health-care systems	Institution of therapeutic committees
	Institution of infection control committees
	Guidelines for antimicrobial use
	Antimicrobial use surveillance
	Antimicrobial resistance surveillance through laboratory networks
Government, policies, strategies, and regulations	Commitment to a national antimicrobial resistance task force with a budget
	National drug policies (essential drug lists, standard treatment guidelines)
	Registration and regulation of all drug outlets (dispensing of antimicrobials by prescription only and by licensed staff)
	Quality assurance for antimicrobials
	Required resistance data for drug licensing
	Undergraduate and continuing education on resistance
	Access to evidence-based drug information and monitoring of promotion
	Monitoring and linking of resistance and use data
Pharmaceutical industry	Incentives for research and development
	Production according to good manufacturing practice standards
	Monitoring and supervision of drug promotion
Non-human antimicrobial use	Surveillance of resistance and use
	Banning or phasing out of growth promoters
	Education of farmers and veterinary practitioners

Source: Okeke, I. N., Klugman, K. P., Bhutta, Z. A., Duse, A. G., Jenkins, P., O'Brien, T. F., ... & Laxminarayan, R. (2005b). Antimicrobial resistance in developing countries. Part II: strategies for containment. The Lancet infectious diseases,5(9), 568-580.

Table 5.   Surveillance Constraints and Improvements – Hospital Infections

Appropriate surveillance constraints
- Paucity of dedicated human resources and funds
- Scarcity of expertise in epidemiology and infection control
- Difficulties in application of standard definitions:
  - limited expertise to distinguish between infection, colonisation, and contamination
  - shortage of reliable microbiological and other diagnostic methods
  - poor-quality information from patients' records
  - need to evaluate clinical evidence
- Absence of skills for data interpretation and use
- Sparse or insufficient microbiological laboratory capacity
- Existence of different payer sources

Perspectives for improvement and research
- Improve reporting of information in clinical records
- Ensure minimum requirements in terms of facilities and resources available for surveillance
- Improve capacity-building for clinical microbiological laboratories
- Ensure that core components for infection control are in place
- Promote staff education on infection control and surveillance of health-care-associated infection
- Undertake research to adapt and validate definitions of health-care-associated infection and protocols for its surveillance on the basis of the reality of developing countries
- Undertake research on patients' and relatives' education and involvement in detection and reporting of health-care-associated infection

Source: Allegranzi, B., Nejad, S. B., Combescure, C., Graafmans, W., Attar, H., Donaldson, L., & Pittet, D. (2011). Burden of endemic health-care-associated infection in developing countries: systematic review and meta-analysis. The Lancet, 377(9761), 228-241.

Table 6.   Antimicrobial Resistance By Resource Limitation Level

	Extreme resource limitation	Extreme to moderate resource limitation	Moderate to minimal resource limitation	Min
Setting	Extremely poor countries or areas	Mainly developing countries	Mainly developed countries	High
Resource use	Minimal to none	Some (inconsistent and/or insufficient)	Inappropriate (excessive use and poor compliance)	'Go
Antimicrobial use and consequence	Little or no antimicrobial use—minimal antimicrobial resistance (limited to that which is naturally occurring)	Inconsistent antimicrobial use (interrupted supply); suboptimal dosing; use of counterfeit drugs, non-prescription antimicrobial use, leading to excessive emergence of resistance; some excessive use as for moderate to minimal resource limitation group	Excessive use of antimicrobials (including those not used in humans); use of broad- rather than narrow-spectrum agents—excessive emergence of resistance	App and supp anti resis
Infection control resource use and consequences	No infection control activities (but limited transmission of resistance still may be a problem)	Inconsistent and incomplete infection control practices in hospitals and community—excessive transmission of resistance	Inappropriate use of infection control strategies (non-compliance, non-timely use)—excessive transmission of resistance	App and (incl of re true
Public health consequences	Excess mortality due to treatable infections—excessive public health cost	Excess mortality, healthcare costs and morbidity due to infection caused by resistant organisms—excessive public health cost	Excess mortality, healthcare costs and morbidity due to infection caused by resistant organisms—excessive public health cost	Una eme publ
Possible responses	Scale-up antimicrobial agents, syndromic surveillance and some surveillance of use, vaccination and infection control strategies (strengthen capacity)	Optimise appropriate and consistent use of good-quality antimicrobials; regulations to avoid OTC antimicrobial use; surveillance/laboratory capacity; prioritise vaccination and infection control practices to decrease transmission	Optimise appropriate antimicrobial use (antibiotic stewardship); surveillance; optimise infection control practices and vaccination; drug, vaccine and diagnostics development	Dru deve deve

OTC, over the counter.

Table 7. Recommendations for Improving AMR Surveillance in Under-Resourced Countries

Recommendation
Laboratory improvement
Address both patient management and surveillance needs
Build sustainable capacity (infrastructure, equipment, human resources)
Provide good coordination between clinics and laboratory
Standardize procedures
Identify appropriate diagnostic tests for antimicrobial drug resistance (e.g., molecular tests for uncultivable or slow-growing bacteria or for resistance is linked to a single gene
Logistical needs
Avoid shortage of reagents; address both resources and supply chain
Ensure appropriate specimen collection and transport to the laboratory
Political will
Backed by hospital management
Endorsed by policy makers
Standardized antimicrobial drug resistance results: resistance index
Leverage successful experiences
Integrate drug resistance surveillance to other public health measures aimed at curbing the spread of pathogens
Start small; increase gradually
Take advantage of existing networks targeting specific diseases (HIV, malaria, tuberculosis)

Source: Vernet, G., Mary, C., Altmann, D. M., Doumbo, O., Morpeth, S., Bhutta, Z. A., & Klugman, K. P. (2014). Surveillance resistance in under-resourced countries. Emerging infectious diseases, 20(3), 434.