brought to you by a CORE

ANTIMICROBIAL RESISTANCE GLOBAL ISSUE

Policy and practice recommendations for addressing antibiotic/antimicrobial resistance in Haiti

By

Marie Lina Excellent, MD

A Master's Paper submitted to the faculty of the University of North Carolina at Chapel Hill in partial fulfillment of the requirements for the degree of Master of Public Health (MPH) in the Public Health Leadership Program (PHLP).

Chapel Hill

Spring 2016

Rohit Ramaswamy, PhD, MPH

04/13/2016

Date

5 ego

Peggy Honoré, DHA

<u>04/13/2016</u> Date

0

Acknowledgments

GOD! who is my all!

The completion of this Master paper was made possible due to the invaluable support of several experts in the field of Medicine, Public Health and English. Nevertheless, as agreed with the interviewees, they will remain anonymous. This list includes: Rohit Ramaswamy, PhD, MPH (*Academic Advisor, First Reader of my Master Paper and Mentor*); Peggy Honoré, DHA (*Second Reader of my Master Paper*); All the interviewees including *Haiti Ministry of Health* (MSPP) for sharing with me in Haiti their precious time and insights; Gigi Taylor, PhD and Alex Funt (UNC-Writing Center).

Abstract

For decades, antibiotics also called antimicrobial agents have been widely used in the treatment of infectious diseases. Nonetheless, the improper use of antibiotics has been reported in the literature globally as one of the primary causes of antibiotic /antimicrobial resistance (Laxminarayan et al., 2013). Indeed, the alarming magnitude of antibiotic/ antimicrobial resistance as a global public health threat deserves our full attention to implement evidencebased interventions aiming at reducing this growing challenge (Tillotson, 2015). This paper will describe the issue of antibiotic/antimicrobial resistance in countries such as the United States, Canada, Europe, India, Pakistan, South Korea, Japan, South Africa, Brazil, Argentina and Haiti to provide an overview of the global burden of antibiotic/ antimicrobial resistance. The overarching goal of this paper is to explore the connections and gaps between the World Health Organization (WHO) strategic action plan on antibiotic/ antimicrobial resistance and the current policy in Haiti. Data was collected from sixteen key stakeholders including the Haitian Ministry of Health & Population (MSPP), the National Laboratory of Public Health (LNSP), the National Tuberculosis Program (PNLT), University teaching Hospitals and International organizations, selected for their ability to influence policy and/or decision making processes regarding antibiotic / antimicrobial resistance challenge in Haiti. Finally, the paper will conclude with the critical role of leadership in implementing the recommendations that aim to reduce the burden of antibiotic / antimicrobial resistance in Haiti.

Keywords: antibiotic / antimicrobial resistance, global issue, World Health Organization (WHO) strategies, Haiti Ministry of Health (MSPP), policy recommendations.

Policy and practice recommendations for addressing antibiotic/antimicrobial resistance in Haiti The burden of antibiotic/antimicrobial resistance affects all nations on Earth, which jeopardizes the control of infection (Marinelli and Genilloud, 2013,2014)., The purpose of this Master paper is to provide a better understanding of antibiotic/antimicrobial resistance in Haiti. This paper will attempt to identify some similarities and gaps between the strategic action plan for addressing antimicrobial resistance suggested by the World Health Organization (WHO) and data collected through sixteen (16) semi-structured key informant interviews conducted in Haiti The interviewees included organizations with strong partnerships with the Ministry of Health of Haiti such as the National Laboratory of Public Health (LNSP), the National Program of Fight against Tuberculosis (PNLT), University teaching Hospitals and some international organizations that have sufficient influence on policy and/or decision-making process. Finally, this paper will conclude with an emphasis on the value of leadership in the implementation of the reported practical recommendations in compliance to WHO guidelines, in order for Haiti to contribute to this global combat along with other countries.

Definition of key terms

Pathogens include all living micro-organisms that have the capacity to quickly multiply and spread in hosts' bodies (NIAID, 2009). These pathogens include bacteria like Mycobacterium Tuberculosis, which causes Tuberculosis; viruses like Hemophilus Influenza, which causes Flu; fungi like Candida Albicans, which causes Yeast infections; and parasites like Plasmodium Falciparum, which causes Malaria. *Antibiotic/ antimicrobial agents* can be defined as medical drugs used to treat infections, which prevent harm from pathogens by either limiting their growth or by killing them (WHO, 2011). *Antibiotic/antimicrobial resistance (AMR)* occurs when a set of mutations in the gene of a pathogen makes it resistant to the antimicrobial drug originally

effective to treat the infection (Lopez-Lozano et al., 2000). Finally, *Hospital Acquired Infection* (*HAI*) happens when pathogens are unintentionally spread across patients and providers in healthcare settings (Deshpande et al., 2007).

Literature review

A wide range of studies reported that methicillin-resistant Staphylococcus aureus (MRSA) and/ or multidrug-resistant Gram-negative bacteria are accountable for the majority of antibiotic/ antimicrobial resistance and hospital-acquired infections globally (David and Daum, 2010). In 2015 multi-drug resistant Tuberculosis (MDR-TB) and extensively drug-resistant Tuberculosis (XDR-TB) led to an estimated 190,000 deaths worldwide (Frieden, 2016). This review illustrates the burden of the global of antibiotic/ antimicrobial resistance by presenting examples from a few select countries and regions around the world. This is not a systematic review, but is intended to demonstrate that the problem of antimicrobial resistance is truly a worldwide phenomenon.

United States

In the United States, an estimated of 23,000 deaths result from antibiotic/ antimicrobial resistance especially in healthcare settings nationwide every year (CDC, 2013). Overall, the most prevalent resistant pathogens reported in the literature across several studies, were: methicillin-resistant staphylococcus aureus (MRSA), multidrug-resistant Escherichia Coli (MDR- E. Coli) and Carbapenem-resistant Enterobacteriaceae (Singh et al., 2015; Sievert et al., 2013; Multari et al., 2013; Hidron et al., 2008; Dan et al., 2016; Ibekwe et al., 2016; Stephen and Jones, 2002). Studies reported that 76% of all Hospital Acquired Infections (HAIs) were found to be methicillin-resistant staphylococcus aureus (MRSA) and that 89% were vancomycin-resistant (Singh et al., 2015). Pseudomonas aeruginosa, another leading cause of Hospital Acquired

Infections (HAIs) has developed resistance to almost all antibiotics (CDC, 2014). Clostridium difficile has also become resistant to standard antibiotics in health care settings (Munro, 2015). Moreover, a report in 2014 mentioned the financial burden of antimicrobial resistance on the health systems showing that it cost the US \$ 150,000 per case of multidrug resistance Tuberculosis (MDR-TB) and \$ 482,000 per case of extensively drug resistance Tuberculosis (XDR-TB) (CDC, 2015).

<u>Canada</u>

A study conducted across several Canadian Hospitals reported that methicillin-resistant staphylococcus aureus (MRSA) was accountable for 68.8% of antimicrobial resistance in hospital settings compared to 27.6% in community settings (Zhanel et al., 2010). Also, every year the pathogen Neisseria gonorrhoeae infects an estimated 13,000 individuals and it found to be resistant to standard antibiotics (Martin et al., 2016).

<u>Europe</u>

Methicillin-resistant staphylococcus aureus (MRSA) has been reported by the European Society of Clinical Microbiology and Infectious Diseases as an alarming public health threat due to its exponential trend (Rossolini and Mantengoli, 2008). Also, in 2013 Estonia, Latvia and Romania in Central Europe represented the leading countries carrying the burden of multidrug resistance Tuberculosis (MDR-TB) (Stagg et al., 2015). A study conducted in Barcelona reported that resistant strains of Escherichia Coli (E. Coli) were highly prevalent in neonatal sepsis (Guiral et al., 2012).

<u>India</u>

A study conducted across several Pediatric centers in Chennai reported a prevalence of 4% of multidrug resistance Tuberculosis (MDR-TB) in children (Swaminathan, 2012).

<u>Pakistan</u>

Pakistan Among the 27 countries highly prevalent with multidrug resistance Tuberculosis (MDR-TB), Pakistan holds the 5th position (WHO, 2014). In 2013 Pakistan managed to link only 13% (1,570/12,997) of the diagnosed cases of MDR-TB to appropriate medical care, (Safdar, 2014).

South Korea

A study conducted from 2005 to 2014 nationwide reported that 41.2% (28/68) of the Salmonella Virchow pathogens were found to be cefotaxime-resistant (Jin Seok et al., 2016). Another research study assessed the antimicrobial susceptibility of Escherichia Coli (E. Coli) from cattle farms across the country and reported a high prevalence of resistance to first line antibiotics like Streptomycin (63.1%) and Tetracycline (54.5%) (Shin et al., 2014).

<u>Japan</u>

A nationwide survey conducted across 27 Medical centers in 2010 reported a very high prevalence (72%) of methicillin-resistant Staphylococcus aureus (MRSA) among 586 hospitalized patients (Takesue et al., 2012).

South Africa

A study from Johannesburg supported the evidence of a high prevalence (8.8%) of multidrug resistance Tuberculosis (MDR-TB) (Fairlie et al., 2011). Similarly, reports from Cape Town argued an increasing trend (2.3 to 6.7%) for the prevalence of MDR-TB in childhood (Schaaf et al., 2009).

<u>Brazil</u>

An exploration of the Brazilian Amazon reported a prevalence of 5.2% (7/135) of the patients infected with Plasmodium Vivax being resistant to the standard treatment with Chloroquine, which hinders the control of Malaria (Marques et al., 2014).

<u>Argentina</u>

A study conducted across several Argentinean medical centers argued a growing prevalence of pathogens resistant to the class of antibiotics called Carbapenem (Tognim et al., 2004).

<u>Haiti</u>

Although in Haiti there is no national data on antibiotic/ antimicrobial resistance overall, some published data are available regarding multidrug resistance Tuberculosis (MDR-TB). In 2000 the "Groupe Haitien d'Etude du Sarcome de Kaposi et des Infections Opportunists (GHESKIO)" Research Center conducted a 2-year study across a few HIV/AIDS management sites involving 330 patients to report a prevalence of 20% (10/49) of MDR-TB from recurrent TB cases (Joseph et al., 2006). Another study from GHESKIO reported a prevalence of 2.9% of MDR-TB among 906 patients diagnosed with TB for the first time (Ocheretina et al., 2012).

Summary of the literature review

Table 1

Summary of the data from this informal review of the literature, showing the pathogens that are most prevalent in the various countries.

Country	Reported resistant-pathogens	Data sources
United States	Methicillin-resistant staphylococcus aureus (MRSA) Multidrug-resistant Escherichia Coli (MDR- E. Coli) Carbapenem-resistant Enterobacteriaceae Pseudomonas aeruginosa Clostridium difficile	Singh et al., 2015 Sievert et al., 2013 Multari et al., 2013 Hidron et al., 2008 Dan et al., 2016 Ibekwe et al., 2016 Stephen and Jones, 2002 CDC, 2014 Munro, 2015
Canada	Methicillin-resistant staphylococcus aureus (MRSA) Neisseria gonorrhoeae	Zhanel et al., 2010 Martin et al., 2016
Europe	Methicillin-resistant staphylococcus aureus (MRSA) Multidrug resistance Tuberculosis (MDR-TB) Multidrug-resistant Escherichia Coli (MDR- E. Coli)	Rossolini and Mantengoli, 2008 Stagg et al., 2015 Guiral et al., 2012
India	Multidrug resistance Tuberculosis (MDR-TB)	Swaminathan, 2012
Pakistan	Multidrug resistance Tuberculosis (MDR-TB)	WHO, 2014 Safdar, 2014
South Korea	Salmonella Virchow pathogens Multidrug-resistant Escherichia Coli (MDR- E. Coli)	Jin Seok et al., 2016 Shin et al., 2014
Japan	Methicillin-resistant staphylococcus aureus (MRSA)	Takesue et al., 2012
South Africa	Multidrug resistance Tuberculosis (MDR-TB)	Fairlie et al., 2011 Schaaf et al., 2009
Brazil	Plasmodium Vivax	Marques et al., 2014
Argentina	Carbapenem-resistant Enterobacteriaceae	Tognim et al., 2004
Haiti	Multidrug resistance Tuberculosis (MDR-TB)	Joseph et al., 2006 Ocheretina et al., 2012

In conclusion, the following points are noteworthy:

- Antibiotic/antimicrobial resistance represents a serious public health issue worldwide
- The pool of pathogens resistant to first line antibiotics displays strong similarities globally, although there might be some regional differences

Based on these evidence, even though Haiti does not have a strong health system to assess the magnitude of antibiotic/antimicrobial resistance and collect data to drive and implement an action plan, it is reasonable to conclude that Haiti will more likely display similar patterns of resistance. Available data on MDR-TB in Haiti support this argument.

WHO strategies to address the global issue of antibiotic/antimicrobial resistance

As a global public health issue, addressing antibiotic/antimicrobial resistance requires a global response. Therefore, the WHO calls for concerted global attack against antibiotic/antimicrobial resistance, which requires strong leadership, ongoing advocacy and sufficient resources (WHO, 2011). A global action plan proposed by the WHO identified the following five key strategies to address antimicrobial resistance (WHO, 2015):

1. Improve awareness and understanding of antibiotic/ antimicrobial resistance through effective communication, education and training

This strategy aims at encouraging nations to react against antimicrobial resistance through promotion and advocacy for antibiotics stewardship and behavioral change. 2. Strengthen the knowledge and evidence-based through research and surveillance

This strategy emphasizes the urgency to reinforce the capacity of laboratories in identifying bacteria and assessing their susceptibility to antimicrobial drugs with the ultimate goal of implementing or strengthening laboratories-based surveillance systems. Systems that would proactively report cases of antimicrobial resistance for further actions.

3. *Reduce the incidence of infection through effective hygiene and infection prevention measures*

This strategy aims at promoting best practices of hygiene, use of vaccines as well as evidence-based infections control in healthcare settings.

4. Optimize the use of antimicrobial medicines in human and animal health

This strategy encourages the control of access to medicines through partnerships across stakeholders involved in authorization, production, distribution, control and use of veterinary antimicrobial agents, as well as the publication of the lists of essential medicines as guidelines for providers.

5. Develop the business case for sustainable investment that considers the needs of all countries, as well as the need for investment in new medicines, diagnostic tools, vaccines and other interventions

This strategy aims at finding cost-effective approaches to engage and incentivize health researchers to develop new medical drugs with the potential of treating current resistant infections.

To understand the extent to which these five strategies are currently applied in Haiti to address antibiotic/ antimicrobial resistance, a set of semi-structured interviews was conducted with key stakeholders in leadership positions including the ministry of Health (MSPP) about their insights. In December 2015. Institutional Review Board (IRB) approval was obtained from both the University of North Carolina (UNC) at Chapel Hill and the National Bioethics Committee of Haiti.

Summary of interviews' results

For confidentiality reasons, the data collected will remain anonymous as agreed with the interviewees. Instead of individual quotes, the responses from all the non-governmental interviewees will be aggregated and compared to the Ministry of Health's (MSPP) perspective for each of the five strategies proposed by WHO.

WHO strategy # 1: *Improve awareness and understanding of antibiotic/ antimicrobial resistance through effective communication, education and training* (Please refer to page 9).

Issues Identified		What has been done	What needs to be done
•	No assessment of antibiotic / antimicrobial resistance.	 Several campaigns have been launched against antibiotic/ antimicrobial resistance. 	• Expansion of the regulation of medical drugs nationwide.
		• Regulation of the use and selling of medical drugs at least in Port-Au-Prince.	

Key Stakeholders perspective

I	ssues Identified	What has been done	What needs to be done
•	Unavailability of data to confirm if antibiotic/ antimicrobial resistance is a public health issue.	• Availability of data for MDR-TB	• Provide national guidelines for healthcare providers to follow to foster a better standardization of care delivery.
•	Lack of motivation of the parliament to pass a policy even to make mandatory MDR-TB treatment.		 Train providers on antibiotics use. Use the partnerships of the
•	Antibiotic/ antimicrobial resistance might be a public health problem because of the current misuse of antibiotics in Haiti.		Ministry to provide scholarships to potential candidates interested in public health and willing to serve Haiti.
•	Not enough trained public health professionals working at the Ministry of Health (MSPP) able to help identifying key priorities and strengthen our Health systems.		

WHO strategy # 2: Strengthen the knowledge and evidence-based through research and

surveillance (Please refer to pages 9-10 for details).

Ministry of Health (MSPP) perspective

	Issues Identified	What has been done	What needs to be done
•	Availability of specific data about antibiotic/ antimicrobial resistance in Haiti requires capacity building of institutions to systematically investigate the patterns of resistance, which is currently not widely available in Haiti.	 Pharmaceutical agencies are required to receive authorization from this Ministry every time they are ordering medicines from abroad in order to track the laboratory producing the medicines imported by Haiti for quality assurance. Partnerships for pharmaco-vigilance with countries like Belgium, USA (FDA) to exchange data on the quality of the medicines on the market to protect the nation. 	 Reinforcement of the policy to regulate the entry of medicines in Haiti, because not all the drugstores are registered with this Ministry.
	resistance in Haiti requires capacity building of institutions to systematically investigate the patterns of resistance, which is currently not widely available in Haiti.	 from this Ministry every time they are ordering medicines from abroad in order to track the laboratory producing the medicines imported by Haiti for quality assurance. Partnerships for pharmaco-vigilance with countries like Belgium, USA (FDA) to exchange data on the quality of the medicines on the market to protect the nation. 	in Haiti, because not all the drugstores are registered with this Ministry.

Key Stakeholders perspective

Issues Identified		W	hat has been done	W	hat needs to be done
•	Lack of microbiology laboratories.	•	Two research projects addressing antibiotic/ antimicrobial resistance in at	•	Provide the Departmental hospitals adequate laboratories with the capacity to do cultures to document
•	Lack of infectious diseases specialists.		risk population for Cholera, MDR-TB using GeneXpert and culture of germs via		antibiotic/ antimicrobial resistance nationwide.
•	Very limited access to microbial cultures and		Drugs sensitivity tests (DST).	•	Improve access to affordable laboratory tests.
	resistance tests.	•	Only three organizations in the public sector have the		
•	30% of 3,000 patients who received Highly Active Antiretroviral Therapy		capacity to do microbial resistance tests.		
	(HAART) failed to reach an undetectable Viral load.	•	Currently a pilot research study on HIV resistance aims to collect data on HIV genotyping to assess if there would be an association between the reported therapeutic failure cases and HAART-resistant HIV.		

WHO strategy # 3: *Reduce the incidence of infection through effective hygiene and infection*

prevention measures (Please refer to page 10 for details).

Ministry of Health (MSPP) perspective

Issues Identified		What has been done	What needs to be done
	People who live in urban areas are likely to be exposed to healthcare settings and at risk for resistant nosocomial infections.	 Reinforce education on hygiene nationwide through campaigns to raise public awareness as done in response to the Cholera epidemic 	• Educate more the population.
	• Practice of self-medication with antibiotics.		

Key Stakeholders perspective

Issues Identified		What has been done	W	hat needs to be done
•	No policy or law to isolate or put in quarantine people diagnosed with MDR-TB.	Nothing reported	•	Train more healthcare professionals especially the University students in infectious diseases and microbiology to promote the control of infections.
•	Lack of asepsis in healthcare settings		•	Availability of running water in all healthcare facilities to foster hand- washing and reduce the spread of resistant nosocomial pathogens.

WHO strategy # 4: *Optimize the use of antimicrobial medicines in human and animal health*

(Please refer to page 10 for details).

Ministry of Health (MSPP) perspective

Issues Identified		V	What has been done	V	What needs to be done
•	No policy in place yet to	•	Within this Ministry, the	•	Availability of incentives to
•	specifically mitigate the occurrence of antibiotic/ antimicrobial resistance. Consumption of imported poultry from countries where antibiotics is heavily used in livestock.	•	direction of care oversees the prescription of antibiotics for clinical sites. Regulations of the registered drugstores have been reinforced by requiring them to hire at least one pharmacist to manage and control their expired medicines.	•	motivate owners of medical drugs to destroy their expired stock. Establish a surveillance system for emergent antibiotic/antimicrobial resistance.
•	The biggest challenge to destroy expired stock of medicines.	•	Shortening of the license renewal period of registered drugstores from 2-3 years to 1 year now.		
•	Lack of resources available for this Ministry to implement sustainable interventions against the current practices.		of private hospitals in this pharmaco-vigilance, where copies of all the prescriptions are available and saved to report to this Ministry for review to see if there was an order for lab tests/culture associated with the prescribed antibiotics.		

Key Stakeholders perspective

Issues Identified	What has been done	What needs to be done
• No existing policy in place to control the entry of donated medicines and assess their quality.	• Nothing reported.	 Training and coaching on antibiotics stewardship for prescribers and dispensers of antibiotics nationwide.
 No national document available addressing antibiotic/antimicrobial resistance. Set of risk factors for antibiotic/ antimicrobial resistance in Haiti: self-medication, selling of medicines in the streets exposed to the sunlight, rain, humidity, misconception of the effects of antibiotics by the general public, adoption of a syndromic approach by healthcare providers in response to limited access to laboratory tests. The well-known practice where many women buy and consume antibiotics without prescription after their periods to clean up and prevent infections (personal 		 Educate the general population on the appropriate use of antibiotics and the consequences of their misuse considering the socio- economic and cultural components as barriers. Some classes of antibiotics should be allowed to be prescribed only by infectious disease specialists. Use legal means to ban the selling of medicines including antibiotics in the streets.
denets).		

WHO strategy # 5: *Develop the business case for sustainable investment that considers the*

needs of all countries, as well as the need for investment in new medicines, diagnostic tools,

vaccines and other interventions (Please refer to page 10 for details).

Ministry of Health (MSPP) perspective

Issues Identified	What has been done	What needs to be done
 No specific issue reported. 	• Progressive removal of the streets vendors of medicines from the market using a trade-off approach, where they received stocks of iodine salt to sell in the streets instead of the medicines that they used to buy.	 Eliminate the streets vendors of medicines by promoting agriculture and the exportation of their food to ensure sufficient income for their living expenses while protecting the population. Support from potential international partners to foster better access to new protocols of antibiotics. Financial assistance to buy these new antibiotics required to handle antimicrobial resistance, in order to subsidize the vulnerable people in need, because otherwise they will more likely die from their resistant infections despite the advances of health research.

Key Stakeholders perspective

Issues Identified	What has been done	What needs to be done
• Nothing reported	Nothing reported	Nothing reported

WHO perspectives on Haiti's Health System capabilities to address antimicrobial resistance

WHO argued that it is critical to prevent infections from occurring in the first place as a costeffective approach to reduce the need for antibiotics by doing the following: "Better hygiene, Access to clean water and sanitation, Infection control in healthcare facilities, Vaccination" (WHO, 2014). However, the Haitian health systems makes it difficult to implement these activities. The lack of infrastructure of the Haitian Ministry of Health has led to the fact that almost 80% of the population rely on traditional medicine as their first resource for healthcare due to several reasons such as access to care, cost, personal beliefs (PAHO/WHO, 2012). Indeed, the sad reality on the ground is that except for HIV/AIDS, TB, and Malaria there are no national standard treatment guidelines and antibiotics are frequently sold over the counter without a prescription which hinders the rational use of pharmaceuticals (PAHO/WHO, 2012). Moreover, the Haitian Government does not have a national policy that sets the price of medical drugs and regulates their prescriptions and selling except for narcotic medical drugs (MSPP, 2014). Fewer than five pharmaceutical laboratories are officially designated to produce drugs for national use and "supply approximately 30% to 40% of the Haitian market", but there is a quasi-absence of official guidelines or regulations for donated medicines which may foster the use of expired medicines by the population (PAHO/WHO, 2012).

Discussion

Based on the results of the interviews, it appears that major gaps exist in the implementation of all WHO strategies in Haiti. Both the Ministry of Health (MSPP) and the key stakeholders acknowledged that the quasi-absence of assessment of antibiotic/ antimicrobial resistance, made it hard to objectively support that it would be a public health issue in Haiti, despite the current unregulated conditions of antibiotics use nationwide. However, the stakeholders identified the following major issues:

- Limited access to microbiology laboratories.
- Misuse of antibiotics, absence of policy to regulate the selling of medical drugs except for the narcotic drugs.
- Misperceptions of antibiotics use by the population.
- Absence of surveillance systems to document cases of antibiotic/ antimicrobial resistance.

The Ministry of Health felt that policies were in place to regulate the selling of medical drugs, but this was not perceived by other stakeholders. However, there was general agreement that there is need for educating the general public and healthcare providers on the dangers of antimicrobial resistance. It is also clear that a significant amount of research is needed to understand the extent of antimicrobial resistance in Haiti. Instead of having the few research organizations work in silo to conduct studies on MDR-TB with a sample size of subjects that is not necessarily representative of the population, it would be more beneficial to work collaboratively. By doing so, Haiti would be able to collect and report reliable data on antibiotic/ antimicrobial resistance from all the well-equipped public and private laboratories that would convene to launch and lead a National assessment of antibiotic/ antimicrobial resistance under the Ministry of Health (MSPP) oversight. Furthermore, the MSPP should expand the practice of peer audit of prescriptions to bring about changes in prescribing behavior across providers in both public and private sectors. Finally, Haiti's Health system needs to be substantially strengthened and capacity should be built in the areas of assessment, awareness, surveillance and vigilance, antibiotics stewardship, training, policy enforcement, and sustainable investment.

Recommendations

In summary, the following *policy and practice recommendations* can be made to further understand and address Haiti's antimicrobial drug resistance problem:

- Educate the general public and the providers on antibiotics stewardship
- Develop and apply policy to regulate and control the selling, consumption and destruction of all medical drugs, not just for the narcotic drugs like morphine

- Request assistance from the International community and partners to strengthen the capacity of at least the Universities and Departmental laboratories to improve access to labs tests
- Integrate a section for antibiotic/antimicrobial resistance into the current surveillance systems that reports to the Ministry of Health data on Cholera, HIV/AIDS, Tuberculosis
- Elaborate national guidelines to standardize the quality of care, in addition to those for Tuberculosis, HIV/AIDS, Cholera, Malaria
- Communicate and disseminate the progress and challenges of this Ministry, to engage more stakeholders and experts in this critical initiative

Role of leadership

Clearly leadership plays a very important role in addressing antibiotic/ antimicrobial resistance. As reported by the key stakeholders, the strategies implemented by the Ministry of Health (MSPP) are unknown by the practitioners, health facilities leaders and possibly by the general public. Therefore, the leadership team of this Ministry needs to become more assertive to articulate not only the needs but also the progress and barriers of its initiatives and to involve a broader set of stakeholders in assessment and in the design and implementation of interventions. This Ministry should also seek strong commitment from the legal system like the Ministry of Justice and the Parliament to enforce the law in support of antibiotics stewardship as well as to implement prospective policy that would allow providers to initiate mandatory treatment and isolation of all diagnosed MDR-TB people for the safety of the entire population.

Conclusion

To date antibiotic/ antimicrobial resistance remains an alarming public health issue globally. And the literature has not yet reported a single country that has fully tackled all the components of this major challenge. As with all health issues, better resourced countries like the United States seem to be more successful in addressing for example MDR-TB compared to others like Pakistan and Haiti. The World Health Organization (WHO) has developed an action plan as guidelines to mitigate the situation. As this paper shows, Haiti has taken some steps to follow these guidelines, but much still needs to be done, as confirmed by both reports in the literature and the opinion of the interviewed stakeholders. The Ministry of Health must be encouraged to take on a strong leadership role to address the policy and practice recommendations outlined in this paper.

References

- 1. Centers for Disease Control and Prevention. (2013). National Summary Data. CDC website. <u>http://www.cdc.gov/drugresistance/pdf/3-2013-508.pdf</u>
- 2. Centers for Disease Control and Prevention. (2014). http:// www.cdc.gov/drugresistance/pdf/carb_national_strategy.pdf. Published 2014.
- 3. Centers for Disease Control and Prevention. 2016. CDC fights against Global TB. <u>file:///E:/UNC%20_%20SPRING%202016%20Classes/PUBH%20992/global_tb_2016.p</u> <u>df</u>
- Dan S, Shah A, Justo JA, Bookstaver PB, Kohn J, Albrecht H, Al-Hasan MN. (2016). Prediction of Fluoroquinolone Resistance in Gram-Negative Bloodstream Infections. Antimicrob Agents Chemother. 2016 Feb 1. pii: AAC.02728-15.
- M. Z. David and R. S. Daum. (2010). "Community-associated methicillinresistant Staphylococcus aureus: epidemiology and clinical consequences of an emerging epidemic," Clinical Microbiology Reviews, vol. 23, no. 3, pp. 616–687, 2010.
- Deshpande LM, Fritsche TR, Moet GJ, Biedenbach DJ, Jones RN. (2007). Antimicrobial resistance and molecular epidemiology of vancomycin-resistant enterococci from North America and Europe: a report from the SENTRY antimicrobial surveillance program. *Diagn Microbiol Infect Dis* 2007; 58:163–170.
- 7. Frieden, Tom, MD, MPH. (2016). We can stop drug-resistant TB if we act now. Centers for Disease Control and Prevention. Posted on January 7, 2016
- Guiral, E., Bosch, J., Vila, J., & Soto, S. M. (2012). Antimicrobial resistance of escherichia coli strains causing neonatal sepsis between 1998 and 2008.*Chemotherapy*, 58(2), 123-8. doi:http://dx.doi.org/10.1159/000337062
- Hidron, A., Edwards, J., Patel, J., Horan, T., Sievert, D., Pollock, D... Participating Natl Healthcare Safe. (2008). Antimicrobial-Resistant pathogens associated with Healthcare-Associated infections: Annual summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2006–2007. *Infection Control and Hospital Epidemiology*, 29(11), 996-1011. doi:10.1086/591861

- Ibekwe AM, Murinda SE, DebRoy C, Reddy GB. (2016). Potential pathogens, antimicrobial patterns and genotypic diversity of Escherichia coli isolates in constructed wetlands treating swine wastewater. Oxford University Press on behalf of FEMS 2016. FEMS Microbiol Ecol. 2016 Feb;92(2). pii: fiw006. doi: 10.1093/femsec/fiw006. Epub 2016 Jan 10.
- 11. Jin Seok Kim, Young-Sun Yun, Soo Jin Kim, Se-Eun Jeon, Deog-yong Lee, Gyung Tae Chung, Cheon-Kwon Yoo, Junyoung Kim, PulseNet Korea Working Group. (2016). Rapid Emergence and Clonal Dissemination of CTX-M-15–Producing Salmonella enterica Serotype Virchow, South Korea Emerging Infectious Diseases. <u>www.cdc.gov/eid.Vol</u>. 22, No.1, January 2016 DOI: <u>http://dx.doi.org/10.3201/eid2201.151220</u>
- Patrice Joseph, Patrice Severe, Severine Ferdinand, Kye Seng Goh, Christophe Sola, David W. Haas, Warren D. Johnson, Nalin Rastogi, Jean W. Pape and Daniel W. Fitzgerald. (2006). Multidrug-resistant tuberculosis at an HIV testing center in Haiti. AIDS 2006, 20:415-418. ISSN 0269-9370
- Laxminarayan, R., Duse, A., Wattal, C., Zaidi, A. K. M., Wertheim, H. F. L., Sumpradit, N., Cars, O. (2013). Antibiotic resistance-the need for global solutions. *The Lancet Infectious Diseases*, 13(12), 1057-98. doi:http://dx.doi.org/10.1016/S1473-3099 (13)70318-9
- Lopez-Lozano, J.M., Monnet, D.L., Yague, A., Burgos, A., Gonzalo, N., Campillos, P., Saez, M., (2000). Modelling and forecasting antimicrobial resistance and its dynamic relationship to antimicrobial use: a time series analysis. Int. J. Antimicrob. Agents 14, 21–31.
- Marinelli, F., & Genilloud, O. (2013;2014;). Antimicrobials: New and old molecules in the fight against multi-resistant bacteria (1;2014; ed.). Dordrecht: Springer Berlin Heidelberg. doi:10.1007/978-3-642-39968-8
- Marques MM, Costa MR, Santana Filho FS, Vieira JL, Nascimento MT, Brasil LW, Nogueira F, Silveira H, Reyes-Lecca RC, Monteiro WM, Lacerda MV, Alecrim MG. (2014). Plasmodium vivax chloroquine resistance and anemia in the western Brazilian Amazon. Antimicrob Agents Chemother. 2014;58(1):342-7. doi: 10.1128/AAC.02279-12. Epub 2013 Oct 28.
- 17. Martin, P. Sawatzky, G. Liu, V. Allen, B. Lefebvre, L. Hoang, S. Drews, G. Horsman, J. Wylie, D. Haldane, R. Garceau, S. Ratnam, T. Wong, C. Archibald, M.R. Mulve. (2016). Decline in Decreased Cephalosporin Susceptibility and Increase in Azithromycin

Resistance in Neisseria gonorrhoeae, Canada. *Emerging Infectious Diseases* <u>www.cdc.gov/eid</u>. Vol.22, No.1, January 2016. DOI:http://dx.doi.org/10.3201/eid2201.151247

 Multari, R. A., Cremers, D. A., Bostian, M. L., Dupre, J. M., & Gustafson, J. E. (2013). Proof of principle for a real-time pathogen isolation media diagnostic: The use of laserinduced breakdown spectroscopy to discriminate bacterial pathogens and antimicrobialresistant staphylococcus aureus strains grown on blood agar. *Journal of Pathogens*,2013, 1-11. doi:10.1155/2013/898106

19. National Institute of Allergy and Infectious Diseases (NIAID), 2009 http://www.niaid.nih.gov/topics/antimicrobialResistance/Understanding/Pages/definitions.aspx

- Oksana Ocheretina, Willy Morose, Marie Gauthier, Patrice Joseph, Richard D'Meza, Vincent E Escuyer, Nalin Rastogi, Guy Vernet, Jean W Pape and Daniel W Fitzgerald. (2012). Multidrug-resistant tuberculosis in Port-au-Prince, Haiti. NIH Public Access. Rev Panam Salud Publica . 2012 March; 31(3): 221–224.
- 21. Pan American Health Organization (PAHO)/ World Health Organization (WHO). (2011). Commit to a Comprehensive, Financed National Plan with Accountability and Civil Society Engagement. A MASTER PLAN TO COMBAT ANTIMICROBIAL RESISTANCE. Available at http://www.who.int/world-health-day/2011 <u>file:///E:/UNC%20_%20SPRING%202016%20Classes/PUBH%20992/PAHO_WHO%2</u> <u>0Website/Policy%20Brief%2011.pdf</u>
- 22. Haiti National Program against Tuberculosis (PNLT). (2014). Epidemiology of MDR-TB in Haiti.
- 23. République d' Haiti. Ministère de la Santé Publique et de la Population (MSPP). 2014. Direction de la Pharmacie, du Médicament et de la Médecine Traditionnelle DPM/MT. Politique Pharmaceutique Nationale (PPN). Septembre 2014. <u>http://mspp.gouv.ht/site/downloads/PPN%20final%20mars%202015.pdf</u>
- 24. Jane Ritchie et al (2013). Qualitative Research Practice. The Framework approach to qualitative data analysis. Nat Gen Learning, Social Research that works for Society. Available at http://www.natcen.ac.uk/events-and-training/our-training

- Rossolini GM, Mantengoli E. (2008). Antimicrobial resistance in Europe and its potential impact on empirical therapy. Clin Microbiol Infect. 2008 Dec;14 Suppl 6:2-8. doi: 10.1111/j.1469-0691.2008.02126.
- 26. Safdar, N. (2014). MDR-TB in pakistan: A challenge in hand. *Pakistan Journal of Medical Research*, 53(3), 54.
- Schaaf HS, Marais BJ, Hesseling AC, Brittle W, Donald PR. (2009). Surveillance of antituberculosis drug resistance among children from the Western Cape Province of South Africa—an upward trend. Am J Public Health 2009; 99:1486–90 [Epub 2009 Feb 5]
- Sievert, D. M., Ricks, P., Edwards, J. R., Schneider, A., Patel, J., Srinivasan, A... for the National Healthcare Safety Network (NHSN) Team and Participating NHSN Facilities. (2013). Antimicrobial-resistant pathogens associated with healthcare-associated infections: Summary of data reported to the national healthcare safety network at the centers for disease control and prevention, 2009–2010.*Infection Control and Hospital Epidemiology*, 34(1), 1-14. doi:10.1086/668770
- 29. Singh, H., Kongo, J. M., Borges, A., D J B Ponte, & Griffiths, M. W. (2015). Lactic acid bacteria isolated from raw milk cheeses: Ribotyping, antimicrobial activity against selected food pathogens and resistance to common antibiotics. *Journal of Food Processing & Technology*, 6(9), 1.
- Shin SW, Byun JW, Jung M, Shin MK, Yoo HS.(2014). Antimicrobial resistance, virulence genes and PFGE-profiling of Escherichia coli isolates from South Korean cattle farms. J Microbiol. 2014 Sep;52(9):785-93. doi: 10.1007/s12275-014-4166-1. Epub 2014 Jul 30.
- Stagg, H. R., Brown, J., Ibraim, E., Riekstina, V., Viiklepp, P., Cirule, A... White, P. J. (2015). Drug susceptibility patterns in MDR-TB patients: Challenges for future regimen design. A cross-sectional study: E0142425. *PLoS One*, *10*(11) doi: 10.1371/journal.pone.0142425
- 32. Stephen JM, Jones RN. (2002). Assessment of pathogens and resistance (R) patterns among intensive care unit (ICU) patients in North America (NA): initial report from the SENTRY Antimicrobial Surveillance Program (2001). In: Programs and Abstracts of the

42nd Interscience Congress of Antimicrobial Agents and Chemotherapy American Society for Microbiology; September 27–30, 2002; San Diego, CA. Abstract C2-297.

- Soumya Swaminathan. (2012). Drug-resistance in childhood tuberculosis invisible and unnoticed. *Pediatric Infectious Disease 2012 April–June Editorial Volume 4, Number 2;* pp. 41–42 doi: 10.1016/S2212-8328(12)60019-8
- 34. Takesue, Y., Watanabe, A., Hanaki, H., Kusachi, S., Matsumoto, T., Iwamoto, A... Yanagihara, K. (2012). Nationwide surveillance of antimicrobial susceptibility patterns of pathogens isolated from surgical site infections (SSI) in japan. *Journal of Infection and Chemotherapy*, 18(6), 816-826. doi:10.1007/s10156-012-0509-1
- 35. Tillotson, G. (2015). Antimicrobial resistance: What's needed. *The Lancet. Infectious Diseases*, 15(7), 758-760. doi:10.1016/S1473-3099(15)00081-X
- 36. Tognim MC, Andrade SS, Silbert S, Gales AC, Jones RN, Sader HS. (2004). Resistance trends of Acinetobacter spp. in Latin America and characterization of international dissemination of multi-drug resistant strains: five-year report of the SENTRY Antimicrobial Surveillance Program. Int J Infect Dis. 2004 Sep;8(5):284-91.
- World Health Organization. Antimicrobial Resistance. Global Report on Surveillance 2014. Geneva: World Health Organization, 2014. Available at www.who.int/drugresistance
- 38. World Health Organization. Global tuberculosis report 2014. World Health Organization. 2014 [cited 2014 Nov 28]; Available: ttp://www.who.int/tb/publications/global_report/en/
- 39. World Health Organization. Global action plan on antimicrobial resistance. Geneva: World Health Organization, 2015. Available at <u>http://www.who.int/drugresistance/global_action_plan/ongoing_activities/en/</u>
- Zhanel, G. G., DeCorby, M., Adam, H., Mulvey, M. R., McCracken, M., Lagacé-Wiens, P... the Canadian Antimicrobial Resistance Alliance. (2010). Prevalence of antimicrobialresistant pathogens in canadian hospitals: Results of the canadian ward surveillance study (CANWARD 2008). *Antimicrobial Agents and Chemotherapy*, 54(11), 4684-4693. doi:10.1128/AAC.00469-10

Appendix

Interview questionnaires

A1) English version of the questionnaire interview for the Ministry of Health Officials of Haiti (MSPP)

<u>Disclosure</u>: Thank you for taking the time to meet with me and please note that the information that you will share with me here will be included in my Master Paper which is about "**Policy and**

practice recommendations for addressing Antimicrobial Resistance in Haiti: using the Public Health Quality Aims"

Interviewer/PI: Marie Lina Excellent (MPH student in PHLP at UNC – Chapel Hill, NC and Fulbright Scholar from Haiti)

Name of interviewee:

Organization:

Role /job position:

For how long have you held this position?

Set of questions for Officials from the Ministry of Health of Haiti, such as:

Minister of Health or Current General Director of the Ministry of Health

Former General Director of the Ministry of Health

Three categories of questions:

A) I would like to understand the current state of antimicrobial resistance in Haiti

- Would you consider antimicrobial resistance be a public health issue in Haiti?
- Would you like to share any relevant information that we should know about the current status of antimicrobial resistance in Haiti?
- □ How would you describe the impact of antimicrobial resistance in Haiti?
- □ Would there be a difference between people living in rural versus urban areas in terms of being at risk for that issue?

- Does the Ministry of Health have a system in place to collect data or reports from hospitals and organizations partners about antimicrobial resistance?
- Based on your perspective what would be the top conditions that have led to antimicrobial resistance in Haiti?

B) I would like to learn about the current policy in place in Haiti regarding Antimicrobial Resistance

- Does the Ministry of Health consider antimicrobial resistance a public health priority?
- Does the Ministry of Health have an existing policy addressing antimicrobial resistance in Haiti? If yes, how was it implemented nationwide?
- Does the Ministry of Health have a strategic plan to address antimicrobial resistance in Haiti? If yes, how was the piloting phase? How was it received by the general public and key stakeholders like healthcare providers, pharmaceutical agencies? What were some identified barriers to implementation?
- □ Is there a surveillance system established by the Ministry of Health to collect and monitor data about antimicrobial resistance?
- Does the Ministry of Health use the resources from the National Lab of Public Health to investigate the threat of antimicrobial resistance in Haiti?
- On September 2014 the Ministry of Health of Haiti published the National Pharmaceutical policy in which it is clearly stated that there are insufficient regulations and legislation to control the selling of medicines at national level? How would you address that?
- Do you have written legislations or process to enforce compliance to regulations regarding prescriptions, selling of antibiotics at National level?

C) I would like to hear about your willingness to accept and implement recommendations

- □ What type of support would be the most helpful to the Ministry of Health in developing and implementing policy related to antimicrobial resistance?
- □ What would be some recommendations for addressing antimicrobial resistance in Haiti?
- Please complete this sentence: As an official of the Ministry of Health, if I was asked by the Ministry of Health to provide one strategy or idea to address antimicrobial resistance in Haiti, I would say
- Has public health quality ever been considered when framing strategies for Antimicrobial Resistance in Haiti? Would Haiti be open to consider using an HHS framework for public health quality (Population-centered, Vigilant, Transparent, Efficient, Risk reducing, Effective, Health promoting, Proactive and Equitable) for developing a set of population-based strategies?
- What kind of support is the needed for (a) the development of policy to address antimicrobial resistance and (b) the implementation of the policy? Among the partners of the Ministry of Health do you in mind who might be able to provide that kind of support?
- Please feel free to provide any recommendations to improve this threat in Haiti

Any final words:

Thank you very much!

A2) English version of the questionnaire interview for key stakeholders/partners of Haiti Ministry of Health (MSPP)

<u>Disclosure</u>: Thank you for taking the time to meet with me and please note that the information that you will share with me here will be included in my Master Paper which is about "**Policy and**

practice recommendations for addressing Antimicrobial Resistance in Haiti: using the Public Health Quality Aims"

Interviewer/PI: Marie Lina Excellent (MPH student in PHLP at UNC – Chapel Hill, NC and Fulbright Scholar from Haiti).

Name of interviewee:

Organization:

Role /job position:

For how long have you held this position?

Three categories of questions:

A) I would like to understand the current state of antimicrobial resistance in Haiti

- Would you consider antimicrobial resistance be a public health issue in Haiti?
- □ Is your organization involved in any surveillance for antimicrobial resistance?
- Would you like to share any relevant information that we should know about the current status of antimicrobial resistance in Haiti? For example, in your hospital have you ever come across cases of antimicrobial resistance? If yes, how were the case managed?
- How would you describe the impact of antimicrobial resistance in Haiti?
 Would there be a difference between people living in rural versus urban areas in terms of being at risk for that issue?
- Based on your perspective what would be the top conditions that have led to antimicrobial resistance in Haiti?

B) I would like to learn about any existing policy in place in Haiti regarding Antimicrobial Resistance

- □ Is antimicrobial resistance a priority for your organization?
- Do you implement in your organization any policy to address antimicrobial resistance?
- Is there an established procedure in your organization to collect data related to antimicrobial resistance and then report them to the Ministry of Health for follow up?
- On September 2014 the Ministry of Health of Haiti published the National Pharmaceutical policy in which it is clearly stated that there are insufficient regulations and legislation to control the selling of medicines at national level. Would you like to share any thoughts about it?
- Based on your perspective what the Ministry of Health should include in a strategic plan to address antimicrobial resistance in Haiti? And what would you anticipate as being the major barriers to the effective implementation of a policy?
- Do you have any plan to implement strategies against antimicrobial resistance?
- □ What are some recommendations for addressing antimicrobial resistance in Haiti?
- □ For Pharmaceutical agencies ONLY: Do you have a process in place to mitigate antimicrobial resistance? Do you have specific procedures on selling medicines to independent individuals, pharmacists, etc?
- □ For Hospitals Seniors ONLY: Do you know if your hospital acknowledges the threat of antimicrobial resistance and what have been done about it? If yes, what is the approach? For example, do you implement educational messages about it to be shared at different levels like in the waiting room with the patients, small handouts or flyers in the outpatient clinics for providers, case studies about during academic activities with the residents and interns?

□ For National Lab of Public Health ONLY: Does the National lab currently work on projects that address antimicrobial resistance in Haiti? If yes, how do you track antimicrobial resistance?

C) I would like to hear about your willingness to accept and implement recommendations

- Based on your perspective what type of support would be the most helpful to the Ministry of Health in developing and implementing policy related to antimicrobial resistance?
- □ Would your organization be willing to consider recommendations from my policy brief which will be sent out to a scientific journal with an attempt for publication regarding antimicrobial resistance in the context of Haiti?
- Have you heard of the public health quality aims? Would your organization be open to consider using an HHS framework for public health quality (Population-centered, Vigilant, Transparent, Efficient, Risk reducing, Effective, Health promoting, Proactive and Equitable) to assist the Ministry of Health in developing a set of population-based strategies?
- Please feel free to provide any recommendations to improve antimicrobial resistance threat in Haiti
- Please complete this sentence: If my organization was asked by the Ministry of Health to provide one strategy or idea to address antimicrobial resistance in Haiti, I would say

Any final words:

Thank you very much!