

ISSUE 2

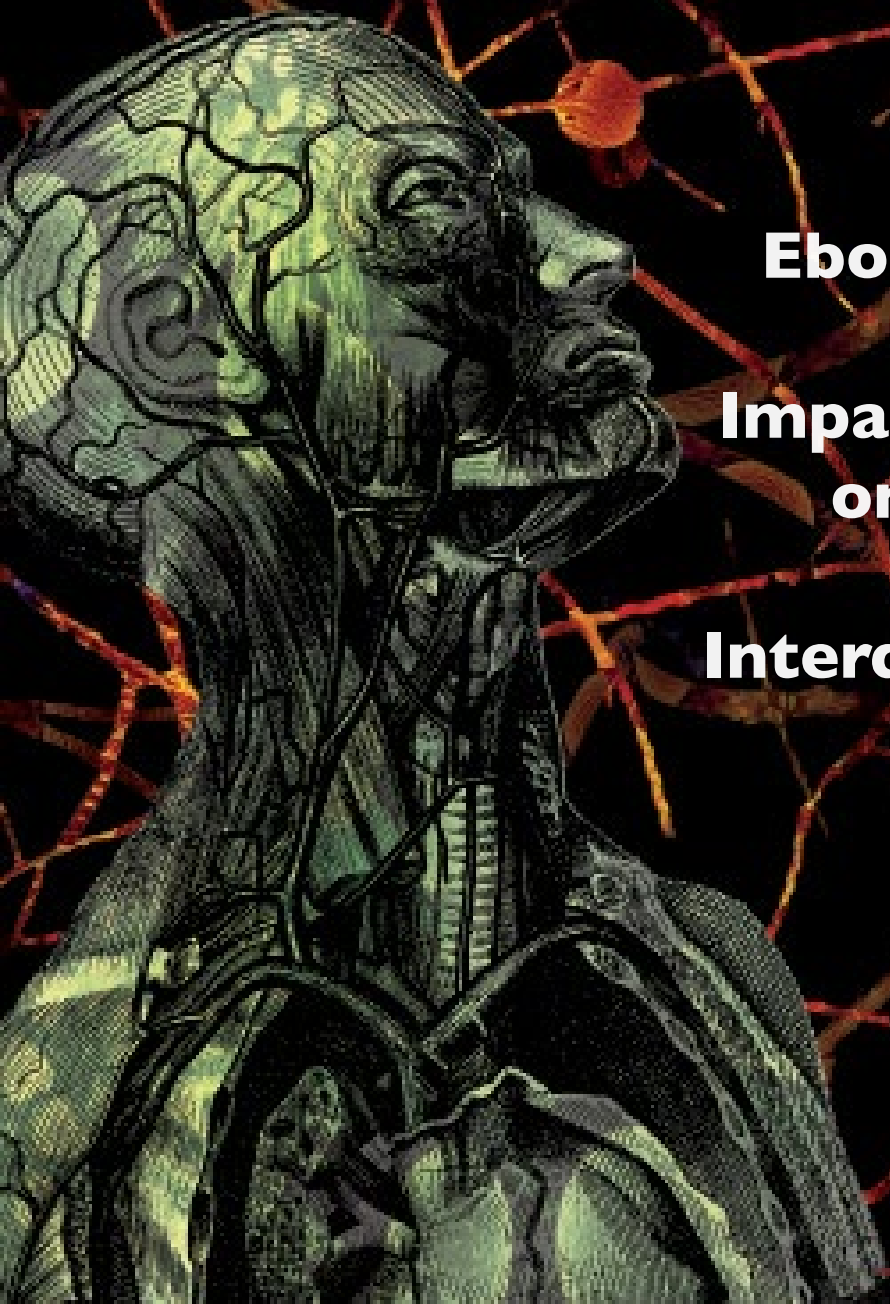
VOLUME 3

---

# THE JOURNAL OF GLOBAL HEALTH

---

FALL 2013



**Ebola Fever Outbreaks**

**Impact of Deforestation  
on Disease Incidence**

**Interdisciplinary Disease  
Education**

## Academic Research Papers

- 1 **Comparison of two Ebola hemorrhagic fever outbreaks**  
Tracey Young, MD  
*Kaiser Woodland Hills, University of California at Los Angeles, Los Angeles, CA, USA*
- 7 **HIV and public policy: Predictors of chronic homelessness in persons living with HIV/AIDS**  
Iman Simmonds, Ena O. Oru  
*Columbia University Mailman School of Public Health, New York, NY, USA*
- 11 **The epidemiology of noroviruses in Ghana: a case study of norovirus detection**  
Chuan-jay Jeffrey Chen,<sup>1</sup> Adel Mahmoud, MD, PhD,<sup>1</sup>  
George Armah, PhD<sup>2</sup>  
<sup>1</sup>*Princeton University, Princeton, NJ, USA*  
<sup>2</sup>*Noguchi Memorial Institute for Medical Research, Ayawaso, Accra, Ghana*

## Perspectives

- 16 **Impacts of deforestation on vector-borne disease incidence**  
Allison Gottwalt  
*George Washington University, Washington, DC, USA*
- 20 **Recommendations for increasing the efficacy & coverage of the rotavirus vaccination program in Ghana**  
Rachel A. Blake  
*Alpert Medical School, Brown University, Providence, RI, USA*
- 26 **Funding the future of global health: A medical student perspective**  
Sara Roberts, Sarah Smith, Juliette Mandel,  
Daniel George, PhD, MSc, N. Benjamin Fredrick, MD  
*Penn State University College of Medicine, Hershey, PA, USA*

## Field Notes

- 28 **“Anansi tricks Mrs. Mosquito”: An interdisciplinary malaria education program for school aged children in Kwahu-eastern region, Ghana**  
Deborah Lardner, DO, DTM&H, Michael Passafaro, DO, DTM&H, Jonathan Giordano, MS IV, Jasmine Beria MPH, MS IV  
*New York Institute of Technology Center for Global Health, New York, NY, USA*
- 33 **Medical neutrality and solidarity in the syrian armed conflict**  
Ravi S. Katari  
*Wake Forest School of Medicine, Winston-Salem, NC, USA*
- 37 **A look into the realities and complexities of tuberculosis as observed amongst zulu populations of durban, south africa**  
Margaret Variano  
*Tulane University, New Orleans, LA, USA*

During the devastating plague of Athens in the 5th century BC, the historian Thucydides noted that survivors of the epidemic could freely care for the sick without any risk of repeated infection. It was not until over two millennia later that Pasteur’s seminal work brought about the widespread acceptance of germ theory, which demonstrated that microorganisms could cause and spread illness. This new paradigm of disease revolutionized the fields of medicine and public health, ultimately enabling our contemporary understanding of infection, immunity and epidemiology. The field of infectious diseases has evidently wielded a powerful influence on medical investigation throughout human history. With Volume III, Issue II of *The Journal of Global Health*, we aim to reexamine this critical subject within the context of the modern era.

Like many important topics in global health, infectious diseases represent a complex interplay of the life sciences, sociology and domestic and international public policy. Breakthroughs in scientific techniques have enabled the accumulation of an unprecedented wealth of knowledge about the biology of many infectious pathogens. As our understanding of the basic science continues to grow, however, current public health efforts also must take into account the practical complications of disease prevention and treatment. Such approaches may focus on accessible education, such as anti-malaria instructional modules designed to prevent spread of the disease among schoolchildren. Additionally, biological differences across strains of related pathogens may combine with distinct geopolitical conditions to affect drastically the relative effectiveness of disease control programs. Chronic infections such as HIV can especially go on to exacerbate existing social concerns such as homelessness, requiring a concerted approach to specific treatment and overall wellness in order to produce any significant gains in actual health. All these issues and more are trenchantly discussed by the pieces featured in this issue of the *Journal*, which presents a broad spectrum of original research and viewpoints in the multifaceted field of infectious diseases.

As JGH commemorates its third year in circulation, we are proud to continue serving as the major voice of students from around the world who are actively engaged in shaping the future of global health. I have been continually impressed by the tremendous success with which the organization has consistently managed to surpass its ambitious goals, and it is therefore my pleasure to present to our readers my final issue both as Editor-in-Chief and as a member of the organization. As I move on, I eagerly look forward to seeing JGH continue to make a difference.

**Amit Saha**  
Editor-in-Chief



*Esther Jung*

Front cover design by Erica Cohenmehr

All articles published, including research articles, perspectives and field notes, represent the opinions of the author(s) and do not reflect the official policy of JGH or of the institution(s) with which the author is affiliated, unless this is clearly indicated.

Manuscripts should be submitted online via our online manuscript submission system at [www.ghjournal.org](http://www.ghjournal.org). All inquiries regarding submissions, advertisements, subscriptions and permissions to republish or adapt material should be addressed to: [info@ghjournal.org](mailto:info@ghjournal.org).

*The Journal of Global Health*  
5464 Lerner Hall  
2920 Broadway  
New York, NY 10027, USA  
[info@ghjournal.org](mailto:info@ghjournal.org)

ISSN: 2166-3602 (Print)  
ISSN: 2166-3599 (Online)

© 2013 *The Journal of Global Health*.  
All Rights Reserved.

### Editor-in-Chief

Amit Saha

### Managing Editor (ERB)

Dana Neugut

### Managing Editor (Online)

Connie Chen

### Executive Editor (ERB)

Frances Cho

### Executive Editors (Online)

Karen Gambina, Cynthia Li

### Creative Director (Online)

Kevin Xu

### Faculty Advisors

Norman J. Kleiman, Ph.D., *Mailman School of Public Health, Columbia University*

Vincent Racaniello, Ph.D., *College of Physicians and Surgeons, Columbia University*

Bhaven Sampat, Ph.D., *Mailman School of Public Health, Columbia University*

### Editorial Review Board

#### Senior Editors

David Gabriel, Jason Kang, Kelsey Roberts

#### Associate Editors

Anjali Agarwalla, Kristy Choi, Anjali Doshi, Koryalys Edwards, Erin Falk, Taylor Gray, Rachel Harrus, Benjamin Joffe, Zhenrui Liao, Diana Ruan, Yasaman Seyedi, Jeremy Sherman, Brahadheeshwar Sundararaju, Merry Sun, Chris Wen, Bitania Wondimu, Ming Zhao, Helen Zhou

### JGH Online & Web Development Team

#### Executive Web Editors

Veronica Li, Ponni Vel

#### Associate Editors

Emma Cheng, Elizabeth DePrato Cochran, Corinne Rodgers Corbett, Stuart Fine, Katherine Patrice Kester, Mariko Kanai

#### Web Developers

Kenneth Li, Kellie Liu, Eric Wei

### Design & Layout Team

#### Executive Design Editors

Esther Jung, Kay Lodge

#### Associate Editors

Erica Cohenmehr, Minah Kim, Gonzalo Paz-Soldan

### Business & Communications Board

#### Executive Director

Grant King

#### Deputy Director

Katherine Jin

#### Executive Publication Strategists

Noah Chodos, Margaret Chou

#### Business Associates

Mitu Bhattatiry, Julie Chen, Olivia Lemons, Polina Porotskaya

### Graduate Student Advisory Board

Sonia Gupta, Seong Jin Kim, Ruch Kumbhani, Ena Oru, Sheila Pande, Kathleen Rees, Richa Singh, Richa Wahi, Ze Zhang

# Academic Research

.....

COMPARISON OF TWO EBOLA HEMORRHAGIC FEVER OUTBREAKS	1
HIV AND PUBLIC POLICY	7
THE EPIDEMIOLOGY OF NOROVIRUSES IN GHANA	11

## Comparison of Two Ebola Hemorrhagic Fever Outbreaks: Uganda 2000-01 and Republic of the Congo 2001-02

Tracey C. Young MD

Kaiser Permanente Woodland Hills, University of California at Los Angeles, Los Angeles, CA, USA

.....

### Abstract

Many factors contribute to the severity of viral epidemics. Two outbreaks of Ebola, one in Uganda and one in the Republic of the Congo, were compared to assess their impact on social and political environment and the impact of viral strain on identification and containment of disease. The outbreaks were similar in many respects, allowing comparison of factors such as duration of outbreak, number affected and mortality. Both outbreaks were the first reported in the region and occurred during the same time of year. Both affected nations had the same access to international resources, such as the World Health Organization (WHO) and other aid groups willing to assist and provide financial support/resources. Data for this study was gathered from the United Nations Office for the Coordination of Humanitarian Affairs, the United States Centers for Disease Control (CDC) and the WHO's published data on the outbreaks in Uganda and Republic of Congo in 2000 and 2001, respectively.

The results demonstrate that the percent of the population infected, percent mortality, length of outbreak and virulence of the Ebola strain were all greater in the Republic of Congo outbreak, arguably due to differences in the social and political climate. The general response to the Ugandan outbreak was more rapid and more effective. Although different strains of the Ebola virus caused the outbreaks, mortality rates were high for both the Ebola-Zaire and Ebola-Sudan strains. Both outbreaks had decreased mortality rates compared to initial predictions. It is argued that the data from the Republic of the Congo outbreak was artificially low due to reporting bias and changes in outbreak parameters, resulting in a greater reported mortality. Indeed, prompt, organized and monitored infection control protocols are imperative to limit the morbidity and mortality of this disease, as seen in both the Uganda and the Republic of the Congo outbreaks on the health and economy of this region and a potential target for medical intervention.

.....

### Introduction

Ebola is among the deadliest of any known virus, with up to 90% mortality in some cases.<sup>1</sup> Named after a river in Zaire (modern-day Democratic Republic of the Congo) where the first known cases were reported, the virus causes Ebola hemorrhagic fever. This disease has claimed many lives throughout central Africa. At present, there is no cure.

It is important to understand several points about Ebola in order to discuss its prevalence as well as strain variation. An RNA virus in the Filoviridae family, Ebola has five identified subtypes according to the CDC; however, only Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast and Ebola-Bundibugyo are known

to affect humans. The last strain, Ebola-Reston, only affects non-human primates.<sup>1</sup> The outbreaks in Uganda and Republic of the Congo were caused by different strains. The outbreak in Uganda was caused by the Ebola-Sudan strain, which has a 60-65% mortality rate and is known to spread more easily than others.<sup>1,2</sup> By contrast, the Republic of the Congo outbreak was caused by the Ebola-Zaire strain, which has a higher mortality rate of 85-95%.<sup>2</sup> The Zaire strain is more virulent but is easier to test for as some tests require only ten viral particles to obtain a positive result.<sup>3</sup> The natural reservoir or animal host of Ebola virus remains unknown, but is generally thought to be a primate native to Africa.<sup>4</sup> Initial Ebola spread is thought to be initiated through

blood contact with an infected primate; the virus then spreads from person to person through contact with contaminated body fluids.<sup>4</sup> This is important to note, as epidemic containment would need to include both the education of local hunting populations and the ability to report sick or dead primates within a region. Furthermore, early studies of the virus in 1979 showed that most cases of Ebola resulted from secondary spread to family members and health care workers. In fact, 29 of the 34 cases first reported in Sudan were attributed to secondary spread, emphasizing the importance of proper infection control measures.<sup>5</sup> Understanding how this virus spreads gives insight into the types of protective gear that health care staff need.

To better prevent viral spread and illness, learning more about how the virus works is crucial. The incubation period for this virus ranges from two to 21 days; thus, outbreaks are declared over when no new cases are found for 42 days—twice the longest incubation period.<sup>6</sup> Symptoms of Ebola infection occur abruptly: fever, headache, muscle ache, sore throat and fatigue occur early, followed by diarrhea, vomiting and abdominal pain. Internal and external hemorrhages, the signature symptoms of Ebola, are only seen in the late stages of the infection.<sup>4</sup> Because the early symptoms are nonspecific, Ebola must be diagnosed with specialized laboratory tests. First, antigen-capture enzyme-linked immunosorbent assays (ELISA) and immunoglobulin M (IgM) testing use antibodies to detect virus in the blood; then polymerase chain reactions (PCR) amplify viral DNA in blood samples; and finally, blood cultures isolate the virus. The presence of immunoglobulin G (IgG), an antibody produced by the body during recovery, can show prior infection in survivors. Although survivors do exist, it is not known why they are able to mount an adequate immune response while others cannot.<sup>4</sup> Antigen-capture ELISA testing, PCR and virus isolation can also be used to confirm post-mortem identification of Ebola. Since there is no specific treatment for Ebola at this time, patients are only able to receive supportive care.

Further, discussions of political and social differences between the regions allow exploration of other sources of differences between the outbreaks. At the time of the outbreak in 2000, Uganda operated a free market economy, which had been growing since its establishment in 1987. The country had an established no-party democracy, and based on an survey in 2000, this was the favored mechanism of government for 90 percent of the voters (although admittedly, there were contentions about the legitimacy of this vote according to US human rights groups).<sup>7</sup> In addition, Uganda held a presidential election in March of 2001, and reelected their previous leader, Yoweri Museveni. Reports suggest that he won with 69.3% of the votes compared to the 27.8% of the next closest competitor, although the election was rife with accusations of intimidation and fraud.<sup>7</sup> Despite these flaws, the margin of victory was large enough that the government was fairly cohesive during his term. As in the case with Ebola, national and international recommendations were more easily instituted as a result of Uganda's stability. Thus, when there is little dissent among ruling parties and local populations support the national leadership, international aid workers can more effectively work to contain the epidemic with the assurance of personal safety.

In stark contrast, the Republic of the Congo's transition from a socialist to market economy was a more difficult one that began in the 1980s and left the country with a substantial budget deficit.<sup>7</sup> Economic instability left some areas with limited resources, especially in healthcare facilities, where a lack of resources would be extremely detrimental in an Ebola outbreak. During this same period, the Republic of the Congo enacted democratic elections and in 1993 Pascal Lissouba became the country's first democratically elected leader. When elections loomed again in 1997, conflict broke out between supporters of Lissouba and supporters of his opponent, Denis Sassou-Nguesso, leading to a five-month civil war.

Sassou-Nguesso's forces won, and he declared himself president. However, more fighting ensued soon after and continued through the end of the millennium. By the start of the outbreak in 2001, no settlement had been reached and the civil war persisted.<sup>7</sup> In the midst of civil war and unclear national leadership, possible warning signs and safety concerns about Ebola were more easily lost, under-reported or not reported at all. Compared to Uganda, the Republic of the Congo was less politically stable and thus unable to assure the safety of aid workers in its volatile climate.

Since the Ebola virus has a high mortality rate and is very infectious, it is a public health imperative to investigate and improve upon ways to manage outbreaks. The outbreaks in Uganda and Republic of the Congo, which spanned 2000-2001 and 2001-2002 respectively, were selected for this study because of several specific similarities and differences that make them appropriate for comparison. Both were the first known outbreak reported in each region, so there would be equally limited community knowledge about the disease and no previous containment policies in place. Furthermore, both occurred during roughly the same time of year in regions with similar weather conditions; thus, temporal and climatic effects are less disruptive to the main object of the paper. Known information and guidelines for care and prevention were the same in both regions, as was access to international resources. Because these variables are similar in the two groups, they may be removed from consideration as reasons for differences in outcome.

In contrast, the two outbreaks occurred in countries with vastly different political and social climates. The other major difference between the outbreaks was the strain of the virus: in the Republic of the Congo it was the Zaire strain, and in Uganda it was the Sudan strain. Controls used for expected mortality and spread for each strain were designated by WHO based on previous laboratory and human outbreaks that occurred without any official outbreak containment practices in place. This comparison was designed to elucidate the differences in the effects of the two viral strains, as well as the effects of social and political environment on identification and containment of the disease, length of outbreak, numbers affected and mortality.

### Review

Ebola is among the deadliest of any known virus, with up to 90% mortality in some cases.<sup>1</sup> Named after a river in Zaire (modern-day Democratic Republic of the Congo) where the first known cases were reported, the virus causes Ebola hemorrhagic fever. This disease has claimed many lives throughout central Africa. At present, there is no cure.

Ebola is among the deadliest of any known virus, with up to 90% mortality in some cases.

It is important to understand several points about Ebola in order to discuss its prevalence as well as strain variation. An RNA virus in the Filoviridae family, Ebola has five identified subtypes according to the CDC; however, only Ebola-Zaire, Ebola-Sudan, Ebola-Ivory Coast

and Ebola-Bundibugyo are known to affect humans. The last strain, Ebola-Reston, only affects non-human primates.<sup>1</sup> The outbreaks in Uganda and Republic of the Congo were caused by different strains. The outbreak in Uganda was caused by the Ebola-Sudan strain, which has a 60-65% mortality rate and is known to spread more easily than others.<sup>1,2</sup> By contrast, the Republic of the Congo outbreak was caused by the Ebola-Zaire strain, which has a higher mortality rate of 85-95%.<sup>2</sup> The Zaire strain is more virulent but is easier to test for as some tests require only ten viral particles to obtain a positive result.<sup>3</sup> The natural reservoir or animal host of Ebola virus remains unknown, but is generally thought to be a primate native to Africa.<sup>4</sup> Initial Ebola spread is thought to be initiated through blood contact with an infected primate; the virus then spreads from person to person through contact with contaminated body fluids.<sup>4</sup> This is important to note, as epidemic containment would need to include both the education of local hunting populations and the ability to report sick or dead primates within a region.

Furthermore, early studies of the virus in 1979 showed that most cases of Ebola resulted from secondary spread to family members and health care workers. In fact, 29 of the 34 cases first reported in Sudan were attributed to secondary spread, emphasizing the importance of proper infection control measures.<sup>5</sup> Understanding how this virus spreads gives insight into the types of protective gear that health care staff need.

To better prevent viral spread and illness, learning more about how the virus works is crucial. The incubation period for this virus ranges from two to 21 days; thus, outbreaks are declared over when no new cases are found for 42 days—twice the longest incubation period.<sup>6</sup> Symptoms of Ebola infection occur abruptly: fever, headache, muscle ache, sore throat and fatigue occur early, followed by diarrhea, vomiting and abdominal pain. Internal and external hemorrhages, the signature symptoms of Ebola, are only seen in the late stages of the infection.<sup>4</sup> Because the early symptoms are nonspecific, Ebola must be diagnosed with specialized laboratory tests. First, antigen-capture enzyme-linked immunosorbent assays (ELISA) and immunoglobulin M (IgM) testing use antibodies to detect virus in the blood; then polymerase chain reactions (PCR) amplify viral DNA in blood samples; and finally, blood cultures isolate the virus. The presence of immunoglobulin G (IgG), an antibody produced by the body during recovery, can show prior infection in survivors. Although survivors do exist, it is not known why they are able to mount an adequate immune response while others cannot.<sup>4</sup> Antigen-capture ELISA testing, PCR and virus isolation can also be used to confirm post-mortem identification of Ebola. Since there is no specific treatment for Ebola at this time, patients are only able to receive supportive care.

Further, discussions of political and social differences between the regions allow exploration of other sources of differences between the outbreaks. At the time of the outbreak in 2000, Uganda operated a free market economy, which had been growing since its establishment in 1987. The country had an established no-party democracy, and based on an survey in 2000, this was the favored mechanism of government for 90 percent of the voters (although admittedly, there were contentions about the legitimacy of this vote according to US human rights groups).<sup>7</sup> In addition, Uganda held a presidential election in March of 2001, and reelected their previous leader, Yoweri Museveni. Reports suggest that he won with 69.3% of the votes

compared to the 27.8% of the next closest competitor, although the election was rife with accusations of intimidation and fraud.<sup>7</sup> Despite these flaws, the margin of victory was large enough that the government was fairly cohesive during his term. As in the case with Ebola, national and international recommendations were more easily instituted as a result of Uganda's stability. Thus, when there is little dissent among ruling parties and local populations support the national leadership, international aid workers can more effectively work to contain the epidemic with the assurance of personal safety.

In stark contrast, the Republic of the Congo's transition from a socialist to market economy was a more difficult one that began in the 1980s and left the country with a substantial budget deficit.<sup>7</sup> Economic instability left some areas with limited resources, especially in healthcare facilities, where a lack of resources would be extremely detrimental in an Ebola outbreak. During this same period, the Republic of the Congo enacted democratic elections and in 1993 Pascal Lissouba became the country's first democratically elected leader. When elections loomed again in 1997, conflict broke out between supporters of Lissouba and supporters of his opponent, Denis Sassou-Nguesso, leading to a five-month civil war. Sassou-Nguesso's forces won, and he declared himself president. However, more fighting ensued soon after and continued through the end of the millennium. By the start of the outbreak in 2001, no settlement had been reached and the civil war persisted.<sup>7</sup> In the midst of civil war and unclear national leadership, possible warning signs and safety concerns about Ebola were more easily lost, under-reported or not reported at all. Compared to Uganda, the Republic of the Congo was less politically stable and thus unable to assure the safety of aid workers in its volatile climate.

Since the Ebola virus has a high mortality rate and is very infectious, it is a public health imperative to investigate and improve upon ways to manage outbreaks. The outbreaks in Uganda and Republic of the Congo, which spanned 2000-2001 and 2001-2002 respectively, were selected for this study because of several specific similarities and differences that make them appropriate for comparison. Both were the first known outbreak reported in each region, so there would be equally limited community knowledge about the disease and no previous containment policies in place. Furthermore, both occurred during roughly the same time of year in regions with similar weather conditions; thus, temporal and climatic effects are less disruptive to the main object of the paper. Known information and guidelines for care and prevention were the same in both regions, as was access to international resources. Because these variables are similar in the two groups, they may be removed from consideration as reasons for differences in outcome.

In contrast, the two outbreaks occurred in countries with vastly different political and social climates. The other major difference between the outbreaks was the strain of the virus: in the Republic of the Congo it was the Zaire strain, and in Uganda it was the Sudan strain. Controls used for expected mortality and spread for each strain were designated by WHO based on previous

When faced with this outbreak of Ebola, the Ugandan government acted decisively, implementing national preventive measures and soliciting the assistance of international groups.

laboratory and human outbreaks that occurred without any official outbreak containment practices in place. This comparison was designed to elucidate the differences in the effects of the two viral strains, as well as the effects of social and political environment on identification and containment of the disease, length of outbreak, numbers affected and mortality.

### Discussion

The substantial disparity in the political environment at the time is inseparable from the differences in outcome between the two countries' Ebola outbreaks. Since the ruling party in Uganda was generally accepted, the economy was growing and there were few shifts in power, political views or policies at the time—as a result, the political climate was more stable than that of the Republic of the Congo. Political stability allowed for easier communication and coordination between local, national and international governing bodies, and therefore easier implementation of outbreak protocols. Ultimately, this led to better infection control.

The Republic of the Congo, on the other hand, had difficulty relaying information from local to national and international organizations and vice versa due to the ongoing civil war. Lack of cooperation between neighboring communities, national government and international aid organizations, secondary to the political climate in the Republic of the Congo, also hindered the rapid administration of adequate surveillance. This led to inconsistent and ineffective implementation of the WHO containment measures.<sup>12</sup> Thus, the Republic of the Congo fell short of using full containment measures.

There are other potential sources of variation between the two outbreaks. There is known variation in strain virulence, so the studied outbreak data was compared to the known data for that strain to establish an expected baseline. The Ugandan outbreak was caused by the Ebola-Sudan strain, whereas the more severe Republic of the Congo outbreak was caused by the more deadly Ebola-Zaire strain. Instead of comparing mortality rates from the different outbreaks to each other, the mortality rates were compared to the expected

mortality rate based on strain type. Discrepancies between expected and actual mortality rates would therefore decrease the influence of strain type when comparing outbreaks. According to data from previous cases of Ebola hemorrhagic fever caused by the Zaire and Sudan strains, human mortality resulting from Zaire strains was expected to be 85–90%, whereas expected mortality resulting from Sudan strains was expected to be 60–65%.<sup>14</sup> The outbreaks from which this expected mortality is derived preceded, and thus did not employ, any official infection control measures. Therefore, there was no difference in strain-specific mortality due to different control measure effectiveness in the control data.

Previous studies of strain virulence performed on mice found that “fewer than ten infectious particles of a Zaire strain were lethal for suckling mice, whereas 10,000 infectious particles of a Sudan strain failed to kill any of these animals,” which further explains the higher mortality of the Zaire strain.<sup>2</sup> However, it was also found that the Zaire strain is easier to isolate in cell culture than the Sudanese agent.<sup>2</sup> Thus, it should be easier to identify the virus in a person infected with Ebola-Zaire, such as those in the Republic of the Congo; this suggests that, had control measures been put into place sooner, they would have been able to effectively identified infections. Unfortunately, the previously discussed political factors delayed implementation of this intervention.

Furthermore, in the original cases with the Sudanese strains, Ebola-Sudan was found to be more contagious.<sup>14</sup> It is expected, therefore, that because it is more contagious, the Ebola-Sudan outbreak in Uganda would have a larger number of people infected. However, when the second wave of data from the Republic of the Congo was included, the number of infections was nearly the same when comparing the two countries.

It has been shown that initial cases are more virulent than later cases or subsequent waves of infection. Interestingly, the cause for this increased initial virulence is not known; the WHO states that “an unexplained phenomenon is that people who catch Ebola in the second or third wave of an outbreak have a better chance of survival.”<sup>12</sup> The mortality rate is sum of all deaths in all waves until the outbreak is declared over; however, cases that occur later within the outbreak have a better survival rate.

Although the Republic of the Congo's actual mortality was slightly lower than expected, this may be a function of inappropriate baseline analysis rather than effective containment. Much of the control data for the Zaire strain, from which the expected mortality was derived, came from an outbreak in the 1970's. In this outbreak, a high proportion of people contracted Ebola-Zaire directly from contaminated hypodermic needles, as opposed to contact with an infected person.<sup>3,5</sup> As discussed previously, those closest to the original exposure source have a higher mortality rate, and many people in this 1970s' outbreak were directly inoculated from a primary source.<sup>5</sup> This creation of multiple primary waves may have caused this strain to appear more virulent in subsequent analyses than it actually was, and thus falsely elevated the 1970's mortality rate. Thus, if the mortality rate in the Republic of the Congo was more



Stig Nygaard

**Table 1: Outbreak Timelines**

	Uganda	Republic of the Congo
First Identified Case	Oct 7, 2000	Oct 21, 2001
Local Authorities Alerted of Abnormal Primate Deaths	None	Nov 17
First Lab Tests Submitted	Oct 7	Nov 30
Local/National Authorities Alerted of Potential Outbreak	Oct 14	Nov 24
National Guidelines Announced	Oct 15	Dec 8
Lab Tests Confirmed Ebola	Oct 14-15	None
Braoder Control Isolation Procedures Implemented	Oct 16	None
WHO Notified	Oct 15	Dec 8
WHO Task Force arrives	Oct 17	Dec 11
WHO Reports End of Outbreak	Feb 28, 2001	May 7, 2002
Next Known Outbreak in Region	Nov 30, 2007	June 21, 2002

**Table 2: Infections and Mortality**

	Uganda	Republic of the Congo (first wave only)	Republic of the Congo (both waves)
Total Number of Infections	425	124	267
Total Number of Deaths	224	97	225
Mortality	53%	78%	84%
Expected Mortality Based on Strain Type	60%-65%	85%-90%	85%-90%

similar to the control or expected mortality, the effect of what little containment measures were applied are diminished.

When looking at the comparison between the two study populations in Uganda and in the Republic of the Congo, even without including the second wave data, the mortality rate was 53% compared to 78%, respectively, both falling seven to 12 percent from the expected values for each strain. However, with the inclusion of the second wave data in the Republic of the Congo data set, the mortality rate was 84%, which is roughly equivalent to the expected values of 85–90% for Ebola Zaire.<sup>1</sup> Further, when considering the argument that the expected value for mortality is artificially elevated, the outbreak in the Republic of

Political stability and a positive interaction with international aid groups decreases the percentage of people infected.

the Congo shows even less improvement in mortality. When comparing the data in this way it is clear that political stability and a positive interaction with international aid groups decreases the percentage of people infected, and therefore decreases the mortality rate when comparing these two study groups.

#### Conclusion

There are clear differences in the manner in which the two Ebola outbreaks were handled, likely because of two countries' divergent political climates. The more stable political environment in Uganda was better able to put infection control measures in place promptly. The unstable political climate in the Republic of the Congo caused identification and implementation of infection control measures to be delayed by approximately 50 days. Furthermore, the safety of international infection control personnel was not assured and the WHO out-

break control staff were evacuated during the outbreak due to political unrest. Thus, as might be expected, the duration of the outbreak in the Republic of the Congo was longer and more poorly contained, allowing further spread of disease than in Uganda, and percent mortality was greater when compared to strain specific controls.

The total number of cases was greater in Uganda; however, given the population of each region, a higher percentage of the population was infected in the Republic of the Congo. The Zaire strain found in the Republic of the Congo is known to be more virulent than Uganda's Sudan strain in both retrospective human studies and prospective mice studies.<sup>2,14</sup> Although there are differences in strain virulence inherent to the viral genome, when compared to strain-specific outbreak mortality controls, in which no standardized infection control measures were used, it is clear that the difference in mortality was not a result of strain variation.<sup>3</sup> Infection control measures were directly correlated with the regional political climate, which therefore played a role in mortality rate and proportion of population infected. These measures limited the number of infections and fatalities in both discussed outbreaks as compared to the expected outbreak mortality data; however, there was better survival and containment of spread when these infection control measures were put in place promptly, as seen in Uganda. It is evident from the mortality, length of the outbreak and the percentage of the population infected that infection control measures helped to contain the spread of disease. When the data with regards to the second wave was added to the original outbreak data in Republic of the Congo, this difference becomes even more evident.

In conclusion, because there is no known treatment for the viral infection, using prompt, organized and monitored infection control protocols is imperative to limit the morbidity and mortality of this disease. Ebola hemorrhagic fever is a deadly disease with extremely high mortality; however, when the WHO-recommended infection control measures were in use, there was a lower mortality rate than expected. Uganda promptly put into effect these control measures while the Republic of the Congo was unable to achieve control measures as quickly due to political instability. The improvement in percent mortality demonstrated that the WHO control measures were effective when compared to expected

mortality, and they become more effective with prompt implementation. Although strain virulence differed, it was controlled in this study with comparisons between each outbreak and the expected mortality rates based on strain. Differences in strain virulence may not be solely a function of viral genetics, as previously thought. As discussed, the expected percent mortality may be artificially elevated since initial calculations of Ebola-Zaire mortality rates came from patients who contracted the virus via direct inoculation. Accounting for all these factors, it becomes clear that political climate in the outbreak region plays a role in mortality and spread of disease, thus showing that sociopolitical differences are an important factor to account for when looking at the global health issue of Ebola.

#### References

- Longo, Dan L. Harrison's Principles of Internal Medicine. New York, NY: McGraw-Hill, 2012.
- J. B. McCormick, S. P. Bauer, L. H. Elliott, P. A. Webb and K. M. Johnson. "Biologic Differences between Strains of Ebola Virus from Zaire and Sudan." The Journal of Infectious Diseases, Vol. 147, No. 2 (Feb., 1983), pp. 264-267
- van der Groen, G., Jacob, W., Pattyn, S. R. Ebola virus virulence for newborn mice. J. Med. Virol. 4:239-240, 1979.
- CDC. "Ebola Hemorrhagic Fever Information Packet." Special Pathogens Branch 2009.
- Baron RC, McCormick JB, and Zubeir OA. Ebola virus disease in southern Sudan: hospital dissemination and intrafamilial spread. Bulletin of the World Health Organization. 1983;61(6):997-1003.
- Fredeking, T. "Ebola hemorrhagic fever: treatment protocols". 2009.
- "Central Intelligence Agency." CIA Site Redirect - . N. p., n. d. Tue 07 Oct 2013.
- "Outbreak of Ebola Fever in Northern Uganda". UN OCHA Integrated Regional Information Network for Central and Eastern Africa (IRIN-CEA), 17 Oct 2000.
- "Concerning the Spread of Ebola hemorrhagic fever to Kitgum". The Monitor (Kampala), Wed 17 Oct 2000.
- "Gulu; the Intersection of War and Disease". Washington Post, Tue, 17 Oct 2000.
- Okware SI, Omaswa FG, Zaramba S, et al. "An outbreak of Ebola in Uganda". Trop Med Int Health. 2002; 7(12):1068-1075.
- World Health Organization. Outbreak(s) of Ebola haemorrhagic fever, Congo and Gabon, October 2001- July 2002. Weekly Epidemiological Report. 2003; 78(26):223-225.
- Formenty P, Libama F, Epelboin A, et al. "Outbreak of Ebola hemorrhagic fever in the Republic of the Congo, 2003: a new strategy?". Medecine Tropicale (Marseille). 2003; 63(3): 291-295.
- "Ebola haemorrhagic fever in Zaire, 1976." Bull. W.H.O. 56:271-293, 1978.
- Population Profiles. US Department of State. 02 Nov 2011. <http://www.state.gov/r/pa/ei/bgn/2825.htm#people>.
- "Ebola." Encyclopædia Britannica. Encyclopædia Britannica Online Academic Edition. Encyclopædia Britannica Inc., 2011. Web. 31 Oct. 2011. <http://www.britannica.com/EBchecked/topic/177623/Ebola>.



**Jack's Art's Gallery**  
*Custom framing · Custom Mirrors ·  
 10% off with CUID*

2855 Broadway  
 (Between 110th and 111th Streets)  
 New York, NY 10025

**Hours:**  
 Monday - Saturday: 10am to 8pm  
 Sunday: 11am to 6pm  
 Friday closed: 1:30 to 2:30

Phone: (212) 749 - 5554  
[www.jacksartframing.com](http://www.jacksartframing.com)  
 Email: [contact@jacksartframing.com](mailto:contact@jacksartframing.com)

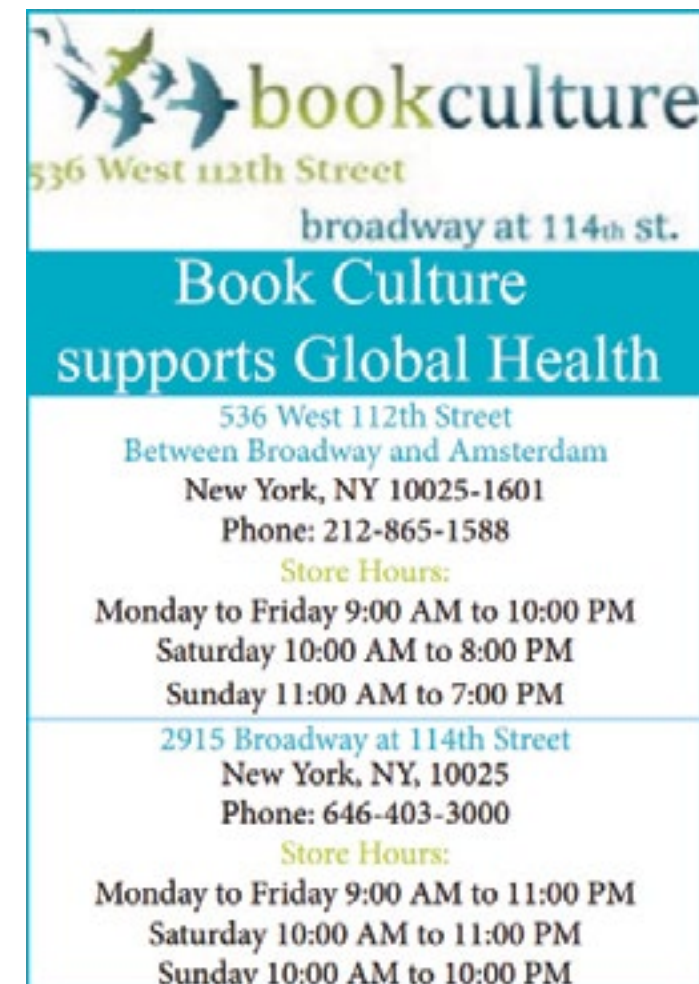


**FAMIGLIA**  
 PIZZERIA

**Hours**  
 Sun-Thu: 11am-1am  
 Fri-Sat: 11am-2am

2859 Broadway at 111th St.  
 New York, NY 10025  
 Tel. 212-865-1234

**We Deliver!**



**bookculture**  
 536 West 112th Street  
 Broadway at 114th St.

**Book Culture**  
 supports Global Health

536 West 112th Street  
 Between Broadway and Amsterdam  
 New York, NY 10025-1601  
 Phone: 212-865-1588

**Store Hours:**  
 Monday to Friday 9:00 AM to 10:00 PM  
 Saturday 10:00 AM to 8:00 PM  
 Sunday 11:00 AM to 7:00 PM

2915 Broadway at 114th Street  
 New York, NY, 10025  
 Phone: 646-403-3000

**Store Hours:**  
 Monday to Friday 9:00 AM to 11:00 PM  
 Saturday 10:00 AM to 11:00 PM  
 Sunday 10:00 AM to 10:00 PM

## UNIVERSITY HOUSEWARES & UNIVERSITY HARDWARE

2901-2905 Broadway  
 @ 113th Street

(212) 882-2798  
 (212) 662-2150

[www.universityhousewares.com](http://www.universityhousewares.com)

"For all your hardware and  
 houseware needs"

# HIV and Public Policy: Predictors for Chronic Homelessness in Persons Living with HIV/AIDS

Iman Simmonds, Ena O. Oru  
Columbia University Mailman School of Public Health, New York, NY, USA

.....  
Abstract

HIV/AIDS is markedly more prevalent in the homeless population than in the population of individuals in stable dwellings. Challenges such as inadequate access to care, HIV-risk behaviors and the costs of healthcare make it difficult for homeless persons living with HIV/AIDS (PLWHA) to improve their health. Conversely, PLWHA are more susceptible to homelessness due to diminished financial agency and emotional support. Recent policies enacted by the U.S. Department of Housing and Urban Development have increased the amount of funding available to supportive housing programs, yet 25% of all homeless PLWHA fall into chronic homelessness and worse health outcomes over time. This paper tests the association between HIV-related risk factors and the likelihood of chronic homelessness in PLWHA. Our results highlighted that incarceration was a significant contributor, Odds Ratio 1.83, after adjusting for illicit substance use.

Considering that the U.S. federal and state governments spend more than \$587 million dollars annually on housing and health support for the homeless, it may prove beneficial to the health of homeless PLWHA and more cost effective to the government over time to combine tailored housing prevention activities with programs known to reduce the transmission of HIV for homeless PLWHA who are more likely to recede into chronic homelessness.

.....

Introduction

Since the introduction of highly active antiretroviral therapy (HAART) in 1996, the mortality rates of persons living with HIV/AIDS (PLWHA) in the United States has decreased. However, HAART is not curative, and as more people are living with HIV/AIDS, the prevalence of the disease has steadily increased in the U.S.<sup>1</sup> At the end of 2009, an estimated 1,148,200 persons aged 13 years or older were living with HIV.<sup>2</sup> Of that population, 476,732 persons were confirmed to have AIDS—91,830 more than in 2002.<sup>3,4</sup> Despite advances in diagnostic interventions and pharmacologic management, HIV/AIDS disproportionately affects certain subsets of the population, such as the homeless. According to the U.S. Department of Housing and Urban Development, 0.12% of the U.S population, an estimated 394,397 persons, were homeless in 2012. 25.3% of those (99,894 persons) were homeless for at least a year or had four or more episodes of homelessness in a span of 3 years, which meets the definition of chronic homelessness.<sup>5</sup> The rate of HIV among homeless and marginally housed PLWHA is five to ten times that of domiciled PLWHA.<sup>6</sup>

The markedly higher rate of HIV among homeless and marginally housed PLWHA can largely be attributed to the social, behavioral and structural

determinants of the disease. Homeless PLWHA frequently have delayed and inadequate access to medical care. Most of them cannot afford to pay for the uninterrupted treatment of their disease and thus display poor adherence to HAART regimens. Homeless PLWHA are also frequently exposed to comorbidities and opportunistic infections prevalent among the homeless population, such as tuberculosis, which further worsen their health.<sup>8,9</sup> Importantly, studies have demonstrated associations between homelessness and the behavioral risk factors for contracting HIV, such as illicit drug use, increased rates of incarceration and sexual exchanges. On the other hand, approximately 50% of domiciled PLWHA in the United States are at risk of homelessness due to job-related discrimination, periodic hospitalization, the high costs of healthcare and a diminished sense of social belonging.<sup>9,11</sup> The increased prevalence of HIV among the homeless, in combination with the aforementioned risk behaviors, exposures and predicaments of homeless individuals, has created an infectious disease reservoir of HIV amongst the homeless population, which is already highly burdened with the illness.

Supportive housing, a combination of housing and services such as job training, assistance with housing placement and the coordination of healthcare through an allocated professional, has been the major accepted solution to this predicament after several

Few studies have outlined issues, such as the effectiveness of the supportive housing program model in reducing individual homelessness over the long term, or explicitly targeted the root causes of chronic homelessness in PLWHA.

studies demonstrated the positive impact of stable housing on the health outcomes of homeless PLWHA. One such study was the 2008 Chicago Housing for Health Partnership study of 407 homeless persons suffering from HIV/AIDS or chronic health conditions, such as diabetes. Participants were randomly assigned to one of two case managers, each of whom assisted in housing placement, a form of supportive housing. Participants were either randomly assigned to case managers who assisted in housing placement, a form of supportive housing or randomly assigned to usual care (homeless shelters). Both groups were followed for 18 months after discharge from the hospital. The study revealed cost savings of \$873,000 for the state-funded housing programs and 110% fewer hospitalizations for the group randomly assigned to supportive housing. In 2003, a multicenter randomized trial enrolled 630 HIV-positive persons in immediate rental assistance against usual housing. The results from the trial showed that before enrollment in immediate rental assistance, homelessness was significantly associated with reduced HAART use and a more detectable viral load (a measure of severity of HIV viral infection). There was however no difference found between the compared results of the cohort in HIV risk behaviors, such as the number of sex partners homeless PLWHA had or their sexual relations

with HIV-negative persons and persons of unknown status. Another observational study of 27 chronically homeless PLWHA, followed for up to three years, indicated that chronically homeless PLWHA who were provided with stable housing were able to maintain their adherence to HAART therapy and thus had lower mean HIV viral loads, a significant predictor of favorable clinical outcomes.<sup>14</sup>

Although such evidence outlines the myriad benefits of supportive housing as a public health solution for homeless PLWHA, few studies have outlined issues such as the effectiveness of the supportive housing program model in reducing individual homelessness over the long term or explicitly targeted the root causes of chronic homelessness in PLWHA. This gap in information prompted the launch of the Enhanced Housing Project Assistance (EHPA) study, a two-year, randomized, controlled trial conducted by the New York Department of Health and Mental Hygiene in collaboration with the U.S. Department of Housing and Urban Development's Housing Opportunities for Persons with HIV/AIDS, a program commonly known as HOPWA. The purpose of the EHPA study was to investigate the different forms of enhanced housing placement assistance and highlight which ones are most beneficial for homeless PLWHA as a measure to increase effectiveness and further save costs for the U.S. federal government. The emphasis of our study was, however, different. As supporting PLWHA constitutes a significant portion of the \$587 million annual budget of healthcare and supportive housing programs for the homeless,<sup>15,16</sup> we thought it imperative to identify those PLWHA who over-utilize these funds by being chronically homeless. In addition, we aim to provide recommendations on how to alleviate the challenges they face and the burden placed on public health systems by their circumstances. Using baseline data collected from the EHPA randomized control trial, this paper uses a cross-sectional analysis to test the association between the risk factors for homelessness and the odds of chronic homelessness in PLWHA.

Table 1: Demographic Information

Variable	Total N (%)
Race	
Black/African American	129 (54.4%)
Hispanic	75 (31.7%)
Other, not Black, Hispanic	33 (13.9%)
Age	
18-40	55 (23.2%)
41-50	89 (37.6%)
51+	93 (39.2%)
Gender	
Male	176 (74.3%)
Female	53 (22.4%)
Transgender	7 (3.0%)
Education	
Less than 12 years	95 (40.1%)
Exactly 12 years	75 (31.7%)
Greater than 12 years	67 (28.3%)
Income Sources	
Received SSDI	196 (82.7%)
Received SSI	154 (65.0%)
Incarceration	
Jail/ Prison/ Juvenile D.	185 (78.1%)
Mental Health	
Diagnosed w/ mental illness	137 (57.8%)
Substance Use	
Binge Drinking	186 (78.48%)
Illicit Substance	155 (65.40%)

Methods

Eligibility criteria for enrollment in the EHPA study included persons who were seropositive for HIV, aged 18 or older, English-speaking and clients of the HIV/AIDS Services Administration (HASA) in New York City. Of the 237 eligible participants enrolled, 225 persons were used in complete case analysis of the covariates of interest. (Incomplete data and loss to follow-up were responsible for the reduction in sample size.) The recruitment began in March 2012 at single-room-occupancy (SRO) hotels. Each SRO was visited door-to-door in a randomly selected order, and eligible participants were followed for at least 12 months. At recruitment, our cohorts were randomly allocated to a treatment or non-treatment group. In the treatment group, individuals were assigned to case managers from CITI-WIDE, a non-profit, community-based housing program designed to help place homeless PLWHA in permanent housing of their choice. The onus to follow up with the manager lay with the participant. Participants in the non-treatment group were not assigned to case managers and did not pursue permanent housing through other avenues. The information regarding the research participants and investigators were neither blinded nor concealed in this study, as all chronically homeless were able to differentiate between the levels and standards of care that were given.

For data collection in the EHPA study, our research investigators in the New York Department of Health and Mental Hygiene utilized a computer-generated survey to conduct one-on-one, in-person interviews of eligible participants. Interviews occurred in the field. All persons gave informed consent to participate in research prior to administration of the survey. Survey implementation took approximately one hour and participants received a \$20 gift card at the end of their baseline and 12-month follow-up assessments. Surveys measured objective data which included social demographics, HAART medication use, self-reported CD4 count, drug and alcohol use, sexual history, income, various sources of financial support and social networks. Data on previous history of homelessness, incarceration, mental health disorders, illicit drugs and alcohol use were also collected.

For specific information on their housing, participants were queried about former housing status, longest length of time spent in an SRO and the number of previous utilizations of SROs. To reduce the likelihood of self-reported bias regarding housing, housing history was verified using the HASA-HIV Surveillance data match system, a supplemental database developed by the New York Department of Health and Mental Hygiene. The outcome variable of chronic homelessness was then classified using two possible values, as participants either met the U.S. Department of Housing and Urban Development's definition of chronic homelessness or failed to meet the definition.

For social and demographic variables, gender was self-reported as male, female, or transgender; the race/ethnicity covariate was collapsed into Black, Hispanic or Other primarily because most participants that were enrolled represented these ethnicities. Age was categorized into three groups: ages 18 to 40, 41 to 50 and 50 and above. Highest level of education was similarly collapsed into three groups: those with less than a high school education, a high school education and more than a high school education. Because this population is predominately disabled and unemployed, income was categorized as those receiving Social Security Disability Income (SSDI) and Supplemental Security Income (SSI).

**Table 2: Crude Model Forward Selection**

Selection	SLE	Model: $\log(P(Y=1) x) - \log(P(Y=1) x)$	Wald Chi-sq.	P-Value
Forward	0.10	$=\beta_0 + \beta_1(\text{incarceration})$	4.8240	0.0281
Forward	0.25	$=\beta_0 + \beta_1(\text{incarceration}) + \beta_2(\text{illicit}) + \beta_3(Dx\_Mental)$	5.9957	0.8737

Information on alcohol and drug use was derived from a series of questions quantifying weekly, monthly and yearly alcohol consumption. Participants were classified as meeting or failing to meet the criteria of binge drinking. Binge drinking was defined using the Centers for Disease Control and Prevention (CDC) criteria of drinking five or more drinks during a single occasion for men and four or more drinks during a single occasion for women. Participants who used drugs were asked to categorize their monthly and yearly drug use as injection or non-injection drug use and were asked to quantify usage of each self-reported drug. Non-injection use included marijuana, methamphetamine, powder cocaine, prescription pills, etc. These variables were then combined to create a single drug use covariate to cover all those that had used injection and non-injection drugs in the past year. It was important to create this singular variable, as intoxication from drug use, for example, is a contributor to HIV-related risk behaviors, such as unprotected sex, in the same manner that sharing needles while using intravenous drugs is an HIV-related risk behavior. Incarceration was classified as a participant reporting ever having been to a jail, prison or juvenile detention center, while the covariate for mental health covered all persons that self-reported having ever being diagnosed with a mental disorder, unspecified.

Statistical Analysis

To determine the variables most common or relevant to chronic homelessness in PLWHA, we used a logistic regression analysis of a full model. (Relationships between all variables were represented in the form of mathematical equations.) We included all possible predictors of chronic homelessness for which data was gathered, which include gender, age, race, illicit drug use, mental illness and incarceration, as well as social demographic variables, including SSI, SSD and education. Variables were computer generated, with the largest frequency group used as the reference category. A crude model was generated using forward, backward and stepwise logistic regression methods (see below)<sup>17</sup> and significance levels of 0.10 and 0.25 were used. Multiplicative interaction, a test for possible extraneous relationships between the variables, was investigated. The results are provided below. The final adjusted model is reported at a level of significance of 0.05. All statistical procedures were run using SAS 9.2.

Results

The demographic summary of the EHPA cohort we used to conduct our study shows that participants were predominantly Black or African American (54.4%), older than 51 (39.2%) and male (74.3%). Notably, the study population had few social and financial resources; 40.1% have less than high school education, 82.7% receive SSDI and 65.0% receive SSI. Additionally, 78.1% had been incarcerated at some point in their lifetime, and 65% had used some form of illicit substance, including marijuana.

The results of our statistical analysis of the risk factors for chronic homelessness in PLWHA in particular showed that incarceration was the only predictor of odds of chronic homelessness among HIV-positive HASA-eligible persons age 18 or older [Odds Ratio (OR): 2.06] at a level of significance of 0.1. Other variables, such as illicit substance use within the past 12 months or a diagnosed mental health disorder, were not ignored. They were indeed considered in the logistic regression model using a level of significance of 0.25. However, the results of these variables in the model were not statistically significant. We could therefore not draw any conclusions from the interactions of any these variables with chronic homelessness in the EHPA cohort.

We decided to further investigate the model that included incarceration for the

presence of effect modification and confounding. These tests are done to ensure that the OR that showed an increased association between incarceration and chronic homelessness in PLWHA was not distorted or modified by the presence of other variables that were being tested. The results showed that, while no variable was an effect modifier, illicit substance use in particular was significantly associated with incarceration (<0.0001) and thus confounds the association between incarceration and chronic homelessness in the EHPA cohort by as much as a 10% change in the OR. After adjusting for substance abuse as a confounder, the final statistical model suggests that the odds of chronic homelessness among the EHPA cohort (HASA clients) who have been incarcerated at any point in their lifetime is 1.827 times those of homeless PLWHA who have never been incarcerated.

Discussion

In May 2009, President Barack Obama signed into law the Homeless Emergency and Rapid Transition to Housing (HEARTH) Act, which consolidated and reauthorized three separate homeless assistance programs carried out previously under the McKinney-Vento Homeless Assistance Act. The purpose of the HEARTH Act was to further mitigate homelessness through a continuum of programs designed to improve administrative efficiency in funding and enhancing response systems that cater to the needs of homeless persons in general.<sup>18</sup> Since its implementation, several urban municipalities, such as New York City, where an estimated 33% of PLWHA are homeless or marginally housed,<sup>19</sup> now rely on the funds it has created to take a secondary prevention-focused approach to tackling the problems of both homelessness and HIV through homelessness prevention programs. The importance of the HEARTH Act in places like New York City cannot be overstated. However, challenges such as recidivism, the continuous relapse into homelessness in as much as 25% of homeless PLWHA, considerably hinder the overarching impact of such policies.

The final conclusion from our analysis of the baseline data of the EHPA cohort suggests that a history of incarceration is an indicator of homeless PLWHA who are like to recede into chronic homelessness despite the previous use of supportive housing services. This result is consistent with studies that explain that individuals who are incarcerated face similar burdens to people living with HIV/AIDS when finding homes. For example, previously incarcerated individuals are also vulnerable to social exclusion, have difficulties in finding a job and are more likely to be under-educated and/or have low wages.<sup>6</sup> Other studies have shown an increased risk of chronic homelessness among certain demographics, such as African Americans, persons with less than a high school education and those with a history of mental illness or illicit substance use.<sup>12,14</sup> In the case of this study, which pertains only to the homeless PLWHA subpopulation, no such associations were discovered at a level of significance of 0.10. The exclusion of these findings is a result of insufficient statistical power, which we attribute to the limited sample size. Further, this sample size is a potential drawback as the study results will likely suffer reduced generalizability if applied to the larger population of homeless PLWHA in urban municipalities throughout the United States. To improve this, a larger cohort size will be needed.

Ultimately, the high percentage of chronically homeless PLWHA, together with the study's results that show the link between incarceration and chronic homelessness in PLWHA, suggests that a call for action is appropriate. In finding solutions for chronically homeless PLWHA, novel strategies that go beyond the one-size-fits-all preventive services approach have to be considered. The major tactics employed at

The odds of chronic homelessness among the EHPA cohort (HASA clients) who have been incarcerated at any point in their lifetime is 1.827 times those of homeless PLWHA who have never been incarcerated.

the moment to prevent homelessness include housing subsidies, supportive housing services, cash assistance for overdue rent and rapid exit from shelter programs. One approach we recommend is to tailor these homelessness prevention activities to homeless PLWHA according to their current predicaments and risks of recidivism. For example, homeless PLWHA who have been incarcerated or those who have a history of chronic homelessness may be better candidates for subsidized housing programs than first-time homeless PLWHA, as subsidized housing strategies have been shown to work better for extremely low-income individuals.<sup>20</sup> With such a strategy, previously incarcerated or chronically homeless PLWHA may not ex-

perience discrimination in obtaining a home. Public and private support from NGO's working at the community level will also be instrumental in carrying out such programs to prevent discrimination. More importantly, these community-level programs may prove useful as an effective tool to carry out programs that are known to reduce the rate of HIV transmission among high-risk groups, such as needle exchanges or behavior modifications. One last shortcoming of the study was that, because we utilized a cross-sectional analysis of baseline data from the randomized control trial, it was not possible to ascertain the direct causality between the multiple variables on chronic homelessness in PLWHA, if any existed. In other words, identifying what variable might have led to the other was not statistically possible and thus remains obscure to us. Our paper is one piece of the puzzle, as it has identified a link between incarceration and chronic homelessness in PLWHA, but it has limited internal validity—the extent to which causality can be declared outright. Moving forward, researchers could improve this by pooling data

from other randomized trials or using a systems-based approach, which could better incorporate the complex cause-and-effect patterns of each structural and behavioral HIV-related variable and simulate how they are relevant to homeless PLWHA. Knowing which actions are causative of chronic homelessness in this elaborate cycle will provide key insights for the government to create and implement more cost-effective public health policies and targeted, program-based interventions. In a time of government sequesters and in a population of homeless individuals where the prevalence of HIV is markedly high, the need for such targeted approaches towards homeless PLWHA is clear, and such approaches could reduce both chronic homelessness and the rates of transmission of HIV among homeless individuals.

References

- Centers for Disease Control and Prevention (2010). HIV surveillance report, 22, 9.
- Centers for Disease Control and Prevention (2012). Monitoring selected national HIV prevention and care objectives by using HIV surveillance data—United States and 6 U.S. dependent areas—2010. HIV Surveillance Supplemental Report 2012, 17 (3, Part A).
- Centers for Disease Control and Prevention (2010). HIV surveillance report, 22, 10.
- Centers for Disease Control and Prevention (2002). HIV/AIDS surveillance report, 14, 7.
- U.S. Department of Housing and Urban Development (HUD) (2012). Annual Homeless Assessment Report to Congress (AHAR). The 2012 Point-in-Time Estimates of Homelessness, 3.
- Milloy, M.J., Brandon, M., Montaner, J., & Wood, E. (2012). Housing status and the health of people living with HIV/AIDS. *Current HIV/AIDS Reports*, 9(4), 364-374.
- Kidder, D. P., Wolitski, R. J., Campsmith, M. L., & Nakamura, G. V. (2007). Health status, health care use, medication use, and medication adherence among homeless and housed people living with HIV/AIDS. *American Journal of Public Health*, 97(12), 2238-2245.
- Palepu, A., Milloy, M. J., Kerr, T., Zhang, R., & Wood, E. (2011). Homelessness and adherence to antiretroviral therapy among a cohort of HIV-infected injection drug users. *Journal of Urban Health*, 88(3), 545-55.
- Aidala, A.A., Lee, G., Abramson, D.M., Messeri, P., & Siegler, A. (2007). Housing need, housing assistance, and connection to HIV medical care. *AIDS and Behavior*, 11(S2), 101-115.
- Zelenev, A. et al. (2013). Patterns of homelessness and implications for HIV health after release from jail. *AIDS and Behavior*. [Epub ahead of print: <https://www.ncbi.nlm.nih.gov/pubmed/23657757/?i=4&from=23668491/related>]
- Holtgrave, D. R. et al. (2013). Cost-utility analysis of the housing and health intervention for homeless and unstably housed persons living with HIV/AIDS and Behavior, 17(5), 1626-1631.
- Sadowski, L. S., Kee, R. A., VanderWeele, T. J., & Buchanan, D. (2009). Effect of a housing and case management program on emergency department visits and hospitalizations among chronically ill homeless adults: a randomized trial. *The Journal of the American Medical Association*, 301(17), 1771-1778.
- Wolitski, R. J. et al. (2010). Randomized trial of the effects of housing assistance on the health and risk behaviors of homeless and unstably housed people living with HIV/AIDS and Behavior, 14(3), 493-503.
- Hawk, M., & Davis, D. (2011). The effects of a harm reduction housing program on the viral loads of homeless individuals living with HIV/AIDS. *AIDS Care*, 24(5), 577-582.
- United States Interagency Council on Homelessness (n.d.). People experiencing chronic homelessness. <http://www.usich.gov/population/chronic>.
- United States Interagency Council on Homelessness (2013). Fiscal Year 2013 Federal Government Homelessness Budget Fact Sheet. [http://www.usich.gov/resources/uploads/asset\\_library/FY13\\_Budget\\_Fact\\_Sheet\\_final.pdf](http://www.usich.gov/resources/uploads/asset_library/FY13_Budget_Fact_Sheet_final.pdf).
- Hastie, T., Tibshirani, R., & Friedman, J. (2009). *The Elements of Statistical Learning*, 11-16.
- U.S. Department of Housing and Urban Development (2013). Homeless emergency assistance and rapid transition to housing: rural housing stability assistance program and revisions to the definitions of "chronically homeless"; proposed rule. 78(59), 18728.
- Greenberg, G.A. & Rosenheck, R.A. (2008). Jail incarceration, homelessness and mental health: a national study. *Psychiatric Services*, 59(2), 170-177.
- Burt, M.R., Pearson, C., & Montgomery, A.E. (2007). Strategies for preventing homelessness: recent evidence. *The Journal of Primary Prevention*, 28(3-4), 213-228.

**WESTSIDE MARKET NYC**  
EST. 1965

**Get it @ the Market**

Locations:

- 2840 Broadway (110th St. & Broadway)
- 2589 Broadway (97th St & 98th St)
- 2171 Broadway (76th St & 77th St)
- 77 7th Avenue (14th St & 15th St)

The highest quality foods and hard-to-find products supported by friendly, personalized, efficient service

**Table 3: Investigation for Effect Modification and Confounding**

Variables	Model 1: Crude = $\beta x$ (Odds)	Model 2: Interaction P Value	Model 3: Confounding = $\beta x$ (Odds)	P Value	= $\beta x$ (Odds)	P Value
Incarceration	0.7213 (2.06)	0.0281	0.4340 (1.54)	0.2763	0.6025 (1.83)	0.0752
Illicit Incarceration			0.3992 (1.59)	0.2205		
Illicit Substance					0.4068 (1.50)	0.1533

# The Epidemiology of Noroviruses in Ghana: A Case Study of Norovirus Detection

Chuan-jay Jeffrey Chen,<sup>1</sup> Belinda Lartey<sup>2</sup>, Chantal Agbemabiese<sup>2</sup>,  
George Armah, PhD<sup>2</sup>, Adel Mahmoud, MD, PhD<sup>1</sup>  
<sup>1</sup>Princeton University  
<sup>2</sup>Noguchi Memorial Institute for Medical Research

## Abstract

Diarrheal diseases cause significant morbidity and mortality worldwide, particularly in children under age five. Most of the 2.5 million annual diarrhea-related deaths occur in developing countries, where access to treatment is limited by geographic, cultural and knowledge-based factors. Noroviruses, the leading cause of diarrhea in adults, are the second leading viral etiology of diarrhea in children behind rotaviruses, causing a roughly estimated 218,000 child deaths a year. The recent introduction of rotavirus vaccines throughout the world may open a path for noroviruses to take over as the leading viral etiology of diarrhea in children. However, while norovirus vaccines are still currently in development, the burden of norovirus disease in many developing nations has yet to be established. Through the analysis of 152 stool specimens collected from Ghanaian children presenting with diarrhea from 3 sites, this study demonstrates that noroviruses are a significant contributor to the childhood diarrheal disease burden in Ghana, responsible for at least 16.4% of all cases. The results help establish the baseline norovirus prevalence in this developing nation prior to the introduction of rotavirus vaccines and explore the potential for future interventions against this major viral etiology of childhood diarrhea. Moreover, a survey of the disparities in norovirus studies around the world leads to a call for standardized detection protocols.

## Introduction

Noroviruses are the second most common cause of viral diarrhea in children under age five around the world, behind rotaviruses. Noroviruses cause an estimated 1.1 million hospitalizations and up to 218,000 deaths in this age group per year.<sup>1,2</sup> Given the effectiveness of current rotavirus vaccines in reducing the most globally common strains of rotaviruses, it is possible that noroviruses will soon take over as the leading cause of viral diarrhea in children. Indeed, noroviruses have recently exceeded rotaviruses as the leading cause of viral gastroenteritis in children under age five in the US.<sup>3</sup>

Diarrheal diseases disproportionately contribute to morbidity and mortality in low-income, developing countries relative to developed nations. For example, of the approximately 527,000 deaths a year of children under age five attributed to rotavirus infection, an estimated 252,000 occur in sub-Saharan Africa and 196,000 in Southeast Asia.<sup>4</sup> In these low-income settings, children suffering from diarrhea often have limited access to medical care and oral rehydration therapy, a formulated solution of water and essential electrolytes that prevents potentially fatal dehydration. Focusing on noroviruses in a specific country provides a closer examination of viral diarrhea in the underdeveloped world. The following case study in Ghana, a developing nation in sub-Saharan Africa, focuses on measuring the disease burden imposed by noroviruses in the country. Given the recent advances in development of a norovirus vaccine, this step is critically important to establishing the potential for interventions against noroviruses.<sup>5,6</sup>

It is possible that noroviruses will soon take over as the leading cause of viral diarrhea in children.

Noroviruses belong to one of five genogroups that are further subclassified by genotype.<sup>7</sup> In general, the nucleotide sequences of norovirus strains belonging to different genogroups can vary by up to 50%.<sup>8</sup> Most noroviruses that infect humans globally belong to either genogroup I or II.<sup>9</sup> Overall, genogroup II noroviruses are believed to be responsible for 80-90% of all cases of norovirus gastroenteritis in the world.<sup>10</sup> The mutation rate of the norovirus genome is estimated to be about 1.21 x 10<sup>-2</sup> to 1.41 x 10<sup>-2</sup> nucleotide substitutions/site/year, higher than most other rapidly evolving RNA viruses.<sup>11</sup> The rapid rate of evolution complicates the constant monitoring of norovirus epidemiology as well as the development of interventions such as vaccines.

Noroviruses infect humans primarily during cool, dry seasons.<sup>11</sup> Often, a single strain is responsible for the majority of norovirus gastroenteritis cases each season. For example, during the 1995-1996 season, GII.4 noroviruses were responsible for about 90% of norovirus gastroenteritis in the United States.<sup>12</sup> GII.4 noroviruses continue to be the leading cause of norovirus outbreaks in the world, responsible for up to 60% of all cases of norovirus diarrhea during most seasons.<sup>13</sup> However, recombination and point mutations drive the rapid evolution of noroviruses, allowing new strains to emerge every season.<sup>13</sup> Moreover, the mutation rate of the norovirus genome is higher than most other rapidly evolving RNA viruses.<sup>14</sup> Together, these factors complicate the constant monitoring of norovirus epidemiology as well as the development of interventions such as vaccines.

As rotaviruses, not noroviruses, have been the predominant cause of acute diarrhea in

children throughout the world, extensive surveillance efforts have monitored the local rotavirus strain distribution in Ghana. In contrast, knowledge of the regional epidemiology of noroviruses is currently limited to two studies that examined samples collected in 2000 and 2005-2006, respectively. Both examined only samples from Northern Ghana and included relatively small sample sizes.<sup>15</sup>

Given the recent introduction of a rotavirus vaccine and the predicted decline in rotavirus gastroenteritis, noroviruses may soon become the most epidemiologically prevalent and clinically relevant cause of viral diarrhea in children in this country. This study aims to provide an updated assessment of epidemiology of noroviruses in Ghana by using samples collected from sites throughout the nation.

## Materials & Methods

**Site Descriptions:** Samples were collected between February 2011 and February 2012 from three distinct locations: Agogo Presbyterian Hospital, a rural medical center with a catchment area containing 55,587 children; Navrongo War Memorial Hospital, a peri-urban facility that serves a district populated by 69,906 children; and the Korle Bu Teaching Hospital in Accra, the capital city of Ghana with a population containing 531,719 children.<sup>16</sup> The cities of Navrongo (Kassena Nankana District), Agogo (Asante Akim North District) and Accra (Accra Metropolitan District), listed in increasing population size, are located in Northern, Central and Southern Ghana, respectively, and provide coverage for both urban and rural populations.

**Study Population:** Fecal specimens were obtained with parental consent from children under five years of age hospitalized with acute diarrhea. In accordance with the WHO's definition of diarrhea, children were eligible if they had at least three episodes of non-bloody watery stools within 24 hours for fewer than seven days. In total, 152 samples were collected for this study: 53 samples from Agogo, 50 from Navrongo and 49 from Korle Bu. Demographic and clinical data was obtained from hospitals and missing values were excluded from analysis.

**Sample Collection and Analysis:** Stool specimens were collected in sterile containers, stored at 4°C and transported to the Noguchi Memorial Institute for Medical Research (NMIMR) near Accra, where they were stored at -20 °C until analysis. Samples were tested on an enzyme-linked immunosorbent assay (ELISA) using the commercially available IDEIA-Rotavirus kit (DAKO; Glostrup, Denmark) following the manufacturer's instructions. This study was approved by the Institutional Review Boards of Princeton University (#5794) and NMIMR at the University of Ghana (#002/12-13).

**Norovirus RNA Extraction and RT-PCR:** RNA was extracted using the guanidinium thiocyanate (GITC) phenol/chloroform method described by Boom et al., eluted with 100 µL DEPC-treated water and purified with the RNAid kit (QBIogene; Carlsbad, CA) according to the manufacturer's instructions.<sup>17</sup> RT-PCR analysis was performed with the protocol described by Kojima et al. with some modifications.<sup>18,19</sup> Briefly, amplification of the cDNA used 1.0 µL of 20 pmol solutions of either the GIFFN or GIIFBN forward primer 2.0 µL of 20 pmol solutions of either the GISKR or GIISKR reverse primer (Table 1). These primers target the 5' end of ORF2, amplifying genogroup-specific sequences of the N-terminal and shell (N/S) region of the VP1 gene.<sup>20</sup> Thus, these primers can distinguish between genogroup I and genogroup II viruses.

**Data Analysis:** Statistical associations between norovirus status and demographic or clinical data were calculated using multinomial logistic regressions performed on the Stata software package (College Station, TX).

**Table 1.** Oligonucleotide primers used for norovirus detection and genogrouping.

Genogroup	Primer (Polarity)	Sequence*
GI	GIFFN (+)	5'-GGAGATCGCAATCTCCTGCC-3'
	GISKR (-)	5'-CCAACCCARCCATRTACA-3'
GII	GIIFBN (+)	5'-TGGGAGGGCGATCGCAATCT-3'
	GIISKR (-)	5'-CCRCCNGCATRHCCRTTRTACAT-3'

\*According to the IUPAC nucleotide ambiguity codes: R = A or G; H = A or C or T; N = A or C or G or T

## Results

**Prevalence of Norovirus Infection:** To determine the burden of norovirus disease in Ghanaian children, diarrheic stool samples were analyzed by RT-PCR for the presence of norovirus RNA (Table 2). Of the 152 fecal specimens collected from children under age five hospitalized with acute gastroenteritis between February 2011 and February 2012, norovirus RNA was detected in 25 (16.4%) samples. The prevalence of norovirus-positive samples differed by study site: 11 (22.4%) in Korle Bu, 11 (20.8%) in Agogo and three (6.0%) in Navrongo, though the lower prevalence in the northernmost site was not statistically significant ( $p = 0.07$ ). A greater proportion of samples obtained from girls tested positive (11/62; 17.7%) than did specimens from boys (9/77; 11.7%). The majority of children who were hospitalized with acute diarrhea and had positive test results for norovirus were less than two years old (71.4%), with the 18-24 month group experiencing the highest rates of infection. The mean age of norovirus-positive children was 20.3 months. Positive norovirus status was significantly associated with the presence of vomiting ( $p = 0.041$ ).

**Prevalence of Rotavirus and Co-Infections:** To further explore other causes of viral diarrhea within the study population, the samples were tested for the presence of rotavirus antigen with a commercial ELISA kit that uses a polyclonal antibody (Table 3). Of the 152 fecal specimens, rotavirus antigens were detected in 73 (48.0%) samples. The prevalence of rotavirus-positive samples also differed by study site: 30 (61.2%) in Korle Bu, 24 (45.3%) in Agogo and 19 (38.0%) in Navrongo. A larger proportion of specimens from boys tested positive for rotavirus (39/77; 50.6%) than did samples from girls (23/62; 37.1%). The vast majority of hospitalized children with rotavirus-positive samples were under two years old (90.5%), with the 6-11 month group experiencing the highest rates of infection. The mean age of rotavirus-positive children was 14.1 months. Rotavirus-positive children (40.0%) were more likely to experience vomiting than rotavirus-negative children (28.9%). Of the 152 samples, ten tested positive for both rotavirus and norovirus infection, equally distributed between boys and girls (five each). Most of these co-infections (seven) were detected in samples obtained from Korle Bu, though three were detected in Agogo, while none were found in Navrongo. The highest rates of co-infection were in the 18-23 month age group.

**Seasonality of Norovirus Infection:** As rotavirus infection has been determined to be seasonal in Ghana as well as in other tropical parts of the world, dates of sample collection of all norovirus-positive, norovirus-negative and rotavirus-positive samples were plotted to determine if noroviruses follow any seasonal patterns of infection in causing acute diarrhea in children (Fig. 1).<sup>21</sup> Only samples collected from October through May tested positive for norovirus on the RT-PCR, which encompasses the entire dry season in Ghana. Only three samples were detected in May, which falls during the transition between the dry and wet seasons. The peak of detected norovirus infections was in December 2011, followed by January 2012, with six and five positive samples respectively. These months fall in the middle of the dry season throughout Ghana. The peaks of norovirus-positive samples coincided with the seasonal peaks in overall diarrhea, including norovirus-negative samples, as well as with the peaks in rotavirus-positive diarrhea; this observation will be explained further in the discussion.

**Distribution of Norovirus Genogroups:** To provide a prelimi-



**Table 2. Norovirus detection in samples from Ghanaian children hospitalized with diarrhea.**

Variable	Norovirus - (%)	Norovirus + (%)	P Value*
All Samples	127 (83.6%)	25 (16.4%)	
Study Site			Ref
Korle Bu	38 (77.6%)	11 (22.4%)	0.777
Agogo	42 (79.2%)	11 (20.8%)	0.072
Navrongo	47 (94.0%)	3 (6.0%)	
Age			
<6 months	16 (88.9%)	2 (11.1%)	
6-11 months	30 (90.9%)	3 (9.1%)	
12-17 months	27 (90.0%)	3 (10.1%)	
18-23 months	18 (72.0%)	7 (28.0%)	
24-35 months	13 (81.3%)	3 (18.8%)	
36-59 months	14 (87.5%)	3 (12.5%)	
Gender			0.208
Male	68 (88.3%)	9 (11.1%)	
Female	51 (82.3%)	11 (17.1%)	
Vomiting			0.041
Present	17 (73.9%)	6 (26.1%)	
Not Present	61 (89.7%)	7 (10.3%)	

\*Multinomial logistic regression against the reference (Ref) variable for norovirus-positive samples

nary understanding of norovirus diversity throughout all parts of Ghana, the fecal specimens were analyzed with an RT-PCR assay using genogroup-specific primers directed at the N/S domain of ORF2 (Table 1).<sup>18</sup> Of the 25 samples that tested positive for norovirus, 23 (92%) were successfully amplified with GII-specific primers and two with GI-specific primers (8%) (Fig. 6). GII noroviruses were detected in samples provided from children of all ages from all three study sites during all months between October and May. GI noroviruses were detected only at Korle Bu Teaching Hospital in children aged 3 weeks and 42 months in the months of March and May, respectively. Thus, in this study of Ghanaian children, detected cases of norovirus diarrhea were more commonly caused by GII viruses, which caused infections in broader ranges of location, age and date, relative to the incidence of GI noroviruses.

### Discussion: A Call for Standardized Norovirus Detection Protocols

The results from the present study suggest that noroviruses contribute significantly to the disease burden of childhood diarrhea in Ghana. Compared to other published studies, the norovirus prevalence of 16.4% was higher than that reported in a pooled analysis of studies conducted in seven developing countries (12.1%), spanning from Malawi to Thailand to Peru.<sup>1</sup> However, the figure in the present study was lower than that found in children in other countries such as the US (21%) and in Nigeria (37.5%).<sup>3,19</sup>

A number of reasons can potentially explain these disparities in norovirus prevalence across different studies. One possible factor is the type of assay used to detect and group noroviruses. The present study used an RT-PCR method described by Kojima et al. in 2002 that uses primers that target the 5' end of ORF2. These primers amplify genogroup-specific sequences of the N-terminal and shell (N/S) region of the VP1 gene.<sup>18</sup> Incidentally, the VP1 gene is the most hypervariable part of the genome (i.e. there are many variations), as it encodes the domain of the virus involved in receptor binding.<sup>22</sup> There is a considerable chance that some of the stool samples in this study contained noroviruses that these primers, developed in 2002, did not fully anneal to in the initial steps of the PCR protocol. Given the constant genetic drift and shift of noroviruses, many viruses in these samples may have

escaped detection with these primers.

Indeed, there are other sets of primers used in RT-PCR assays to detect and group noroviruses. The primers in this study amplify a segment known as "Region C" within the norovirus genome. Correspondingly, Regions A and B are within ORF1, while Region D is downstream of Region C within ORF2.<sup>20</sup> Studies have shown that different assays have varying sensitivities to different norovirus genotypes, with overall sensitivities ranging from 52-73% depending on the strain.<sup>23</sup> The most broadly reactive norovirus primers target Region B within ORF1, which codes for the viral RNA polymerase.<sup>24</sup> This region contains the most conserved sequence within the entire norovirus genome.<sup>25</sup> However, because the region is so well conserved, primers targeting this area are used only for detection rather than distinguishing between different virus genogroups. Thus, assays targeting Region B using real-time quantitative RT-PCR, which enables the detection of extremely low titers of norovirus, are now a gold standard in labs around the world for the diagnosis of norovirus infection.<sup>26</sup>

Overall, of the protocols capable of genogrouping viruses, the Region C primers used in the present study yield the highest sensitivity assays.<sup>23</sup> Even still, these primers likely provide a low estimate of the norovirus prevalence in Ghanaian children. A study examining norovirus infection in Nigerian children under age five compared the same RT-PCR assay to a commercially available norovirus ELISA kit.<sup>19</sup> In this case, the Region C protocol yielded norovirus-specific gene amplicons for only 53.3% of all ELISA-positive samples, failing to amplify the remaining samples. A possible explanation of the dismal norovirus sensitivity is the diversity of norovirus strains circulating within the region that are non-reactive to the specific primers and antibodies used in the RT-PCR and ELISA assays respectively. In nearby Ghana, the molecular epidemiology of noroviruses is presumably just as diverse. Thus, genogrouping and detection tests face many challenges given the rapid mutation and evolution of noroviruses, especially in this developing region.

After extrapolating the data using the extremely low sensitivity value in the Nigerian study and a higher value from a multi-center pooled analysis (78%), a reasonable estimated range for the norovirus prevalence in the present study in Ghanaian children is 21.1-30.8% (ie the prevalence in the present study divided by the sensitivity values from the other studies). This figure, taking into account the possibility that the Kojima et al. RT-PCR assay missed a number of norovirus-positive samples, better aligns with most other published studies. Extrapolating from the sensitivity values presented in the 2010 study in Nigeria, which likely had a similar norovirus strain epidemiology based on the geographical proximity to Ghana, the actual prevalence of viruses in children from Navrongo is closer to 11.3%. This figure is more comparable to that reported in the 2006 norovirus study in Navrongo, which used multiple sets of primers and both single and sensitive seminested RT-PCR protocols.<sup>16</sup>

Another factor contributing to the disparities among results was the variance in inclusion criteria among the various study populations. In the present study, the duration of diarrhea was restricted to less than seven days and children had to be less than five years of age, which is the age range most affected by diarrhea. Samples were selected randomly from those collected between February 2011 and February 2012 without regard to rotavirus status, age, sex or clinical symptoms. In the 2006 norovirus study conducted in Navrongo, the study population was restricted to rotavirus-negative samples collected from children under two years of age. As the peak age group of norovirus infection in the present study was 18-23 months, limiting this population to younger children would have increased the prevalence.<sup>16</sup>

Moreover, while the 2006 report neglected to list limits in the duration of illness, many other studies in Africa enroll children up to 14 days after onset of symptoms.<sup>27</sup> Rotavirus and norovirus

**Table 3. Rotaviruses and co-infection in samples from Ghanaian children hospitalized with diarrhea.**

Variable	Norovirus + (%)	Co-Infection (%)	P Value*
All Samples	25 (16.4%)	10 (6.6%)	
Study Site			Ref
Korle Bu	11 (22.4%)	7 (13.3%)	0.722
Agogo	11 (20.8%)	3 (5.7%)	0.138
Navrongo	3 (6.0%)	0 (0.0%)	
Age			
<6 months	2 (11.1%)	1 (5.6%)	
6-11 months	3 (9.1%)	2 (6.1%)	
12-17 months	3 (10.1%)	2 (6.7%)	
18-23 months	7 (28.0%)	4 (16.0%)	
24-35 months	3 (18.8%)	0 (0.0%)	
36-59 months	3 (12.5%)	0 (0.0%)	
Gender			0.093
Male	9 (11.1%)	5 (6.5%)	
Female	11 (17.1%)	5 (8.1%)	

\*Multinomial logistic regression against reference (Ref) variable

shedding generally peaks within the first week of illness but can last for nearly two months, reflecting how the duration of illness can affect the outcome of each study.<sup>28</sup> Furthermore, while the 2006 norovirus study failed to report the dates of sample collection, the study in Nigeria only examined samples collected between November 2007 and May 2008. As these dates coincide with the dry season in West Africa, it is unsurprising that the norovirus prevalence in that study was so high (37.5%). Clearly, the inclusion criteria of a study can influence the calculated prevalence of the viruses.

Nonetheless, the distribution of norovirus genogroups in the present study was consistent with other reports. In this report, 92% of all detected noroviruses belonged to genogroup GII, while the remaining 8% belonged to GI. Similar ratios were detected in other studies examining the norovirus molecular epidemiology throughout the world, including Ghana.<sup>3,15,16,29</sup> Indeed, GII noroviruses generally comprise the most predominant genotype, depending on the season.<sup>10</sup> Thus, the molecular epidemiology surveyed in this study is consistent with previously published literature.<sup>3,15,16,29</sup>

These disparities in practices illustrate that for noroviruses, a standardized set of inclusion criteria and assays used for analysis would greatly benefit global molecular surveillance. For comparison with other etiologies of childhood diarrhea, children in norovirus studies should be five years of age or under and follow the WHO definition of diarrhea, i.e., pass loose or liquid stools at least three times a day for at most seven days.<sup>30</sup> Samples that test positive for rotavirus infection should not be excluded from study, as co-infections can comprise a non-negligible portion of detected norovirus cases. The assays used to detect and classify noroviruses should also be standardized. Currently, various studies use different primer sets that target disparate regions within the norovirus genome. These regions experience different degrees of variability, leading to inconsistent results. Until more sensitive and accurate assays are developed, a standardized primer set should be used. Ideally, studies would all start with a round of RT-qPCR using primers targeting the conserved Region B, allowing the detection of noroviruses even in low titers. Subsequent failure of amplification in Region C or D would then prompt sequencing analyses, enabling the discovery of entirely novel norovirus strains. However, given the limited funding and tools available in the surveillance lab in Ghana, these sensitivity-boosting steps were not possible. Nonetheless, it is crucial that norovirus prevalence is reported in accordance with standard criteria so that the burden of disease can be reliably monitored and compared in different regions of the world. These data would indicate the areas in most need of specific interventions

such as a norovirus vaccine.

Most of the demographic, temporal, and clinical characteristics of the norovirus and rotavirus infections in Ghanaian children were consistent with those in other studies. As reported in other studies, children infected with rotaviruses and noroviruses were more likely to experience vomiting than those whose disease was caused by other agents.<sup>29,31</sup> As both of these viral etiologies of childhood diarrhea are spread through the fecal-oral route, the implications for transmissibility are considerable. Noroviruses in particular are infamous for the ability to spread through infectious vomitus, especially within enclosed settings such as hospitals.<sup>31</sup>

Moreover, both rotavirus and norovirus infection followed a distinct pattern of seasonality, peaking during the dry season months of October-May while all but disappearing during the wet season. These patterns are consistent with previous studies in Ghana as well as other countries with tropical wet and dry climate such as Kenya and Nicaragua.<sup>15,21,29,32</sup> This seasonality is often attributed to the airborne transmission of virus particles through dust and fecal matter, which occurs more easily during the colder and windier dry season.<sup>19</sup> Nevertheless, the patterns of seasonality are less pronounced areas with tropical climates as in regions with temperate climates, such as Europe and the US.<sup>33</sup>

The age distribution of noroviruses was also similar to that of other studies, proportionally affecting infants younger than age two more than older children.<sup>3,29</sup> Interestingly, prior to the introduction of rotavirus vaccines, norovirus infection in developed countries was more prevalent in children older than two years of age.<sup>15</sup> Meanwhile, children have been experiencing norovirus infections at younger ages in the US and elsewhere following the introduction of rotavirus vaccines.<sup>3</sup> This trend suggests that following the 2012 introduction of Rotarix in Ghana, noroviruses could begin to impose a larger disease burden upon younger age groups throughout the nation. Due to their greater body surface-volume ratios, higher metabolic rates, and smaller fluid reserves, younger infants are especially prone to dehydration.<sup>34</sup> Moreover, previously unexposed infants are less immunologically primed against the agents that cause acute gastroenteritis. Consequently, the morbidity and mortality of norovirus diarrhea would be disproportionately higher in younger age groups.

Future studies will need to continue to monitor noroviruses in Ghana as well as other developing nations to measure the changes in the viral etiologies of childhood diarrhea over multiple years. Longitudinal monitoring is especially crucial following the recent introduction of a rotavirus vaccine into the national immunization program. Ultimately, continued surveillance of the burden of norovirus disease in Ghana can help determine the necessity of further preventative interventions targeting noroviruses.

### Acknowledgements

To Dr. Adel Mahmoud and Dr. George Armah, thank you for your invaluable mentorship, both regarding my thesis and beyond. To Belinda Lartey, Richmond Asamoah, Helena Chibuah, Collins Bamfo and the rest of the Noguchi Memorial Institute for Medical Research, thank you for your assistance in collecting and transporting samples, gathering demographic and clinical data, and welcoming me to Ghana. To the Princeton Environmental Institute, Department of Molecular Biology and Princeton University Center for Health and Wellbeing, thank you for your financial and educational support in providing the opportunity for this research experience.

References available at  
JGH Online,  
www.ghjournal.org



# THAI market

First class cuisine inspired by the delicious food found in the marketplaces and street vendors of Thailand.

960 Amsterdam Avenue  
(West 107th Street)  
New York, N.Y. 10025

Phone  
212-280-4575

**\$8 LUNCH SPECIAL**  
12:00pm to 3:30pm everyday



**Business Hours**  
Monday - Thursday: 12pm - 11pm  
Friday - Saturday: 12pm - 11:30pm  
Sunday: 12pm - 10:30pm

**Delivery Hours**  
Monday - Saturday: 12:00pm - 10:45pm  
Sunday: 12:00pm - 10:30pm

[www.thaimarketny.net](http://www.thaimarketny.net)

**CHE BELLA**  
fast • fresh • tasty

1215 Amsterdam Avenue  
New York, NY 10027

**Hours:**  
Monday - Friday: 11:00 am - 10:00 pm  
Saturday - Sunday: 11:00 am - 9:00 pm

**Pizza, pasta, calzones,  
stromboli, gyros, falafel, fresh  
salads, wings, sandwiches, and  
more!**

**Phone:**  
(212) 864 - 7300  
[www.chebellapizza.com](http://www.chebellapizza.com)



## Perspectives

DEFORESTATION ON VECTOR-BORNE DISEASE INCIDENCE	16
ROTAVIRUS VACCINATION PROGRAM IN GHANA	20
MEDICAL STUDENT'S PERSPECTIVE ON FUNDING GLOBAL HEALTH	26

# Impacts of Deforestation on Vector-borne Disease Incidence

Allison Gottwalt  
Department of Epidemiology and Biostatistics, The George Washington University,  
Washington, DC, USA

## Abstract

Forest clearance alters ecosystem dynamics and leads to new breeding habitats for disease vectors, such as mosquitoes, fleas and ticks, by reshaping existing ecosystem boundaries. Such boundaries are often sites of contact between humans and forest pathogens. There is a well-documented, positive association between the increased deforestation of an area and the emergence of zoonotic, vector-borne diseases. Populations living within or near these fragmented forests are at a much higher risk of infection due to increased contact with vectors at forest edges and the reduced biodiversity of the area. This paper explores studies that have demonstrated that human-vector contact in newly created forest edges has led to increased risk of malaria in Peru, American Cutaneous Leishmaniasis (ACL) in Costa Rica and hantavirus in Panama. It is important to identify at-risk populations and develop strategies to minimize their exposure in order to prevent wider spread of these diseases and help implement targeted control strategies.

## Introduction

Developing countries continue to clear forests for agriculture to meet the demands of their growing populations. Populations living within or near these fragmented forests are at a much higher risk of contracting zoonotic infectious diseases because of increased contact with vectors at forest edges and the reduced biodiversity of the area.<sup>1,2</sup> These diseases represent a significant threat to humans living in affected areas. In the interest of public health, it is important to identify the land alterations that are putting these people at risk in order to better mitigate their effects and ultimately reduce the disease burden. In this paper, I address the association between the conversion of forested areas to agricultural land and the emergence of zoonotic, vector-borne diseases. To illustrate the effects of forest clearance on the incidence and prevalence of infectious diseases, I will discuss the examples of malaria in Peru, American Cutaneous Leishmaniasis (ACL) in Costa Rica and hantavirus in Panama. I will then focus on what can be done in the future to prevent wider spread of these diseases and implement targeted control strategies. These countries and diseases were chosen because of the availability of existing case studies from each, which examine the relationship between deforestation and disease incidence, that will be used here to examine this important and often overlooked issue.

Deforestation, an ongoing problem in the developing world, creates ideal conditions for vectors to breed and spread infectious diseases.<sup>1</sup> The Food and Agriculture Organization of the United Nations (FAO) published a report stating

that between 1990 and 2010, Latin America lost 88 million hectares to deforestation and that the leading cause of this deforestation was the conversion of forests to farmland and pasture.<sup>3</sup> Often, developing countries, such as those in Latin America, are the ones that carry the heaviest burden of infectious diseases and lack the resources to cope adequately with the problems they present. It is difficult to determine how the conversion of land will affect the rate of infectious disease spread in a particular area, mainly because of the variable vulnerability of exposed populations and the complicated relationships between disease transmission, habitat modification and ecosystem function.<sup>4</sup> By gaining more insight into how deforestation and other land-use changes are putting vulnerable populations at risk for infection, we can better tailor intervention strategies to suit particular regions.<sup>5</sup>

While the increase in infectious disease is not the only threat posed by deforestation, it has arguably the most direct, measurable impact on health.<sup>2</sup> Infectious disease emergence in areas affected by deforestation acts as an important diagnostic measure of the health of these human populations. Malaria, ACL and hantavirus illustrate the complex relationship between deforestation and infectious disease and can all behave as the "canary in the coal mine" for population health, as illustrated below. This paper aims to identify the impact of deforestation on infectious diseases and health through the creation of new vector habitats, loss of biodiversity and increased contact between humans and disease reservoirs and vectors.

## Malaria

Malaria is an often-fatal disease found primarily in tropical areas of the world. It is caused by Plasmodium protozoans and spread by anopheline mosquitoes. Malaria represents a significant disease burden on developing countries, annually infecting an estimated 300-500 million people worldwide and killing approximately 1.5-2.7 million.<sup>6</sup> Sixty-five out of every 1,000 people in the world are at risk of contracting malaria, the majority of whom are concentrated in developing countries.<sup>7</sup>

Malaria has been historically prevalent in the northeastern region of Peru, but incidence rates were dramatically reduced in the late 1960s due to mosquito eradication programs. In the 1990s, corresponding to a jump in population growth that led to land clearing for subsistence-scale agriculture, malaria prevalence increased from 641 cases in 1992 to more than 120,000 cases in 1997.<sup>8</sup> The epidemiology of malaria in the Peruvian Amazon is being altered because of changes in the abundance of the Anopheles mosquito vectors.<sup>9</sup> The anopheline mosquitoes breed in standing water, where eggs and larvae can hatch and grow undisturbed. Deforestation and land alteration facilitate environmental and climatic conditions that impact the ecology of mosquito habitats and create new places for water to accumulate. Mosquitoes then have a much wider variety of areas in which to breed, creating a larger vector population to spread the Plasmodium parasite.<sup>9</sup>

*Anopheles darlingi*, the most common malaria vector in eastern Peru, is most often found in areas with shade and submersed vegetation.<sup>11,12</sup> Changes in the forest cover, hydrology and vegetation of areas that have been cleared of their natural forests have increased the number of such ideal breeding sites for *A. darlingi*.<sup>9</sup> The human activities, such as farming, in these cleared areas tend to create artificial bodies of water on the ground or in objects that can collect water, which have also contributed to the increase in available mosquito breeding sites, consequently increasing the distribution of *A. darlingi*.<sup>9,13</sup>

The Northern Amazonian region of Peru has been particularly affected by deforestation due to its rapid population growth and urban expansion. This deforestation is thought to have led to increased rates of malaria. To test this hypothesis, researchers at the University of Pennsylvania conducted a study in the northern part of the Peruvian Amazon to determine the location of *A. darlingi* breeding sites and whether this correlated with deforestation. *A. darlingi* larvae were most often found in modified landscapes with little to no forest vegetation remaining, such as shrub, village or farm sites; they were least frequently found in forested areas. Larvae were found in irrigation canals, pastures, rice fields and flooded cane fields.<sup>9</sup> These data indicate that *A. darlingi* tend to flourish in conditions created by the typical human settlement patterns of non-nomadic farmers in Peru's Amazon basin. These non-nomadic populations often settle in an area and subsequently clear all of the surrounding forest around the village for farming. When this land becomes infertile from overuse, it is then abandoned and the farmers clear the adjoining forested lands to begin the process anew.<sup>14</sup> It has been shown that there are 278 times more *A. darlingi* bites in these deforested areas than in predominantly forested areas.<sup>8</sup> Eighty-three percent of the breeding sites identified as containing *A. darlingi* larvae were within 500 meters of human settlements,<sup>8</sup> which is likely due in part to the availability of humans for adult mosquitoes to feed on and the human alteration of the surrounding landscape. These land alteration practices create favorable conditions for *A. darlingi* larval breeding and lead to an increased incidence of malaria in

these populations that are now in higher contact with the vector mosquitoes in fragmented habitats.

However, increased malaria incidence due to deforestation is not limited to just the Amazon basin. Malaria has spread to new areas across the globe, such as Sri Lanka and Madagascar. Furthermore, even in countries where it was already endemic, such as Uganda and Burundi,<sup>15,18</sup> malaria incidence has increased significantly in recent years. The higher level of contact between humans and malaria vectors increased the size and spread of the vector population.<sup>13</sup>

As the rate of deforestation throughout the world is expected to continue to rise in the foreseeable future, its effects on vector-borne infectious diseases are also projected to increase,<sup>19</sup> and both the scope and spread of malaria will continue to grow if nothing is done.

## American cutaneous leishmaniasis

According to the World Health Organization (WHO), "Neglected tropical diseases affect more than 1 billion people, primarily poor populations living in tropical and subtropical climates. These populations are frequently geographically clustered and individuals are often afflicted with more than one parasite or infection. More than 70% of countries and territories that report the presence of neglected tropical diseases are low-income or lower middle-income economies."<sup>20</sup>

American Cutaneous Leishmaniasis (ACL) is classified as a neglected tropical disease by the WHO and represents one of the foremost emerging and re-emerging vector-borne diseases in the Americas.<sup>21</sup> The disease, caused by species of the Leishmania parasite, is transmitted by sand flies that have previously fed on an infected animal reservoir, usually a rodent.<sup>22</sup> Once infected, a patient will develop one or multiple lesions or ulcers on the skin that can take over a year to heal. Secondary bacterial infections occur in nearly one-fifth of patients and may lead to serious pain and disability.<sup>23,24</sup> About 10% of patients who are treated for ACL experience relapses of the disease that can be even more severe than the initial

infection.<sup>25</sup> According to the WHO, there are an estimated 1.5 million new cases each year and an estimated 12 million people infected worldwide,<sup>16</sup> placing a significant and increasing burden on all populations in endemic areas.

As with the case of malaria, there has been a documented association between deforestation in tropical and subtropical regions and the re-emergence of leishmaniasis.<sup>26</sup> It has been found that ACL infection rates are highest in populations that live close to forest edges and/or work in the forests to harvest natural resources.<sup>27,28</sup> Leishmaniasis, especially ACL, is becoming more of a burden in areas of Central and South America as widespread urbanization and changing agricultural practices increase the rates of deforestation.<sup>29</sup> During the 1960s and 1970s, Costa Rica had the fastest rate of land-use alteration and population growth in the Americas and thus provides an important case study on the effects of deforestation.<sup>30</sup> The prevalence of ACL infection in rural Costa Rica has been linked directly to contact with forests near agricultural land.<sup>22</sup>

Deforestation in Costa Rica is especially associated with rapid human population growth and the expansion of large-scale commercial agriculture. Such expansion often leads to the singular cultivation of a number of commercial crops in which ACL reservoirs tend to be concentrated.<sup>31,32</sup> These population and agricultural shifts bring imbalances in land ownership, raise the numbers of displaced and landless farmers and increase pressure to clear land for the harvesting of natural resources and local subsistence farming.<sup>30,33</sup> The resulting land-use change

and deforestation lead to a higher level of contact between socially marginalized populations and ACL vectors and sylvatic reservoirs.<sup>28</sup>

In addition, human populations that live within or near fragmented forests mixed with crops are at a much higher risk of ACL infection due to the reduced overall biodiversity of the local environment.<sup>34</sup> It has been well-documented in environmental studies that in fragmented, isolated and disturbed landscapes, habitat destruction and related biodiversity loss lead to the loss of keystone species and eventually result in niche changes that significantly reduce landscape biodiversity in a positive feedback loop.<sup>34</sup> These keystone species, such as large mammals and predators, play a critical role in the structure of an ecosystem. Since the main reservoirs of the Leishmania species that transmit ACL are small mammals, such as rodents and sloths, deforestation and the resulting loss of biodiversity have a significant impact on the incidence of the disease.<sup>27</sup> Forest fragmentation significantly alters the inter-species relationships within the ecosystem and leads to a decrease in mammal biodiversity. First, large predators disappear resulting in rodent population increases.<sup>35</sup> While only a relatively small number of mammals exposed to sand fly vectors are actually infected with Leishmania and act as reservoirs, deforestation increases their populations and changes disease transmission dynamics by increasing human contact with the sand fly vectors, increasing the spread of ACL in nearby populations.<sup>35</sup>

The number of annual cases of ACL in Costa Rica increased from 690 in 2002 to 1,870 in 2007, in association with population growth and a changing landscape in highly endemic regions.<sup>36</sup> Marginalized populations, such as Nicaraguan refugees, living in areas affected by deforestation and land-use changes have suffered epidemics that affected more than 200 people.<sup>36</sup> Brazil has suffered similar effects from deforestation. Between 1998 and 2002, ACL incidence in Brazil increased from 21,800 cases to 40,000 cases.<sup>29</sup> As can be seen in both rural Costa Rican populations and Brazilian populations, deforestation and the ensuing effects on the landscape and ecosystem are putting human populations at an increased risk for ACL. There are now more reservoir animals, and the forest edges of their habitats are becoming more fragmented. Not only are the reservoir species now more likely to leave the forest occasionally, but the humans who have cleared the land for farming are also now living much closer to the forest edges. Altogether, humans and ACL reservoirs are coming in contact with each other much more frequently now than before and therefore disease transmission has increased.

## Hantavirus

Hantaviruses are transmitted by a large number of rodent species in the Cricetidae family, found in Asia, Europe and the Americas. Transmission to humans occurs through direct contact with the rodent, such as through a bite or inhalation of the aerosolized virus in rodent urine, feces and saliva.<sup>37</sup> The strains of hantavirus present in the Americas cause hantavirus pulmonary syndrome, which can have a mortality rate as high as 38%.<sup>38</sup> While the disease is not very common in the United States, it is a significant burden in countries in Central and South America. Hantavirus prevalence has been increasing throughout South America, especially in Argentina, Brazil and Paraguay, where rodent host populations have flourished following deforestation.<sup>39</sup> The prevalence of the disease has also increased in Panama, where intermittent cases of hantavirus pulmonary syndrome occur every year. Rodent species represent the main reservoirs of hantaviruses in Panama, so researchers from the University of New Mexico conducted a study to determine the

effect of deforestation on those reservoir species populations. The researchers compared communities of small mammals from habitats such as national parks, pastures, forests and forest edges, each with varying levels of land change and fragmentation.<sup>40</sup>

Ecological communities such as those studied in Panama are comprised of generalist and specialist species. Generalist species tend to be highly adaptable to a wide range of habitats and environments, whereas specialist species are highly adapted to thrive in a very narrowly defined environment. Not surprisingly, specialist species are more vulnerable to habitat change and destruction.<sup>40</sup> Analysis of the data from Panama exhibited discernible differences among the studied habitats in the composition and abundance of small mammals. Forest habitats tended to have higher species diversity and more specialist species, while pastures and forest edges tended to have more generalist species.<sup>40</sup> As generalist species are often the ones involved in transmitting zoonotic infectious diseases,<sup>40</sup> the fact that they are found in areas that humans are likely to have contact with means that these populations are at a higher risk of contracting hantavirus pulmonary syndrome. These data show that the increased species diversity among small mammals in forests is clearly linked to the decreased absolute abundance of hantavirus reservoir species in those areas.<sup>40</sup> These hantavirus reservoirs are found in greatest numbers in disturbed and forest-edge habitats and in agricultural land and pastures, known as the "seminal matrix," the ecological niche in which more human activities tend to take place.<sup>40,41</sup>

The highest proportion of the reservoir species was found in two national parks on the Azuero Peninsula, where the majority of the Panamanian cases of hantavirus pulmonary syndrome are reported.<sup>40,42</sup>

The prevalence of hantavirus has significantly increased in areas that have undergone deforestation and other ecological changes due to the decreased biodiversity of the regions and the increased contact between humans and the rodents that carry hantavirus.<sup>29,43</sup> Increases in the local distribution and abundance of generalists and hantavirus reservoir species in Panama can be attributed to the changes in local environments occurring due to deforestation in tropical areas, as has also been the case in other countries such as Venezuela and Costa Rica.<sup>44,45</sup> While not much is understood about the underlying mechanisms for the changes observed in rodent communities in disturbed habitats, the decrease in specialists and the increase in generalists have been shown to be the result of changing species interactions due to habitat loss.<sup>46</sup>

In fragmented habitats from the study conducted in Panama, many specialist species were either present at very low numbers or were absent completely.<sup>40</sup> Seroprevalence was measured to determine the level of the pathogen in the blood serum of populations from the studied habitats. It was found that the seroprevalence of hantavirus increases three-fold in these disturbed habitats over areas that still retain specialist species.<sup>47</sup> If the current rate of deforestation and loss of forest cover in tropical regions continues, many specialist species are likely to go extinct, and this will have serious implications not only for the function of important ecosystems, but also for human health.<sup>48</sup>

## Recommendations

The increasing incidences of malaria in Peru, ACL in Costa Rica and hantavirus in Panama following deforestation all support the idea that populations near these fragmented forests and new forest edges are at a much higher risk of infection due to their increased contact with vectors, the increased vector and reservoir populations and the reduced biodiversity of these areas. These

Deforestation is ongoing in much of the developing world, creating ideal conditions for vectors to breed and spread infectious diseases.

Deforestation and the ensuing effects on the landscape and ecosystem are putting human populations at an increased risk for ACL.



Allison Gottwald

cases are just a few examples of a larger trend. The relationship between deforestation and infectious disease emergence has also been observed in Uganda, Sri Lanka, Madagascar, Rwanda and numerous other countries throughout the world,<sup>15,16,18</sup> and its impact will only continue to grow if it is not mitigated. Here, I provide recommendations for steps that should be taken to reduce this growing problem in Central and South America.

Deforestation is not easily regulated due to the political and economic climates in which it usually occurs. As we will not be able to stop this process fully in the near future, it is vitally important that surveillance methods are improved and implemented in the most affected areas in order to reduce the rate of ongoing deforestation. More data on changes in vector populations, the environment, disease incidence and human migration and behavior patterns are needed to better understand the complex dynamics of this process. This information will play an essential part in early detection of disease emergence or re-emergence and in developing predictive models that can prevent future disease epidemics, especially in the most vulnerable populations.<sup>2,10</sup>

The loss of forests and their accompanying biodiversity is a key environmental issue in tropical regions. It is the determining factor through which social marginalization increases the rates of Leishmania transmission. Socioeconomic factors play an important role in determining which marginalized populations are ultimately at highest risk. Based on ACL incidence data for all of the cantones (subdivisions of provinces) in Costa Rica between 1996 and 2000, it was discovered that the spatial distribution of ACL could not be explained by landscape alteration alone.<sup>22</sup> There was a high level of correlation between clusters of ACL incidence and clusters of social marginalization, a pattern demonstrated by other studies done on small spatial scales to show the tendency of other common infectious diseases to disproportionately affect populations that have been socially marginalized.<sup>49,50</sup> The study of ACL in Costa Rica shows that this pattern observed in the smaller-scale studies can also be true of large, geographic scales in explaining disease incidence rates through social marginalization and will be demonstrated below.

Case studies and epidemiological research into the impacts of different land-use changes and social situations are also important, as they will give us a more complete understanding of how best to approach the disease problems associated with deforestation and land alteration in various parts of the world.<sup>51</sup> Further research must still be done into how this information can be used to implement targeted, community level interventions in order to minimize the effects of growing agriculture and other industries in developing countries, such as Peru and Costa Rica.

While ecological mechanisms associated with infection risk and the observed disease patterns in areas affected by land-use change have been identified, new policies must still be implemented in order to work toward better control of infectious diseases, conservation of biodiversity and promotion of human well-being.<sup>22</sup> These policies can work to control the extent of deforestation by limiting the allowed amount of clear cutting each year, requiring replanting to reduce the impact of tree cover loss and implementing other disease control measures in those areas most affected by the increase in susceptibility to infectious disease. It is important that new policies work to balance conservation with agriculture and economic growth, so as not to impact negatively the very populations

they are trying to protect.

One possible way to mitigate the problems of deforestation and infectious disease prevalence is to target them from many angles at once: implementing policy changes, as cited above; educating communities, especially more rural and agricultural populations, about disease prevention; and promoting interdisciplinary research involving social, environmental and biological scientists on the relationship between deforestation and increasing rates of infectious disease. Colloquia, such as the Working Group on Land Use Change and Disease Emergence, help compile resources on interrelated topics and work not only to design and promote education and research, but also to effect policy changes to protect other vulnerable populations worldwide. This particular colloquium has suggested a three-fold approach to begin to address the issue of deforestation and the emergence of zoonotic, vector-borne diseases. They propose the implementation of programs to promote research that combine the natural, health and social sciences and the training of professionals to do this research. It is also important to educate local communities about the relationship between public health and environmental degradation.<sup>52</sup> Communication across disciplines, such as anthropology, environmental science and biology, and assessment of the current situation are essential to create policies that will promote sustainable ecosystems and health objectives specific to each country's particular situation and the needs of its population.<sup>16,52</sup> The neglected natures of these infectious diseases and the heavy burden they place on developing countries make this an important area of future research and development. If steps such as the ones presented above are implemented in the most impacted countries, the negative interactions between deforestation and disease incidence may diminish.

References available at  
**JGH Online,**  
[www.ghjournal.org](http://www.ghjournal.org)



# Recommendations for Increasing the Efficacy & Coverage of the Rotavirus Vaccination Program in Ghana

Rachel A. Blake

Warren Alpert Medical School, Brown University, Providence, RI, USA

.....

## Abstract

Rotavirus is the most prevalent cause of severe diarrhea in children worldwide, accounting for up to 600,000 preventable deaths in young children each year. The burden of rotavirus is particularly high in sub-Saharan Africa, the site of 150,000 to 200,000 of these annual deaths. There are two live, oral rotavirus vaccines available globally: RotaTeq, administered in three doses and Rotarix, administered in two doses. In May 2012, Ghana became one of the first countries in the sub-Saharan region to administer a rotavirus vaccine, namely Rotarix. However, when comparing results of clinical trials conducted on children in developing nations to those conducted on children in higher-income nations, it is evident that there is a decreased level of success of rotavirus vaccines in Ghana and other developing nations. In Ghana, longer rotavirus infection seasons, younger ages of infection, poorer health and nutrition of children and decreased access to adequate healthcare are the most relevant obstacles to the success of the rotavirus vaccination program. Therefore, there is a need for a unique set of vaccine delivery strategies to maximize the success of the rotavirus vaccination program in Ghana. This paper explores the most relevant issues through literature reviews, in-person forums with mothers in Ghana and on-site interviews with the Head of Program Planning and Evaluation at Ghana's Ministry of Health and a rotavirus expert from the University of Ghana's Noguchi Memorial Institute for Medical Research. Recommendations for improving vaccine success in Ghana include administering a probiotic and micronutrient supplement with the vaccine and broadening age restrictions for the vaccine from eight months up to two years old. In addition, further studies should be conducted to evaluate the risks and benefits of a neonatal dose at two weeks of age, examine the potential impact of restricting breast-feeding 30 minutes before and after immunization and determine the safety and effectiveness of the vaccine in HIV-positive infants. Importantly, the investigation of new candidate vaccines may ultimately be necessary to provide protection against uncommon viral strains found at increasingly higher rates in children in developing nations. These recommendations aim to circumvent the challenges to vaccination to maximize performance of rotavirus vaccines in Ghana and in other developing nations worldwide.

.....

## Introduction

### Global burden of rotavirus

Rotavirus-induced gastroenteritis is the single most prevalent cause of severe diarrhea worldwide, accounting for about 400,000 to 600,000 preventable deaths annually in children younger than five years old.<sup>1</sup> According to the World Health Organization (WHO), the burden of rotavirus is particularly high in sub-Saharan Africa, which is the site of 150,000 to 200,000 of the aforementioned annual deaths. This increased disease burden is due to longer rotavirus infection seasons, younger ages of infection, poorer health and nutrition of children and decreased access to adequate healthcare.<sup>1</sup> There are currently two rotavirus vaccines available for use: RotaTeq and Rotarix. These are both live, oral vaccines that as of 2011 have been licensed for use in over 123 nations around the world. However, clinical trials of these vaccines have demonstrated decreased efficacy in low-income nations in sub-Saharan Africa.<sup>2</sup> Moreover, as of November 2013, of the 123 nations in which these vaccines are licensed for use, only 50 nations, the vast majority of which are in Europe and the Americas, have incorporated them into their national infant immunization programs.<sup>3,4</sup>

### Rotavirus in Ghana

Ghana is a nation in sub-Saharan Africa that has a relatively

well-developed healthcare system and infant immunization program compared to surrounding countries.<sup>5,6</sup> I chose Ghana as a case study because I believe that policy makers in this country are extremely dedicated to creating a rotavirus vaccine program that can effectively decrease the burden of this disease and can provide coverage to all children throughout the country. Throughout my work in Ghana, I interacted with community members, physicians and government workers who are passionate about improving the country's infant immunization program as well as the overall healthcare infrastructure.

Data from a recent multi-center study conducted by the Department of Child Health at the University of Ghana Medical School from January 2008 to December 2009 showed that of the over 16,000 children hospitalized during the study time period, 13% were hospitalized due to acute gastroenteritis (infectious diarrhea causing abdominal pain, cramping, vomiting and dehydration). Of those hospitalized for acute gastroenteritis, 49% of them were confirmed as rotavirus-positive. The majority of children affected by rotavirus were between the ages of three and 14 months old, with peaks between six and 12 months old.<sup>7</sup> Due to the high morbidity and mortality rate of rotavirus in Ghanaian children, the incorporation of a rotavirus vaccine has been a top priority for Ghana's Ministry of Health in recent years. In May

2012, Ghana, along with Morocco, South Africa and Sudan, became one of the first African nations to administer a rotavirus vaccine.<sup>8,9</sup> The Ministry of Health in these nations chose Rotarix because this vaccine is administered in two doses unlike RotaTeq, which must be administered in three doses. A two-dose vaccine is more likely to yield higher rates of compliance as opposed to a three-dose vaccine, which could ultimately lead to higher vaccination rates.<sup>9,10</sup>

#### Decreased performance in developing nations

It is important to note that trials conducted by the African Rotavirus Surveillance Network in Ghana and other developing countries in Africa and Asia have demonstrated decreased performance of RotaTeq and Rotarix compared to performance in higher-income nations. In a large-scale placebo-controlled study (during which half of participants received the vaccine and the other half received a “placebo” or inactive vaccine) conducted on infants in six nations in Europe, two doses of Rotarix demonstrated 90.4% protection against severe rotavirus disease.<sup>12</sup> However, data from a separate study conducted by the African Rotavirus Surveillance Network showed that two doses of Rotarix induced only 58.7% protection against severe rotavirus disease in children in South Africa and 49.4% in children in Malawi. In that same study, two years post-vaccination, the RotaTeq vaccine protected against severe disease at rates of 55.5% in Ghana, 63.9% in Kenya and merely 17.6% in Mali.<sup>13</sup>

Though discouraging, these results are consistent with results from previous trials in the region with other live oral vaccines, namely poliovirus and cholera. These studies, published in highly-regarded journals including the *Journal of Infectious Disease* and the *International Journal of Epidemiology*, among others, demonstrated that these live oral vaccines showed decreased rates of protection against polio and cholera in children in developing nations.<sup>13</sup> Importantly, these studies show that the decreased success of the

Of the over 123 nations in which these vaccines are licensed for use, only 50 nations have incorporated them into their national infant immunization program.

vaccine may be due to a higher severity of rotavirus infection in poorer nations, which is attributed to longer lengths of rotavirus infection seasons, younger ages of onset of rotavirus infections and higher instances of malnutrition and affliction with multiple other diseases.<sup>14-17</sup> These findings render even more crucial the urgency to modify policies regarding vaccine administration in order to optimize delivery and efficacy of these vaccines.<sup>12</sup>

Though the Rotarix vaccine has been used in Ghana for more than a year, experts have begun to identify a number of outstanding issues that must be further investigated and policies that should undergo revision in order to maximize the success of the new vaccine program.<sup>2</sup> These recommendations include administering a probiotic and micronutrient supplement with the vaccine and broadening age restrictions for vaccine administration up to two years old. In addition, further studies should be conducted to evaluate the risks and benefits of a neonatal dose at two weeks old, examine the potential impact of restricting breast-feeding 30 minutes before and after immunization and determine the safety and efficacy of the vaccine in HIV-positive infants. Importantly, the investigation of new candidate vaccines may ultimately be necessary in order to provide protection against uncommon viral strains found at increasingly higher rates in children in developing nations. This paper presents in-depth rationales for each of these recommendations, with the in-

attention of circumventing outstanding issues to ultimately maximize performance of rotavirus vaccines in Ghana and developing nations worldwide.

#### Recommendations for vaccine administration

##### Administer vaccines with a micronutrient and probiotic supplement

The overall nutritional status of children in developing countries like Ghana is much poorer than children in more affluent nations. Young children in these areas often experience malnutrition and are frequently afflicted with bacterial, viral and parasitic infections.<sup>2,18</sup> Studies published in the *Pediatric Infectious Disease and Pediatrics* journals suggest that infants in developing nations are more likely to have diseases in their gut, including viruses that are not normally present in the guts of otherwise healthy infants.<sup>2,18,19</sup> Consequently, these studies demonstrate that infants who are experiencing upset stomachs or any diarrheal symptoms from infections other than rotavirus at the time of vaccination show a decreased absorption of the rotavirus vaccine.<sup>19,20</sup> One of these studies, which examined the oral cholera vaccine in children in Chile, showed that bacterial overgrowth from infections other than cholera in the small intestine impaired response to the vaccine.<sup>19</sup> Similarly, an additional study in Bangladesh with the live oral poliovirus vaccine indicated that rates of response to the vaccine were decreased in children who were experiencing diarrheal symptoms resulting from infections other than polio at the time of vaccination.<sup>19</sup>

Previous literature overwhelmingly suggests that a child's enteric balance can be properly maintained with probiotic and micronutrient supplements, especially in the context of childhood diarrhea.<sup>2,20,21</sup> Recently, a study published in *Pediatrics* demonstrated that continuous zinc supplementation significantly reduced the severity and frequency of diarrheal morbidity in infants, further suggesting that micronutrients may play a role in stabilizing the environment within an infant's gut.<sup>19</sup> In addition, probiotics have been shown to increase an infant's absorption of a live oral vaccine. For example, a successful intervention study in Finland of a previous rotavirus vaccine, RotaShield, showed that administering a probiotic *Lactobacillus GG* supplement at the time of vaccination improved infants' response to the vaccine.<sup>20</sup> These few studies provide evidence supporting a widely understood concept in pediatric medicine that micronutrient supplements and probiotics are beneficial for infant digestion and immune function.<sup>19-21</sup>

In order to maximize absorption and effectiveness of the rotavirus vaccine in Ghanaian children, policymakers should require administration of a micronutrient and probiotic in conjunction with rotavirus vaccination. Ideally, continuous probiotic and micronutrient administration would be the most successful way to ensure optimal health in children in developing nations. However, administering a supplement that contains a probiotic such as *Lactobacillus*, at least during the actual time of vaccination, would support a more optimal balance in gut flora by supplying beneficial bacteria that can combat any ongoing infections other than rotavirus that are occurring in the gut.<sup>20,21</sup> Moreover, since infants who are experiencing upset stomach or any diarrheal symptoms at the time of vaccination show a decreased absorption of the vaccine, a micronutrient supplement could help promote maximal absorption of the vaccine.<sup>19</sup> According to the World Health Organization (WHO), these types of campaigns are currently in operation in numerous developing nations worldwide, including the coupling of measles vaccines with Vitamin A supplements in order to combat Vitamin A deficiencies in young children.<sup>22</sup> Since this type of intervention is already widely used in developing regions for measles vaccines, it could also serve as a potentially feasible intervention for rotavirus vaccines in these regions.

##### Broaden vaccine age restrictions for infants in Ghana

In addition to optimizing an infant's absorption of the vaccine, the age range for vaccination should be broadened in order to maximize the number of infants who can be successfully vaccinated in Ghana. Currently, infants in Ghana receive the vaccine at six and ten weeks of age, with the final dose administered sometime prior to

eight months of age. However, this age range should be broadened to extend the age limit of the final dose up to 24 months old.

##### Rationale for current age restrictions

Currently, infants in the US receive doses of Rotarix at two and four months old. In Ghana, infants receive Rotarix at six and ten weeks old, per recommendations made by the Centers for Disease Control and Prevention (CDC).<sup>23</sup> This recommendation is based on the fact that infants in Ghana are often susceptible to rotavirus infections at younger ages than children in the US and it is important to ensure that infants receive the vaccine before they contract natural rotavirus infection.<sup>24,25</sup> The first dose given at six weeks old in Ghanaian children corresponds to the approximate age at which an infant's digestive tract is mature enough to be able to absorb the majority of the vaccine.<sup>3</sup>

The CDC recommends that the worldwide maximum age for the first dose of vaccine is 14 weeks and six days, while the maximum age for the second dose is eight months old.<sup>23,26</sup> This recommendation was created after the removal of the previously licensed RotaShield vaccine just a year after it was implemented in the United States because it increased the risk of intussusception.<sup>26</sup> Intussusception is the most common cause of intestinal obstruction in children under 5 years old and is characterized by the invagination of a proximal portion of the bowel within a more distal portion. This condition often requires emergency surgery.<sup>27,28</sup> Merck & GlaxoSmithKline, the manufacturers of RotaTeq and Rotarix, respectively, recommend a maximum vaccination age of eight months due to the fact that in normal infants, the risk of intussusception peaks just before eight months old.<sup>28</sup>

However, large-scale global trials of RotaTeq and Rotarix vaccines demonstrate that these currently licensed vaccines, unlike their predecessors, do not show any increase in rates of intussusception.<sup>29-31</sup> Therefore, the risk of intussusception may no longer be relevant for these newer vaccines. A top priority during post-licensure surveillance studies will be to confirm that RotaTeq and Rotarix indeed do not increase intussusception risk, in order to ensure the safety of extending the vaccination age limit beyond eight months.

##### Extend age limit to eight months for first dose, 24 months for second dose

In order to prevent infants who are above the vaccination age limit from being denied the vaccine, the age maximum for vaccination should be increased to 24 months old. As a result of limited access to health clinics in more rural areas of Ghana, delays in vaccination and missed follow-up doses are not uncommon. These delays and missed follow-up doses can lead to infants becoming too old to receive the second dose of vaccine.<sup>2,12</sup> A recent study published in the *Journal of Infectious Disease* conducted in the rural Kassena-Nankana district projected that 70% of rotavirus-related deaths in Ghana could be prevented if there were no age restrictions on the vaccine, while only 53% of deaths would be prevented if children were required to receive all three doses between the age of 12 and 32 weeks.<sup>32</sup> Similarly, a study published in *Vaccine* estimated that extending the age of vaccination up to one year would save 28% more additional lives worldwide.<sup>33</sup>

A study published in the *New England Journal of Medicine* demonstrated that at 24 months old, nearly 100% of children have some degree of natural immunity against severe rotavirus infection due to previous naturally acquired rotavirus infections.<sup>34</sup> Namely, it is crucial to vaccinate infants all the way up to two years of age, because before this age, it is not certain that all children would have naturally-acquired protection against severe rotavirus disease. Therefore, many children will still be susceptible to severe infection before the age of two. After two years old it is almost 100% certain that infants would have gained some degree of protection against severe rotavirus disease, so an infant presenting after the age of two would no longer need to be vaccinated.<sup>34</sup>

Similarly, the age limit on the first dose should be extended to eight months old, at which time only about 40% of infants are likely to have contracted their first natural rotavirus infection.<sup>37</sup> In addition, there should be no restriction on the length of time between doses, provided that the first dose is given by eight months old, and the second dose is administered within this broadened 24-month time frame. Though patients should still be highly encouraged to

receive the vaccine on the recommended dosing schedule of six and ten weeks, extending the age maximums will allow for much wider vaccine coverage and fewer infants who are turned down due to late arrival to scheduled immunizations.<sup>32,33</sup>

#### Areas where further studies are needed

##### Benefit of restricting breast-feeding 30 minutes before and after vaccination

In order to maximize Ghanaian infants' response to live oral vaccines, the effect of breast-feeding directly before and after administration of the vaccine must be considered. Experts have suggested that a correlation could potentially exist between breast-feeding and decreased effectiveness of live oral rotavirus and poliovirus vaccines. Although circulating antibodies (proteins of the immune system that fight off infection) acquired maternally are considered to be important in protecting a young infant against natural rotavirus infection, during vaccination with a live oral vaccine, the presence of these antibodies may actually decrease vaccine efficacy.<sup>2</sup>

##### Studies needed to address the effect of breast-feeding during immunization period

A review conducted by the University of Maryland cited multiple studies that suggest that breast-feeding can interfere with immune reaction to rotavirus vaccines. However, the results of these studies were not always statistically significant.<sup>35</sup> On the other hand, more recent large-scale trials of both currently licensed vaccines have shown negligible differences in vaccine efficacy between mothers who self-reported breastfeeding and those who did not.<sup>26,29,36</sup> However, these studies showing no correlation between breast-feeding and decreased immune response to the vaccine only examined whether mothers self-reported breast-feeding their infant, but did not specifically examine the feeding practices directly surrounding administration of the vaccine.<sup>26,29</sup> Therefore, there is a need for further studies to investigate whether breast-feeding specifically during the time frame surrounding vaccination decreases effectiveness of the vaccine.

A study published in the *Journal of Infectious Disease* supports the notion that further investigation of this issue is warranted. This study showed that when breast milk and rotavirus were mixed outside of the body, 60% of the breast milk samples were able to neutralize (destroy) at least 90% of the virus and 30% of the breast milk samples were able to neutralize up to at least 99% of the virus.<sup>2,35</sup> These data suggest that if an infant has breast milk in the digestive tract from a recent feeding specifically during the time at which the vaccine is administered, maternal antibodies may be able to neutralize the relatively small amounts of live rotavirus contained in the vaccine. This initial neutralization could subsequently decrease the potential protective effect of that dose of vaccine compared to an infant who did not have breast milk present in the gut.<sup>2,35,36</sup>

A priority for clinical investigators should be to conduct trials that examine whether withholding breast-feeding 30 minutes before and 30 minutes after immunization has an effect on immune response to the vaccine. This time frame is based on the estimated 30 minutes to one-hour period that is required for infants of this age to digest breast-milk. Upon presenting to the clinic, health workers would require mothers to restrict feeding 30 minutes before giving their infants the vaccine. Health workers would then observe mothers for an additional 30 minute period after immunization during which breast-feeding would be prohibited. This approach is not completely novel, given that during recent trials of novel candidate rotavirus vaccines (namely, 1321 and 116E), investigators required that mothers withhold breast-feeding 30 minutes before their infants were given the vaccine so that the presence of breast-milk would not interfere with vaccine absorption.<sup>37</sup>

##### Evaluating cultural feasibility of breast-feeding regulations

Before trials of this potential breast-feeding regulation can be performed in lower-income nations like Ghana, the feasibility of this type of feeding restriction must be examined. In Ghana, nearly all infants are breastfed at least up to six months of age, as the Ministry of Health encourages breast-feeding to protect infants from a host of diseases that can result in premature death.<sup>38</sup> My hypothesis is that confusion stemming from this contradiction may cause ob-

stacles such as non-compliance with the feeding restriction and could possibly cause a decreased willingness of mothers to bring their infants to vaccination appointments.

In an effort to provide a preliminary exploration of the feasibility of regulating breast-feeding for the one-hour immunization period, I travelled to Ghana to conduct forums with mothers. Participants were recruited during their infant's six-week-old immunization visit as a part of an ongoing randomized controlled trial of Rotarix conducted by the Noguchi Memorial Institute for Medical Research. Mothers were recruited at two sites: the Navrongo Health Research Center in the rural Kassena-Nankana district in Northern Ghana and the Agogo Presbyterian Hospital in the urban city of Agogo in the Ashanti Region of Southern Ghana. A total of 11 mothers were surveyed from the Navrongo Health Research Center (divided into two separate forums of four and seven participants each) and a single forum of eight mothers was held at the Agogo Presbyterian Hospital. Translators from the Navrongo Health Research Center and the Agogo Presbyterian Hospital aided with the questionnaires.

During the forums, I asked the mothers about their current breast-feeding practices and their willingness to adhere to a potential 30-minute feeding restriction directly prior to and following immunization of their infant with the rotavirus vaccine. Health status and HIV status of mothers was not recorded during these forums. Results demonstrated that all of the mothers self-reported exclusive or partial breast-feeding of their infants. However, the forum discussions revealed an overall enthusiasm of these few mothers to comply with a proposed breast-feeding restriction surrounding vaccination.

In all three forums, 100% of the women reported that they would be willing to comply with this feeding regulation. Due to the very real threat of rotavirus diarrhea in young children in these communities, the participants agreed that they would be willing to restrain the child from feeding for one or two hours in order to protect the child from this potentially deadly disease. Overall the participants were very willing to comply with these regulations in hopes of improving the success of the vaccine and ultimately benefiting their infants. One woman remarked that the women in the community do their best to adhere to the current vaccine schedules in order to protect their children, and that she would be enthusiastic and willing to adhere to any further rules for a future vaccine. Similarly, another participant cited the success of the measles vaccine in eliminating that disease from their communities and expressed her enthusiasm that these new rotavirus vaccines could help to do the same for rotavirus in their communities. A few women did express concern that breast-feeding is one of the only ways that they can console their infant when he or she is crying. However, since the restriction is only one hour, they were hopeful that they would be able to withhold feeding their infant during this short period of time.

Though these forums represented a very limited sample of mothers from two health centers in Ghana, these preliminary discussions are certainly encouraging. Much larger and more comprehensive studies should ultimately be performed in order to determine whether this breast-feeding restriction would indeed be feasible and well received in Ghana and other developing nations worldwide.

#### Studies examining safety & effectiveness of a neonatal dose

During the period between two weeks old and the first Rotarix dose at six weeks old, infants in Ghana remain susceptible to rotavirus infection. Though maternal antibodies protect infants from

rotavirus during the first two weeks of life, after two weeks the protective effect of maternal antibodies largely declines.<sup>18</sup> A recent study published in *Vaccine* suggested that a neonatal dose of the rotavirus vaccine could further decrease rotavirus hospitalizations and deaths in extremely young infants in developing nations.<sup>39</sup> In terms of safety, a study published in the *Pediatric Infectious Disease Journal* demonstrated that infants given the first dose of the previous rotavirus vaccine, RotaShield, during the neonatal period did not develop any adverse reactions.<sup>40</sup> However, since the digestive tract of neonates is not yet fully mature, a neonate's absorption of this live oral vaccine may not be significant enough to induce protection against rotavirus this early on in life.<sup>40</sup> Therefore, further clinical trials of a neonatal dose at two weeks old should be conducted in order to discern whether this early dose would be effective and beneficial for children in developing nations. If trials are successful, the suggested age range of immunization should be broadened to include a neonatal dose.

#### Studies examining the vaccine in HIV-positive infants

In addition to children who are afflicted with bacterial, parasitic and other viral infections, children in Ghana who are infected with HIV are at equal risk of acquiring rotavirus infections during early infancy and childhood. To date, both Merck and GlaxoSmithKline, the producers of RotaTeq and Rotarix respectively, affirm that their vaccines have not yet been evaluated in HIV-positive populations.<sup>41,42</sup> Therefore, vaccination is not recommended for HIV-positive infants until further trials have confirmed its safety. However, this recommendation effectively excludes an equally susceptible cohort of infants from receiving this important immunization. In Ghana, there are over 21,000 children under the age of 15 who are HIV-positive, many of whom acquired the virus at birth as a result of limited access to anti-retroviral therapy to

prevent transmission of HIV from the mother to the child.<sup>43</sup> Preliminary data from a moderate-sized study in the African nation of Malawi conducted by the University of Malawi showed that severity of rotavirus disease and response to treatment with oral rehydration therapy did not vary significantly between HIV-positive and HIV-negative infants. However this study did not examine whether HIV-positive infants respond in a similar manner to rotavirus vaccines as HIV-negative infants.<sup>44</sup> It should therefore be a priority to conduct studies to determine whether rotavirus vaccines are safe and effective in HIV-positive infants in order to potentially extend the use of these vaccines to thousands more infants in Ghana and millions more worldwide.

#### Develop new vaccines that can fully protect Ghanaian children

Studies have shown that there are significant differences in rotavirus strain types between children in developing nations and children in higher income nations.<sup>2</sup> Rotavirus strains are classified using both a G and a P type, which corresponds to the two proteins on the outer surface of the virus particle. Globally, the most common strains are G1P[8], G3P[8], G4P[8], G9P[8], G9P[6] and G2P[4].<sup>45</sup> Though the G1P[8] strain contained in Rotarix has been shown to be one of the most prevalent strains in both Ghanaian children and children worldwide, the incidence of rare viral strains is higher in Ghanaian children than in children of higher income nations. Therefore, it may ultimately be necessary to design novel vaccine candidates that are able to target the variety of strains found in Ghanaian children and other children living in poorer regions around the world.<sup>2,46</sup>

#### Higher Incidence of Uncommon Viral Strains in Ghanaian Children

In the multi-center study conducted with 16,000 infants in Ghana, the most common G strains were G1 and G2, which are also reported as two of the most common strains in infants worldwide.<sup>7,45</sup> In addition, the P[6] strain was the most common P strain, which is known to be the second most prevalent P strain worldwide (second to the P[8] strain).<sup>47,48</sup> However, a study on global rotavirus strain distribution published in the *Review of Medical Virology* showed a 27% prevalence of strains in African children that were not among the top six most globally prevalent strains. Children in Europe and North America demonstrated significantly lower rates of these uncommon strains, ranging from rates of 1.4% to 5%.<sup>46</sup>

Specifically in Ghana, recent national surveillance studies have identified emerging strains that are becoming more prevalent, including the G8, G9, G10 and G12 strains. These strains are thought to have come about from transmission of the virus from animals to humans due to people living in close contact with livestock and other animals.<sup>14,49</sup> A few regional surveillance studies in Ghana have identified the G9 strain as the most predominant G strain in these regions, at rates ranging from 26% to 29%.<sup>50,51</sup> Similarly, the G8 strain was first isolated in Ghanaian children in 1999 and subsequent studies to date have shown the persistence of this strain in children in this nation.<sup>7,49-51</sup> The very rare G10 and G12 strains are detected at rates of up to 5% and 3.5% respectively in Ghanaian children as compared to approximately 0% in children elsewhere.<sup>6,52,53</sup>

In nearly all of the rotavirus surveillance studies conducted on Ghanaian children, there is also a prevalence of "mixed" G-type and "mixed" P-type infections. This means that instead of having an infection with a virus that has only a single G and a single P type, these viruses contain hybrid or mixed G or P strains. A host of mixed G genotype infections have been detected in Ghanaian children, including G1G2, G2G8, G3G8, G3G12 and G10G12. In the large multi-center study, these mixed G strains accounted for 7.6% of all rotavirus cases, while mixed P strains accounted for 26.5% of the P strains.<sup>6,54</sup> By comparison, these mixed strains are detected at much lower rates, if at all, in children in higher-income nations. One such study published in the *European Journal of Epidemiology* detected a mixed G strain prevalence of merely 2.0% in children in Spain.<sup>37</sup> This emergence of uncommon strains in Ghanaian children is a result of the tendency of these infants to be infected with multiple different rotavirus strain types at the same time, allowing for mixing of multiple strains to create new, hybrid strains.<sup>14,49</sup>

#### Development of New Vaccines to Target Uncommon Strains

Due to the increased incidence of rare strains in Ghanaian children and in children in other developing nations, it is crucial to prioritize development of novel vaccines that can effectively target these emerging strains.<sup>46</sup> Though the Rotarix vaccine contains only a single strain, namely G1P[8], it has demonstrated its ability to protect against a variety of different rotavirus strains during multiple large-scale, multi-nation clinical trials, the review of which is published in *Expert Review of Vaccines*.<sup>38</sup> However, as the Rotarix and RotaTeq vaccines begin to decrease the incidence of the more globally common strains, there may be a global trend towards an even further increased prevalence of rare and mixed strains. This effect has been seen with mass treatment for other multi-strain viruses such as HIV.<sup>55</sup> It is therefore crucial to focus efforts towards designing and evaluating novel vaccine candidates that can effectively target a wide range of strains in hopes of affording maximal protection against rotavirus infection worldwide.<sup>7,27</sup>

#### Priorities for improving vaccine delivery

Before these important recommendations can be implemented in Ghana, it is crucial to consider the most relevant improvements that must be made to Ghana's healthcare infrastructure in order to support the incorporation of this new live oral vaccine into the infant immunization program.

In September 2011, I conducted an in-person interview with the Head of Program Planning and Evaluation at Ghana's Ministry of Health. During the interview, which occurred less than a year

before the rollout of the Rotarix vaccine, the representative stressed that prior to the introduction of this vaccine, a top priority for the Ministry of Health was to ensure that all aspects of vaccine transport and delivery were adequately prepared. She noted that temperature control is especially important during transport and storage of this live oral vaccine, as it must be maintained precisely between 2° and 8° C for quality assurance purposes.<sup>41</sup> At the time of the interview, funds were still needed to address the most relevant improvements, including improving the cold chain (vaccine transportation) system, training regional staff to properly administer the vaccine and updating the medical records systems to allow ample space to record this additional vaccine. The representative explained that the Ministry of Health was in the process of updating their cold chain system to include large, walk-in refrigerators with a reliable monitoring system that would provide alerts when appliances required maintenance or replacement. The representative seemed very hopeful that these necessary improvements would be implemented before the introduction of rotavirus vaccines to Ghana.

To date, the Ministry of Health has since successfully undergone these previously outlined revisions to their infrastructure as the rotavirus vaccination program has begun and continues to expand. Importantly, the Ministry of Health has updated their cold chain system to support massive quantities of these live oral vaccines at the required temperature of 2° to 8° C.<sup>41</sup> Consistent with the agenda set forth two years ago by the Head of Program Planning and Evaluation at the Ministry of Health, this agency must continue to allocate adequate funding towards closely monitoring the integrity of vaccine transport and delivery in order to ensure optimal quality and effectiveness of these vaccines.

#### Update on rotavirus vaccination program in Ghana

Recently in August 2013, I conducted an interview with George Armah, Ph.D., to discuss the progress of the Rotarix vaccination program in Ghana. Dr. Armah is a specialist in rotavirus gastroenteritis and chair of the Department of Electron Microscopy and Immunohistochemistry at the University of Ghana's Noguchi Memorial Institute for Medical Research. He estimated that currently 75% of infants are being vaccinated against rotavirus in Ghana, a number that he projects will continue to rise. Importantly, he reported that as of March 2013, researchers have begun national post-licensure surveillance studies of the vaccine's performance in Ghana. This two-year-long nation-wide investigation will provide important efficacy and coverage data surrounding the performance of rotavirus vaccines, ultimately helping to inform crucial changes to rotavirus vaccine policies.

#### Conclusion

In the United States and many European nations, rotavirus vaccines have demonstrated ample success at preventing severe rotavirus disease in young children. However, this is not yet the case in low-income countries around the world. Though rotavirus vaccines are now fully integrated into Ghana's infant immunization schedule, the ultimate success of these vaccines is contingent upon the adoption of immunization policies that aim to enhance performance of these vaccines in infants throughout the country.

The recommendations presented in this paper attempt to identify and overcome the most relevant challenges to the current rotavirus vaccination program in Ghana. A series of risks and benefits was weighed to take into account the specific conditions of Ghana, which differ greatly from the conditions in more affluent nations in which these vaccines have previously been used successfully. These recommendations include administering a probiotic and micronutrient supplement with the vaccine and broadening age restrictions for the vaccine up to two years old. The cost-effectiveness, however, of coupling vaccine administration with a probiotic and micronutrient supplement has yet to be examined, which would be necessary prior to introduction of this type of program. In addition, further studies should be conducted to evaluate the risks and benefits of a neonatal dose at two weeks old, examine the potential impact of restricting breast-feeding 30 minutes before and after immunization and determine the safety and effectiveness of the vaccine in HIV-

It is crucial to vaccinate infants all the way up to two years of age, because before this age, it is not certain that all children would have naturally-acquired protection against severe rotavirus disease.

positive infants. Importantly, the investigation of new candidate vaccines may ultimately be necessary in order to provide protection against uncommon viral strains found at increasingly higher rates in children in developing nations.

I used Ghana as a case study for this paper due to the relatively well-developed healthcare infrastructure, the readiness of officials to introduce rotavirus vaccines and my personal passion for healthcare policy in this nation. Consequently, the climate, rotavirus epidemiology and access to resources in Ghana are very similar to conditions in most other developing nations around the world. Therefore, the vaccination policies suggested here could ultimately be applied to other countries in Africa, Asia and Latin America once rotavirus immunization programs have been launched in these regions. In the coming years, as rotavirus vaccine coverage continues to expand globally, it will remain crucial that officials prioritize important policy interventions surrounding vaccination that could greatly enhance the life-saving potential of these vaccines.

### Acknowledgments

I would like to acknowledge my advisors Thomas Shenk, Ph.D., George Armah, Ph.D. and Adel Mahmoud, Ph.D., for their guidance on this project. I would also like to acknowledge the researchers at Noguchi Memorial Institute for Medical Research in Ghana and Pearl Duncan for their expertise and support. This work was made possible by generous grants from Princeton University Grand Health Challenges and Princeton Environmental Institute.

### References

1. World Health Organization. Rotavirus, <http://www.who.int/nvui/rotavirus/en/> (2011).
2. Patel, M. et al. Oral rotavirus vaccines: How well will they work where they are needed most? *Journal of Infectious Diseases* 200, S39-S48 (2009).
3. O’Ryan, M., Lucero, Y. & Linhares, A. C. Rotarix®: Vaccine performance 6 years postlicensure. *Expert Review of Vaccines* 10, 1645-1659, doi:10.1586/erv.11.152 (2011).
4. PATH. Rotavirus vaccines: The facts. <http://sites.path.org/rotavirusvaccine/about-rotavirus/rotavirus-vaccines/> (2013).
5. World Health Organization. Ghana: Health Profile, <http://www.who.int/gho/countries/gha.pdf> (2013).
6. Asante, A. D. & Zwi, A. B. Factors influencing resource allocation decisions and equity in the health system of Ghana. *Public Health* 123, 371-377 (2009).
7. Enweronu-Laryea, C. C. et al. Prevalence of severe acute rotavirus gastroenteritis and intussusceptions in Ghanaian children under 5 years of age. *Journal of Infection in Developing Countries* 6, 148-155 (2012).
8. PATH. Rotavirus disease and vaccines in Ghana, <http://www.path.org/publications/files/VAD\_rotavirus\_ghana\_fs.pdf> (2013).
9. Biritwum, R. B. et al. Community-based cluster surveys on treatment preferences for diarrhoea, severe diarrhoea, and dysentery in children aged less than five years in two districts of Ghana. *Journal of Health, Population and Nutrition* 22, 182-190 (2004).
10. McCormack, P. L. & Keam, S. J. Rotavirus vaccine RIX4414 (Rotarix™): A review of its use in the prevention of rotavirus gastroenteritis. *Pediatric Drugs* 11, 75-88 (2009).
11. Vesikari, T. et al. Efficacy of human rotavirus vaccine against rotavirus gastroenteritis during the first 2 years of life in European infants: randomised, double-blind controlled study. *Lancet* 370, 1757-1763 (2007).
12. Armah, G. E. et al. Efficacy of pentavalent rotavirus vac-

13. Levine, M. M. Immunogenicity and efficacy of oral vaccines in developing countries: Lessons from a live cholera vaccine. *BMC Biology* 8 (2010).
14. Kirkwood, C. D. Genetic and antigenic diversity of human rotaviruses: Potential impact on vaccination programs. *Journal of Infectious Diseases* 202, S43-S48 (2010).
15. Levy, K., Hubbard, A. E. & Eisenberg, J. N. S. Seasonality of rotavirus disease in the tropics: A systematic review and meta-analysis. *International Journal of Epidemiology* 38, 1487-1496 (2009).
16. Armah, G. E. et al. Seasonality of rotavirus infection in Ghana. *Annals of Tropical Paediatrics* 14, 223-229 (1994).
17. Haffeejee, I. E. The epidemiology of rotavirus infections: A global perspective. *Journal of Pediatric Gastroenterology and Nutrition* 20, 275-286 (1995).
18. Cunliffe, N. & Nakagomi, O. Introduction of rotavirus vaccines in developing countries: Remaining challenges. *Annals of Tropical Paediatrics* 27, 157-167 (2007).
19. Lagos, R. et al. Palatability, reactogenicity and immunogenicity of engineered live oral cholera vaccine CVD 103-HgR in Chilean infants and toddlers. *Pediatric Infectious Disease Journal* 18, 624-630 (1999).
20. Aggarwal, R., Sentz, J. & Miller, M. A. Role of zinc administration in prevention of childhood diarrhea and respiratory illnesses: A meta-analysis. *Pediatrics* 119, 1120-1130 (2007).
21. Isolauri, E., Joensuu, J., Suomalainen, H., Luomala, M. & Vesikari, T. Improved immunogenicity of oral D x RRV reassortant rotavirus vaccine by lactobacillus casei GG. *Vaccine* 13, 310-312 (1995).
22. World Health Organization. Vitamin A supplementation, <http://www.who.int/vaccines/en/vitamina.shtml> (2003).
23. Cortese, M. M. & Parashar, U. D. Prevention of rotavirus gastroenteritis among infants and children: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR. Recommendations and reports : Morbidity and mortality weekly report. Recommendations and reports / Centers for Disease Control* 58, 1-25 (2009).
24. Offit, P. A. Rotaviruses: Immunological determinants of protection against infection and disease. *ADV.VIRUS RES.* 44, 161-202 (1994).
25. Gentsch, J. R. et al. Serotype diversity and reassortment between human and animal rotavirus strains: Implications for rotavirus vaccine programs. *Journal of Infectious Diseases* 192, S146-S159 (2005).
26. Ciarlet, M. & Schödel, F. Development of a rotavirus vaccine: Clinical safety, immunogenicity, and efficacy of the pentavalent rotavirus vaccine, RotaTeq®. *Vaccine* 27, G72-G81 (2009).
27. DiFiore, J. W. Intussusception. *Seminars in Pediatric Surgery* 8, 214-220 (1999).
28. Kombo, L. A., Gerber, M. A., Pickering, L. K., Atreya, C. D. & Breiman, R. F. Intussusception, infection, and immunization: summary of a workshop on rotavirus. *Pediatrics* 108 (2001).
29. Ruiz-Palacios, G. M. et al. Safety and efficacy of an attenuated vaccine against severe rotavirus gastroenteritis. *New England Journal of Medicine* 354, 11-22 (2006).
30. Ciarlet, M., Crawford, S. E. & Estes, M. K. Differential infection of polarized epithelial cell lines by sialic acid-dependent and sialic acid-independent rotavirus strains. *Journal of Virology* 75, 11834-11850 (2001).
31. Shui, I. M. et al. Risk of intussusception following administration of a pentavalent rotavirus vaccine in US infants. *JAMA - Journal of the American Medical Association* 307, 598-604 (2012).
32. Arvay, M. L. et al. How much could rotavirus vaccines reduce diarrhea-associated mortality in northern Ghana? A model to assess impact. *Journal of Infectious Diseases* 200, S85-S91 (2009).
33. Patel, M. M. et al. Broadening the age restriction for

- initiating rotavirus vaccination in regions with high rotavirus mortality: Benefits of mortality reduction versus risk of fatal intussusception. *Vaccine* 27, 2916-2922 (2009).
34. Velázquez, F. R. et al. Rotavirus infection in infants as protection against subsequent infections. *New England Journal of Medicine* 335, 1022-1028 (1996).
35. Rennels, M. B. Influence of breast-feeding and oral poliovirus vaccine on the immunogenicity and efficacy of rotavirus vaccines. *Journal of Infectious Diseases* 174, S107-S111 (1996).
36. Wobudeya, E. et al. Breastfeeding and the risk of rotavirus diarrhea in hospitalized infants in Uganda: A matched case control study. *BMC Pediatrics* 11 (2011).
37. Buesa, J. et al. VP7 and VP4 genotypes among rotavirus strains recovered from children with gastroenteritis over a 3-year period in Valencia, Spain. *European Journal of Epidemiology* 16, 501-506 (2000).
38. O’Ryan, M. & Linhares, A. C. Update on Rotarix™: An oral human rotavirus vaccine. *Expert Review of Vaccines* 8, 1627-1641 (2009).
39. Halvorson, E. E., Peters, T. R., Snively, B. M. & Poehling, K. A. Potential impact of accelerating the primary dose of rotavirus vaccine in infants. *Vaccine* 30, 2738-2741 (2012).
40. Vesikari, T. et al. Neonatal administration of rhesus rotavirus tetravalent vaccine. *Pediatric Infectious Disease Journal* 25, 118-122 (2006).
41. GlaxoSmithKline. Rotarix Prescribing Information. (2011).
42. Co., M. RotaTeq Prescribing Information. (2011).
43. Tchidjou, H. K. et al. Paediatric HIV infection in Western Africa: The long way to the standard of care. *Journal of Tropical Pediatrics* 58, 451-456 (2012).
44. Cunliffe, N. A. et al. Effect of concomitant HIV infection on presentation and outcome of rotavirus gastroenteritis in Malawian children. *Lancet* 358, 550-555 (2001).
45. Bernstein, D. I. Live Attenuated Human Rotavirus Vaccine, Rotarix™. *Seminars in Pediatric Infectious Diseases* 17, 188-194 (2006).
46. Santos, N. & Hoshino, Y. Global distribution of rotavirus serotypes/genotypes and its implication for the development and implementation of an effective rotavirus vaccine. *Reviews in Medical Virology* 15, 29-56 (2005).
47. Todd, S., Page, N. A., Steele, A. D., Peenze, I. & Cunliffe, N. A. Rotavirus strain types circulating in Africa: Review of studies published during 1997-2006. *Journal of Infectious Diseases* 202, S34-S42 (2010).
48. Armah, G. E. et al. The Global spread of rotavirus g10 strains: Detection in Ghanaian children hospitalized with diarrhea. *Journal of Infectious Diseases* 202, S231-S238 (2010).
49. Armah, G. E. et al. Prevalence of unusual human rotavirus strains in Ghanaian children. *Journal of Medical Virology* 63, 67-71 (2001).
50. Navrongo Health Research Centre. Incidence and risk factors of paediatric rotavirus diarrhoea in northern Ghana. *Tropical Medicine and International Health* 8, 840-846 (2003).
51. Armah, G. E. et al. Changing patterns of rotavirus genotypes in Ghana: Emergence of human rotavirus G9 as a major cause of diarrhea in children. *Journal of Clinical Microbiology* 41, 2317-2322 (2003).
52. Esona, M. D. et al. Genomic characterization of human rotavirus G10 strains from the African Rotavirus Network: Relationship to animal rotaviruses. *Infection, Genetics and Evolution* 11, 237-241 (2011).
53. Silva, P. A. et al. Molecular characterization of enteric viral agents from children in Northern Region of Ghana. *Journal of Medical Virology* 80, 1790-1798 (2008).
54. Armah, G. E. et al. Diversity of rotavirus strains circulating in West Africa from 1996 to 2000. *Journal of Infectious Diseases* 202, S64-S71 (2010).
55. Griffiths, P. D. A perspective on antiviral resistance. *Journal of Clinical Virology* 46, 3-8 (2009).

# Funding the future of global health: A medical student perspective

Sara Roberts, Sarah Smith, Juliette Mandel, Andy Hoover, Alex Falvo, Kim Faldetta, Kyle Lewis, Ki Chang, Derek McCleaf, Daniel R. George, Ph.D, M.Sc., N. Benjamin Fredrick, M.D.  
Penn State University College of Medicine, Hershey, PA, USA

As students from the Penn State College of Medicine (PSCOM) who are engaged in medical research projects in Ecuador, Kenya, Ethiopia and Peru, we recognize we are at a defining crossroad in global health; yet, our voices are seldom invited into public debate. For decades, global health has been synonymous with prevention and treatment of infectious diseases such as malaria and tuberculosis; today, however, the disease burden is shifting toward non-communicable diseases (NCDs) and future physicians will face the likelihood of having to make difficult decisions about the distribution of the scarce resources devoted to health care.<sup>1</sup> The 2011 United Nations General Assembly Summit on Non-Communicable Diseases sparked a debate when members proposed increased funding for NCDs without acknowledging the negative impact such allocations would have on funding for preventing and treating infectious diseases.<sup>1</sup> With our future careers and past experiences in mind, students from PSCOM have explored this conflict in depth and concluded that it is critical that we fight for continued funding of neglected tropical diseases (NTDs).

### Argument for increasing funding for NCDs

Non-communicable diseases, which include cardiac disease, cancers, chronic respiratory diseases and diabetes, are rapidly consuming health care dollars worldwide.<sup>2</sup> Although NCDs are classically considered “diseases of the developed world,” because they often result from unhealthy food choices and sedentary lifestyles, they have quietly become ubiquitous in developing nations as well.<sup>3</sup> Chronic diseases currently account for 60% of all deaths globally. Perhaps surprisingly, 80% of these deaths occur in low- or middle-income countries.<sup>4,5</sup> The reasons for this high death toll are numerous: globalization has made alcohol, tobacco and unhealthful processed foods available worldwide, and unplanned urbanization rapidly exposes populations to these risk factors.<sup>1</sup>

Despite the fact that NCDs represent a large global burden of disease, a mere 2% of international global health funding is allocated to these diseases.<sup>6</sup> A 2011 cost-benefit analysis shows that this lack of funding could lead to major repercussions in the future, estimating the cost of inaction on NCDs as \$4,000 per individual, while the cost of prevention is estimated to be only \$2 per individual.<sup>7</sup> Margaret Cho, Director-General of the World Health Organization (WHO), referred to the growing threat of NCDs as “a slow-motion disaster,” emphasizing the need to confront the spread of diseases which are projected to cause five times the deaths worldwide by 2030.<sup>1</sup>

The 2011 United Nations General Assembly Summit on Non-Communicable Diseases sounded the alarm on the growth of NCDs, detailed specific trends, and also offered recommendations for a number of public health “best buy” interventions.<sup>1</sup> Several large-scale preventative measures—including warnings about tobacco and bans on its advertising, raising taxes on harmful substances, using mass media to promote physical activity or restricting marketing of unhealthy foods/beverages to children—have proven successful in reducing diseases such as cancers and respiratory diseases in developed nations. Evidence demonstrates that preventative measures can also be highly cost-effective (costing less than 50 cents a person) in ameliorating chronic diseases in developing nations.<sup>7</sup>

These small per capital numbers can be misleading, however, as the summit recommended such interventions on a grand scale, stating that “the greatest reductions in non-communicable diseases will come

from a complete Government approach to adopting population-wide interventions that address risk factors.”<sup>1</sup> From the perspective of medical students and future clinicians who are trained to think of the patient as an individual or part of a small panel, a grand scale advertisement campaign is much more difficult to incorporate into our own future practice. While risk-reduction strategies (tobacco and healthy lifestyle counseling, for example) could certainly be mimicked in our smaller scale global health ventures, it would not be done with confidence that such activities are efficacious or valuable uses of time and resources. Certainly some smaller scale risk factor reduction efforts are being made in the developing world—for example, the “Know Your Numbers” campaign to reduce hypertension run by doctors based in Guayaquil, Ecuador—but the data suggests that efforts on a larger scale are more effective.<sup>8</sup> Perhaps in the future, a strongly evidenced model of smaller scale interventions will be established. We understand that devoting funds to NCDs today could help mitigate the impending chronic disease burden that is expected to otherwise consume an even greater share of future resources. However, we are convinced that, considering the limited funds for global health outreach, efforts to ameliorate the chronic disease burden will direct money and attention away from more productive international medical efforts.

### Argument for funding neglected tropical areas

Although it is important to increase funding for NCDs, there may be negative implications for other global health ventures. A significant shift of funding toward NCDs—and recall that the UN spoke of interventions on a Government scale—will siphon money and interest from low-cost, life-saving interventions for preventable infectious diseases that have long been the sine qua non of global health. A group of infectious diseases known as the neglected tropical diseases (NTDs) disproportionately afflict more than a billion of the world’s poorest people, half whom are children.<sup>9</sup> This diverse group of infections tends to cause disabling diseases, resulting in blindness, limb deformities and/or brain and other organ damage. Consequently, afflicted individuals often miss out on school and work opportunities and face social isolation. For example, in Ecuador, a group of Penn State students met with patients stricken with leprosy, many of them blind, scarred and with amputated limbs. In essence, the disease had left these people unemployable and requiring nursing home care. More appallingly, our students who worked in Ethiopia saw disfigured sufferers of polio paraded around the streets for money. From an economic perspective, NTDs are among the most cost-efficient diseases to prevent and cure, costing 50 cents per person treated per year to eliminate these infections with currently available vaccines and/or antibiotics.<sup>9</sup> While some efforts aimed at NCD prevention have been successful, the interventions are behavioral and based on large-scale campaigns, and thus far more complex and difficult to implement, particularly from the viewpoint of a physician or medical student attempting a medical intervention abroad.

The difference in ease of intervention for representative infectious and non-communicable diseases was illustrated to our student group in Ecuador. In a small fishing village with dirt roads and dirt floors, we screened patients for the intestinal parasite *Giardia lamblia*, found a 20% carriage rate and sent patients to the pharmacy for the single dose of metronidazole needed to clear up the infection. We also screened patients for hypertension. We found a similarly high rate of positive re-

sults, and knew that unless the patients decided to purchase lifelong antihypertensive medication or understood and planned to implement diet changes, they were destined to live with hypertension and its long-term ill effects. Though we were aware of the asserted cost-effectiveness of behavioral interventions, from our vantage point on the ground, the difference between ease of treating the giardia infection versus hypertension was astronomical. We acknowledge that the types of projects frequently undertaken by the medical community are often short term visits intended to diagnose and treat acute illnesses, and are not suited to address the growing burden of chronic diseases. These sorts of zeitgeist interventions are generally more effective in treating infectious processes.

We are concerned that shifting funding from NTDs towards NCDs may widen the wealth gap and increase the inequity in distribution of healthcare. Eradicating NTDs has an economic benefit. Experts estimate that hundreds of millions of children would be afforded the opportunity to live longer and healthfully enough to contribute to their country's workforce, thereby stimulating economic and social development if not stricken with NTDs. For instance, the WHO reports that, in Kenya, deworming could potentially increase per-capita earning by 45%.<sup>10</sup> In addition, a 1950s Japanese de-worming campaign was credited as being partly responsible for the nation's economic surge.<sup>11</sup> The impoverished and unhealthy state of the world's poorest billion would only worsen if the global health community averts its eyes

to their plight in favor of the ever-expanding public health problem of NCDs.

### Conclusion

With internationally prevalent NCDs emerging as a big contender for global health funding, this is truly a pivotal time to be a medical student with aspirations to work abroad. The UN's plea for re-allotment of funding inspired us to reconsider what global health really means and how best to support global health ventures in a changing world. Against the new back-drop of global NCDs now clamoring for funding of their own, we challenge our fellow health workers to educate themselves and advocate for causes they believe in by presenting at conferences, raising the issue in classrooms and discussing with peers across disciplines. As future doctors poised to take on a share of responsibility for the health of the world, we have explored this topic at length through the literature, but we have also seen in our own experiences abroad how NTDs disproportionately affect the world's poorest, and how easily and cost-effectively infectious diseases can be treated by smaller scale ventures—the modality most frequently employed by groups of US medical teams such as ours. Fully acknowledging how important the issue of NCDs has already become, we implore that pure prevalence of these diseases not overshadow the low-hanging fruit to be had in both prevention and treatment of NTDs.

### References

1. "Prevention and control of non-communicable diseases: Report of the Secretary-General" May 2011. [http://www.un.org/ga/search/view\\_doc.asp?symbol=A/66/83&Lang=E](http://www.un.org/ga/search/view_doc.asp?symbol=A/66/83&Lang=E)
2. WHO Fact sheet. Media center. Sept 2011. <http://www.who.int/mediacentre/factsheets/fs355/en/index.html>
3. Anderson, G. "Chronic conditions: making the case for ongoing care." Baltimore, MD: John Hopkins University; 2004. [http://www.fightchronicdisease.org/sites/fightchronicdisease.org/files/docs/ChronicCareChartbook\\_FINAL\\_0.pdf](http://www.fightchronicdisease.org/sites/fightchronicdisease.org/files/docs/ChronicCareChartbook_FINAL_0.pdf)
4. Daar AS, Singer PA, Persad DL, et al. "Grand challenges in chronic non-communicable diseases." *Nature* 2007;450:494-496.
5. Yach D, Hawkes C, Gould CL, Hofman KJ. "The global burden of chronic diseases: overcoming impediments to prevention and control." *JAMA* 2004;291:2616-2622
6. World Health Organization [WHO] : Preventing chronic diseases: a vital investment. World Health Organization. 2005.
7. Harvard School of Public Health: "The Global Economic Burden of Non-Communicable Disease." 2011. [http://www3.weforum.org/docs/WEF\\_Harvard\\_HE\\_GlobalEconomicBurdenNonCommunicableDiseases\\_2011.pdf](http://www3.weforum.org/docs/WEF_Harvard_HE_GlobalEconomicBurdenNonCommunicableDiseases_2011.pdf)
8. Del Brutto OH, Montalvan M, et al. "The et al. al. t al. WEF\_Harvard\_HE—A pilot study aimed to reduce cardiovascular diseases and stroke burden in rural communities of developing countries." *International Journal of Cardiology*. 2013.
9. O'Brien, S. "The Neglected Tropical Diseases: A challenge we could rise to — will we?" Report for the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases 2008-2009. [http://www.who.int/neglected\\_diseases/diseases/NTD\\_Report\\_APPMG.pdf](http://www.who.int/neglected_diseases/diseases/NTD_Report_APPMG.pdf)
10. "The evidence is in: Deworming Helps Meet the Millennium Development Goals." World Health Organization. 2005. [http://whqlibdoc.who.int/hq/2005/WHO\\_CDS\\_CPE\\_PVC\\_2005.12.pdf](http://whqlibdoc.who.int/hq/2005/WHO_CDS_CPE_PVC_2005.12.pdf)
11. "Priority Communicable Diseases." Chapter in *Health in Asia and the Pacific*. World Health Organization. 2008. [http://www.wpro.who.int/health\\_research/documents/dhs\\_hr\\_health\\_in\\_asia\\_and\\_the\\_pacific\\_12\\_chapter\\_7\\_priority\\_communicable\\_diseases.pdf](http://www.wpro.who.int/health_research/documents/dhs_hr_health_in_asia_and_the_pacific_12_chapter_7_priority_communicable_diseases.pdf)

## Field Notes

AN INTERDISCIPLINARY MALARIA EDUCATION PROGRAM | 28

MEDICAL NEUTRALITY AND SOLIDARITY IN THE SYRIAN ARMED CONFLICT | 33

TUBERCULOSIS IN ZULU POPULATIONS | 37

# “Anansi tricks Mrs. Mosquito”

An interdisciplinary malaria education program for school aged children in Kwahu-East District, Ghana

Deborah Lardner, DO, DTM&H, Michael Passafaro, DO, DTM&H,  
Jonathan Giordano, MS IV, Jasmine Beria MPH, MS IV

New York Institute of Technology (NYIT), Center for Global Health, New York, NY, USA

### Abstract

Malaria, although a preventable infectious disease, still has negative long-term economic and social consequences on the lives of children in developing nations. This project describes the creation of an educational intervention based on West African folktales designed to increase awareness regarding the vector, the signs and symptoms and the prevention of malaria in the Kwahu-East district, Ghana. An interdisciplinary approach was instrumental for the creation of the play “Anansi tricks Mrs. Mosquito.” Using Anansi the spider, an established folk character, as the protagonist, the interactive play was performed at local schools and community health clinics during June, 2012. The educational content was reinforced by a question and answer session and the distribution of an illustrated book at the end of the performance. Field reports indicated that the children were consistently engaged and able to recognize and identify with the characters. After the performance, they had immediate recall of the signs and symptoms of malaria, the disease vector and prevention by the use of bed nets. The books were also used as teaching tools in some classrooms. This deceptively simple twenty-minute performance was created over a period of several months in order to be implemented in the field. By combining local talents from a number of specialties—education, medicine and visual arts—the authors were able to create a culturally appropriate model for the creation of this malaria prevention tool that could be expanded to address a number of diverse backgrounds and disease burdens.

### Introduction

Since the discovery of malaria transmission by Sir Ronald Ross in 1897, extensive research has been conducted about the Plasmodium parasite, the vector as the Anopheles mosquito, its life cycle and the transmission process of the disease.<sup>1</sup> However, there is still a need for ongoing malaria education and prevention in endemic areas such as Africa. Globally, malaria still causes approximately 655,000 deaths per year. In 2010 alone, an estimated 216 million new cases arose.<sup>2</sup> Malaria remains one of the top three killers of preventable infectious diseases.<sup>3,4</sup> This paper describes our experience in malaria education in West Africa, and proposes a low cost, low technology model that could be expanded into other countries.

Malaria continues to be a leading cause of mortality, particularly in the rural regions of Africa where medical resources are scarce,<sup>2</sup> and the symptoms of the disease significantly interfere with daily living activities. It contributes to the vicious cycle of missed educational opportunities through poor school attendance,

leading to increased poverty, shortened life expectancy and disability. These economic consequences of living in endemic areas have been measured in Disability Adjusted Life Years (DALYs), where in 2002, the total global burden of disease from malaria was estimated by World Health Organization (WHO) to be over 46 million DALYs lost,<sup>5</sup> and in Africa 15% of all DALYs.<sup>6</sup> This makes it the fourth most costly disease burden in Africa.<sup>7</sup>

In his review of economic and social burden of malaria, Jeffrey Sachs, economist and renowned scholar on sustainable development, notes, “where malaria prospers most, human societies have prospered least.”<sup>4</sup> The unequal distribution of malaria means the world's most impoverished populations are twice hindered by disease burden and economic disadvantage, both impeding development. The Center for Disease Control (CDC) estimated the direct costs of treating the disease to be over ten billion dollars per year,<sup>8</sup> with indirect costs to governments, including maintenance and stocking of health facilities, public health education, insecticide spraying and distribution of insecticide-

**mill**

The Mill Korean Restaurant

**Address:**  
2895 Broadway  
(between 111th St & 112th St)  
New York, NY 10025

**Hours:**  
Monday - Friday: 11:00 am - 10:00 pm

**Phone:**  
(212) 666-7653

**www.millkorean.com**





Courtesy of the Author

treated bed nets (ITN) equally significant. Even more striking are the long term consequences, which have been demonstrated to decrease economic growth of a country's Gross Domestic Product (GDP) in highly endemic countries,<sup>9,10</sup> and works against poverty eradication efforts.<sup>11</sup>

The United Nations Millennium Development Goal, Target 6.C was created to reverse the incidence of malaria and other major diseases by 2015.<sup>12</sup> This global commitment has resulted in an estimated decrease of the incidence of malaria by 17%, and a 26% decrease in mortality rate from 2000 to 2010.<sup>2</sup> The success was due in part to an aggressive prevention program sponsored by the World Bank and Roll Back Malaria Partners in which nearly 100 million ITN were distributed in African countries from 2006 to 2012.<sup>13</sup> Experts consider this intervention to be the simplest and most cost effective prevention strategy in developing countries, as it requires no significant upkeep or interventions other than behavioral changes. Nonetheless, many bed net control policies have mistakenly overlooked community perceptions and attitudes that can have a substantial role in behaviors affecting malaria transmission, recognition and treatment.<sup>14</sup>

Our project was conducted in Ghana, where malaria accounts for 9% of overall country mortality and 40% of all malaria deaths occur in children under the age of five.<sup>15</sup> Although many Ghanaians are well informed about the classical symptoms of malaria, the understanding of malarial transmission in rural communities may be clouded. These community misconceptions can result in behaviors that contribute to increased vector exposure. For example, several articles describe community beliefs that heat from the sun was a cause of malaria. Other misconceptions were that overworking during the day or stagnant water itself could cause malaria.<sup>14,15,16</sup> The use of bed nets was therefore inconsequential. Adongo et al. investigated community knowledge about malaria and ITN use in Ghana and concluded that interventions require more social and behavioral research in order to explain the

influence of local beliefs. More specifically, bed nets were perceived as mere "nuisance reducers"<sup>17</sup> rather than a preventive measure. This resulted in bed net use by adults rather than children, since adults required a superior sleeping environment to function better during the following workday.

### Background

The Center for Global Health at The New York Institute of Technology (NYIT) headed this interdisciplinary educational intervention. The Center, established in 2007, is a collaborative effort between a variety of schools and colleges within the University system. Each specialty is invited to contribute to the sustainable improvement of healthcare in host countries. Part of the Center's mission statement includes collaborative international teaching, research and service. Partnering with a non-governmental organization (NGO), The Jesse Rohde Foundation, in a small community of Oworobong, Ghana, we conducted a background research project entitled "School Age Children's Attitudes and Perceptions

of Hygiene and Transmission of Infectious Disease in Rural Ghana." With permission from our Institutional Review Board (IRB), a consultant from the Noguchi Memorial Institute for medical research at the University of Accra and the local Ministry of Health official, a preliminary medical record review at the Oworobong Health clinic for the period from January 2011 to July 2011 was conducted. A total of 1027 medical records were reviewed. Of the 453 cases of malaria diagnosed, 64.2% (n=291) were children 18 years of age or younger. Although a small community health clinic serves the area, its remoteness complicated immediate follow-up for severe malaria cases including cerebral malaria, severe anemia, acute renal failure or respiratory distress syndrome.

### Project Description

Our goal was to develop a simple, concise message that would increase the use of bed nets by adults and children, thereby decreasing vector contact. The community health clinic on Oworobong also serviced a number of surrounding agrarian villages (Awesasu, Ohema, Miasu and Ofamase); therefore our intervention needed to be general enough that it could apply to a number of localities.

Since the target community is isolated with limited resources including a lack of electricity and reliable phone service, the proposed program design would have to be self-contained and adaptive. It could not rely on technical or electronic equipment that might not function in environmental conditions of extreme heat or high humidity. Furthermore, it would need to be culturally appropriate, use recognized characteristics of the community and trigger discussion among different age groups. There is a high level of both adult and youth illiteracy in several of these communities; therefore our method could not require extensive amounts of reading to convey the message. Based on the above community requirements and resources, the most effective intervention was in the form of "edutainment,"<sup>18</sup> that could be offered through the health clinic. It was decided that an animated story or

"play" that encouraged the use of bed nets as malaria prevention would reach the largest number of community members. Specifically, we targeted school aged children and their parents regarding malaria recognition, transmission and prevention.

### Background research

A multidisciplinary team approach was taken to develop this educational programming between the NYIT faculty from the College of Medicine, the Center for Global Health, School of Education, the university librarians, the partnering NGO and a local New York artist. Multiple brainstorming meetings were conducted over a period of months. Since there often existed a language barrier with the target audience on the ground, it was decided that a single narrator with the assistance of a translator would be the most effective tool. It was then agreed that lightweight puppets would be the most effective means of animating the story, since they could be carried across difficult terrain in order to reach more remote sites and could be used either day or night depending on how they were illuminated.

### Artistic design and cost

With the help of the artist, materials were chosen that were durable, lightweight and portable. Supplies were purchased from local art supply stores or larger home improvement stores where materials could be repurposed for the project. The vibrant African-design based puppets served as the characters on a mobile backdrop—a painted fabric set that could be easily displayed and transported. The artist also created foam shadow puppets that could be illuminated from behind at night with flashlights as well as brightly painted thin flat wooden puppets that would be better seen during the day.

To further reinforce the educational objectives, an illustrated book, "Anansi Tricks Mrs. Mosquito" published by the NYIT Publications and Advertising Office, was distributed to the children at the end of the performance to emphasize the learning objectives. Although English is the official language of education in Ghana, it is not always used in rural communities. Accordingly, the books were printed in English but targeted to early readers. Another artist completed the book illustrations based on the puppets and photographs of the target area.

The authors believe this project is unique because of the low cost in conveying our educational objectives thereby increasing the potential for wider distribution. The cost of supplies for the educational component of this pilot project was minimal (less than \$500 USD). Costs included artistic supplies, paints, backdrop, etc. The cost of the illustrated paperback book production was covered by the university Publication and Advertising Office (approximately \$1500 USD). Professional services by the artists for this project were given gratis. If similar projects were to be repeated, these professional artistic services would need to be appropriately compensated, as the design requirements for the field conditions were important.

### Character selection and story creation

Research conducted by the university librarians and School of Education team resulted in the choice of Anansi, a recognizable character in the region of West Africa, as the protagonist. Anansi tales are some of the best-known in West Africa specifically among the Ashanti culture, where they were carried down through the generations by storytelling.<sup>19</sup> In these folktales, also known as Anansesem or "spider tales" in the Ashanti language, Anansi is usually portrayed as a trickster who often gets into and subsequently out of trouble.

Based on physician input of the malaria-causing plasmodium life cycle, a storyline and later script was created that emphasized means of transmission, signs and symptoms and prevention of malaria by the correct use of bed nets. Project members who had firsthand knowledge of the target communities contributed culturally appropriate details for the play, including names and everyday events in the play, such as market days and the name of the local clinic. Even the name of the mosquito, locally known as a tumtum, was considered. The language in the book is simplistic and

formal in order to encourage adults with poor reading skills to practice with their children thereby reinforcing the learning objectives.

### Excerpts from the story

The antagonist, Tammy Tum Tum, the mosquito, enters the village and bites the children who then get ill. The local nurse emphasizes the signs and symptoms of malaria to the mother before the children become ill by visiting the home.

"Welcome, Akwaba!" Anna calls out.

"Hello, I am going from home to home today to let mothers know that we have had several malaria cases in the area. I wanted to make sure that you were aware of all of the signs and symptoms."

"Well," Anna says, "I know that the main symptom is when you get very hot, your bones hurt."

"Right," Nurse Mary says, "it is caused by being bitten by a mosquito. Many pesky bugs fly around, but the mosquitoes that come out at dusk and when we are sleeping are most worrisome. It is very important that you come to the clinic as soon as anyone in your family is feeling sick. The malaria in this region of Ghana is very dangerous."

"Thank you for stopping by," Anna says, "I will remember. Good-bye."

To target younger children, the plot uses traditional elements of folk tales that include fantasy in the form of talking animal characters. A classical epic battle between the protagonist and antagonist where Anansi is victorious occurs and often engages slightly older children.

Later that night, the whole family gets ready for bed and goes to sleep. Anansi spins a web, climbs to the center of it, and falls asleep. In the other corner of the room, Tammy Tum Tum buzzes in.

Anansi startled, awakens from the noise. He sees Tammy hovering over Sarah, and Anansi reacts, quickly spinning a web over Sarah to protect her. Tammy Tum Tum sees Anansi's protective web over Sarah, rapidly changes directions, and heads for Ralph. Anansi reacts swiftly, jumps over to where Ralph is sleeping, and spins a web as fast as he can. Just then, Tammy Tum Tum gets to Ralph, sees the web and backs away!.....

"Tammy, you hurt too many people!" Anansi explains. "You need to get out of here! Get out of this village, or I will have all the children hit you when they see you!"

Tammy furiously flies toward Anansi, who weaves another web, and Tammy gets caught in it. Anansi jumps to get Tammy, who struggles successfully frees herself, and flies away, far away from the village!

The end of the story uses nature and the metaphor of the spider's web to remind people of the importance of bed nets.

"The next night, the family is at dinner. Just then, father comes over and points toward the corner of the wall. He asks, "Mother do you SEE THAT?"

The whole family stares in the corner and sees a spider's web.

"There is a hidden message written out in the spider's web," says father Benjamin. "It reminds us that we must protect ourselves from the mosquitoes. So every time we see a web, remember what Anansi did for us, and how we must continue to fight off Tammy Tum Tum, by using our mosquito nets every night."

"Anansi made these web nets to protect all of us! We will use them every day to prevent our family from getting malaria!" Mother Anna exclaims.

### Field implementation

The interactive play was performed in five villages with approximately 150 children in attendance at each performance. Students and faculty from the Center performed the play in English, Twi and other local dialects with the assistance of trained translators. The play was performed by medical students as part of a field research curriculum, but could easily be taught to community members, as the performers required little more than a backdrop, puppets and a single narrator/translator. Daytime performances were usually conducted in the schools of the surrounding villages and evening performances were conducted at the health clinic.

Following each performance, a question and answer session was conducted when the children were asked to recall the above stated objectives. As the parents were also in the audience, the dis-

Community misconceptions can result in behaviors that contribute to increased vector exposure.



Courtesy of the Author

discussion often included questions about medical treatment and bed net availability. The project team felt it was important to provide the means as well as the knowledge for malaria prevention. To that end, we were able to procure a donation from an international bed net company who generously provided ITN for the community. The nets were distributed to a number of schools at the conclusion of the performance. Since data has indicated a significant drop (up to 75%) in bed net ownership when even minimal payment or cost sharing of ITN was required when compared to free distribution,<sup>20</sup> the nets were provided free of charge to those in the community who did not have one. Community leaders and teachers were responsible for distributing bed nets, as they were most aware of the individual situation.

## Discussion

It has been demonstrated that early intervention for health and hygiene can make a significant difference in disease transmission.<sup>21</sup> The reinforcement of healthy habits in childhood can result in permanent changes as children age. Examples of this can be found in the literature related to hand washing<sup>22,23,24</sup> It has also been repeatedly demonstrated that children, once educated about the issue, will go on to educate other members of the family and community.<sup>25,26,27,28</sup> Using this model, our goal was to create a malaria health intervention that targeted children so they could grasp the learning objectives, and emphasize healthy behaviors that could be used in the home.

The children were consistently engaged in the play and were able to recognize and relate to the characters. A local teacher who was interviewed on camera after witnessing the performance said, "I liked the analogy between the spider webs and the nets. One thing that really helped is that the children are familiar with the spider webs so it helped them to get the understanding very quickly. The interpretation was done very well and they were able to get all the necessary information from the play. Overall it was very impressive." Children demonstrated immediate recall of the signs and symptoms of malaria, the disease vector as the mosquito and the prevention of malaria by the use of a bed net after the presentation, and the

Health providers, educators and community leaders were often present at the play, which served as a catalyst for discussion about malaria prevention at home and in schools.

publications were reported to be teaching tools in some classrooms.

We were able to engage with other community members through this project. Health providers, educators and community leaders were often present at the play, which served as a catalyst for discussion about malaria prevention at home and in schools. Their involvement was critical for the success of the program since most of the research on the misuse of bed nets has been conducted on adults and parents in the home. By having them participate in the program, we believe they will be reminded on the proper use of bed nets that will protect their children and themselves from malaria.

## Future Directions

Ongoing validation of this intervention is focused on two areas: (1) evidence of the effects of the intervention on participants' understanding of the importance of bed nets in preventing malaria, and (2) evidence of the effects of the intervention on the actual use of bed nets. However, both of these areas have experienced several obstacles.

It has been difficult to administer a test that can be completed without well intentioned but intrusive assistance in order to accurately assess students' knowledge. The administration of pre- and

post-tests to children who have limited educational resources and literacy has introduced a Hawthorne Effect bias, where subjects reported an improved aspect of their behavior in response to the fact that they know that they are being studied, or through primary educators or secondary translators who also have a bias of how their country is being portrayed in the medical literature. Although English might be the official language of education in Ghana, it is not always the lingua franca in isolated communities. We are working with colleagues in the School of Education to design an approach

that will assess pre- and post-performance knowledge of malaria prevention with the least distortion of data due to the support needed to implement testing.

In regard to the second area of validation, we are developing a plan to assess actual behavioral changes in children through parental interviews. Determining their actual use involves more than counting the total number of nets available in village



Courtesy of the Author

households. Not every family has the financial means to obtain a net for every child in the house and children often share a sleeping space. We will need to rely on parents' reports of the number and actual use of bed nets by each of their children before and after the experience of seeing the Anansi presentations. An expanded avenue of research might include investigating the prevalence of malaria in the targeted communities, and monitoring changes in these health measures. At this point, the required laboratory testing would be cost prohibitive. In addition, other confounding factors, such as the distribution of free nets from government health ministries or international organizations, also interfere with these validations as it changes the number of safe sleeping spaces, but supersedes experimental methods since it is vital to child welfare.

Although repetition of the play might increase bed net use temporarily, as with most interventions, diminishing returns can be expected. The effect of the message may stagnate and decrease over time. There is a probable finite number of times we can successfully convey the message of our play before it loses its effectiveness, but we rejected the idea of increasing the visual effect of the presentations by implementing more intense music, lighting or complicated sets. This would decrease the simplicity of the production, add to cost and logistically limit our ability to bring the play to the most isolated at-risk areas.

Since the project was a pilot and most of the professional services, bed nets, time and on-the-ground cost were donated, a question remains of the actual cost for up-scaling. The implementation in the field for a performance team could be decreased significantly by the incorporation of local public health advocates. The cultural expertise of local healthcare professionals and educators would be dynamic additions to this project. In-country production cost would be significantly less, and they could create a sustainable method for malaria prevention.

The authors believe that the Anansi program and other models of "edutainment" can be effective in conveying health objectives and, furthermore, that they are transferable from child to child. Although this project is specific to malaria prevention in West Africa, the concept of implementing culturally identifiable folktales, disease burdens, and a form of edutainment can be tools to design programs that encourage healthy behavior in children, and that these behaviors are transferable.

## Conclusions

Using the ancient art of storytelling, the authors repurposed folktales into modern disease control programs for children by simplifying public health issues to an elementary level. Stories regarding Anansi and other folk characters are used as part of the current Ghanaian curriculum in some schools. Stories like "Anansi

Tricks Mrs. Mosquito" could be incorporated into classrooms to convey a simple, but vital health message. Expanding this model into other countries is also possible. The number of folktales with potential protagonists available in different cultures is the only limit, and each country might have a different health objective to be achieved. For example, the Center for Global Health is investigating opportunities to use this model in other international communities including El Salvador (Chagas' disease or American trypanosomiasis prevention) and Haiti (where there is a widespread water sanitation concern). But other public health objectives, like vaccination campaigns, nutrition or dental hygiene could also be considered. The authors suggest that the use of the model described in this paper might be a practical method for reaching populations most vulnerable to specific disease burdens.

The Center's stated mission to enhance communication across different specialties and academic communities by creating innovative partnerships to improve overall health of communities has been achieved. By using an interdisciplinary approach incorporating education, medicine and visual arts, we each addressed our specific areas of expertise, thereby enhancing the overall project. We were also able to educate and inspire students with a special interest in global health by providing exposure to and immersion in international experiences through the lens of public outreach and disease prevention. The future of global health requires creative cooperative partnerships in order to be successful. When follow-up evaluations on the Anansi program are completed, we believe the study will provide important information on the efficacy of using culturally appropriate tools as a low cost, low technology method to influence community health behavior in remote areas of the world.

## Acknowledgements

Thank you to Dr. Edward Gotfried, Dr. Jesse Rohde, Dr. Zehra Ahmed, Charles Asiedu Bofo, Benjamin Dei Boadu, Jennifer LaCava, Karen Chandler, Shanacy Marler, Kenneth Ditley, Dr. Michael Uttendorfer, Dr. Janice Sawyer, Dr. John Kappenberg, Susan Gude, Michelle LaCour, Gail Sachs, Joan Baron Drury, and Doreen Weatherby (Bestnets). A special thanks to the students and residents involved in the performance of the play, without whom this project would not have been possible.

References available at  
JGH Online,  
[www.ghjournal.org](http://www.ghjournal.org)



# Medical neutrality and solidarity in the Syrian armed conflict

Ravi S. Katari

Wake Forest School of Medicine, Winston-Salem, NC, USA

## Abstract

Noninterference with health workers treating the sick and wounded during civil unrest and armed conflict is an ethical principle that has been legally recognized across the globe for 150 years, under the term “medical neutrality.” However, in the Syrian conflict, now in its third year, the deliberate targeting of health workers, including students, and hospitals as a warfare tactic has become widespread. Consequently, work performed under dangerous circumstances by the international medical community’s peers and colleagues deserves recognition, through declarations and demonstrations of international solidarity, in order to bolster the legitimacy of medical neutrality in diplomatic affairs. This article discusses the issue of medical neutrality as applied to the Syrian conflict and, furthermore, underscores the relevance of condemnation as a tactic for influencing policy.

## Introduction

Syria’s ongoing armed conflict has claimed over 115,000 lives (including over 41,000 civilians) and has left more than 6 million displaced, according to the latest figures. However, its war-torn medical infrastructure, characterized by a shortage of hospitals, physicians and medicines, threatens to claim even more lives than the violence.<sup>1</sup> Zaher Sahloul, president of the Syrian American Medical Society (SAMS), estimated that because of the lack of access to drugs and treatment, as many as 200,000 Syrians have succumbed to chronic conditions such as diabetes, hypertension and cancer.<sup>2</sup> The situation was poignantly described in a Lancet editorial published in 2012.<sup>3</sup> It was one of the earliest articles to highlight the targeted destruction of the health infrastructure in Syria and underscore the implications of such circumstances for the international medical community. The authors noted that modern conflicts are disturbingly characterized by “flagrant disregard for the Geneva Conventions, including targeting of civilians, persecution of health workers and attacks on hospitals, alongside the failure of the UN system to prevent these violations.” The situations necessitating this assessment of the loss of the principle of “medical neutrality” in contemporary affairs remains an abundant reality to this day, particularly in Syria.

These violations are, indeed, quite significant, as they threaten the very foundations of international standards of war. The Geneva Conventions refer to a body of treaties and amendments which form the foundation of modern international humanitarian law regarding the protection of victims in armed conflicts. In addition to their critical role in jurisprudential scholarship and world order, they solidified the notion of respect for the life and dignity of the individual into global consciousness. The earliest implementation, at the 1864 Geneva Convention, outlined provisions for wounded or sick soldiers and civilians and officially recognized the International Red Cross’ activities in war zones (making protection of health workers standard). These provisions were majorly updated in 1949 in response to the atrocities of the Second World War that had come to light during the Nuremberg Tribunals. Since then, the conventions are currently recognized by virtually the entire world, including Syria, and enforced by the United Nations (UN) Security Council.

Though the deliberate targeting of the sick and wounded and of health practitioners is specifically prohibited by international law, as codified in the Geneva Conventions, such targeting has become increasingly commonplace in the Syrian conflict.<sup>4</sup> The

Independent International Commission of Inquiry on the Syrian Arab Republic, established through the UN Human Rights Council (UNHCR), has confirmed multiple instances of the shelling and bombardment of hospitals, attacking and kidnapping of hospital personnel and refusal of treatment for the sick and wounded.<sup>5</sup> In their report, the investigators listed specific examples including the bombing of state and field hospitals in and around Dara’a, Damascus and Aleppo; the positioning of snipers, tanks and artillery at the Al-Houlah hospital in Homs; and the rendition of Zarzor hospital employees to an Air Force Intelligence base in Aleppo. Other organizations have presented similar findings; SAMS, a humanitarian group of physicians that has been active during the conflict, released a report which stated “All of SAMS’ doctors who attended medical missions and contributed to this report have personally witnessed attacks on hospitals, ambulances, health workers or rescue volunteers.”<sup>6</sup> Additionally, Reuters recently reported that during its two-year occupation by state security forces, Syrian snipers fired on the sick and wounded trying to enter the National Hospital in Dara’a, until the occupation finally ended in March 2013. The same hospital was attacked in May by opposition forces because 50 patients were believed to be linked to the government.<sup>7</sup> These attacks are all explicit violations of international humanitarian law.

On the issue of human rights breaches in Syria, the world’s attention is currently focused on the usage of chemical weapons in the conflict, particularly the sarin gas incident that took place on August 21, 2013 in Ghouta. It is important to recognize that the same body of laws that prohibits the use of chemical weapons in international armed conflicts also prohibits the targeting of the sick and wounded. As is discussed in what follows, violations of medical neutrality have regularly occurred since the beginning of the conflict, yet concern for these crimes has not been nearly as prominent. Syria’s legal obligations in the context of chemical weapons dominated discourse in the elite media and scholarly literature, whereas discussion of the obligation to respect health workers, civilians and the wounded has been relatively sparse. This discrepancy is inappropriate, given that the respective death tolls of the crimes differ vastly: approximately 1400 civilian victims after the Ghouta attack versus the 200,000 estimated to have succumbed to chronic diseases since the beginning of the conflict.<sup>8</sup>

Accordingly, the authors of the Lancet editorial remark that the world’s medical community “may feel hopelessness” while observing helplessly from the periphery of the quagmire.

Nevertheless, the editorial correctly and encouragingly goes on to conclude that “there is much that it [the world’s medical community] can do to monitor, report, and prevent the impact of conflict on the health of populations, as well as condemning attacks on civilians and breaches of medical neutrality.” Indeed, an important lesson learned from the chemical weapons affair is that diplomatic and regulatory pressures from the U.S. and peacekeeping bodies such as the UN can be successful: the Syrian government has been compliant in destroying its chemical weapons stockpile.<sup>9</sup> Another recent example was the Bahraini government’s decision to nullify the severe prison sentences issued to 20 medical workers during the 2011 civilian uprising, in response to international pressure and condemnation. Former secretary general of the United Nations, Ban Ki-moon, and Physicians for Human Rights (PHR), a human rights advocacy group had criticized the government for sentencing doctors and nurses for treating demonstrators wounded by security forces.<sup>10</sup> Thus, international pronouncements of solidarity and support for the principle of medical neutrality can generate the necessary diplomatic momentum to enforce the protection of health workers and patients.

## An escalating health and humanitarian crisis

The frequency with which reports of conflict-related violence in the Middle East reach American and European audiences dulls the sting of such news via attrition. This phenomenon perhaps inspired another comment published in the Lancet by Mohamed Al-Khaled, a Syrian physician-scientist, who counts relatives amongst the list of casualties in Aleppo: “The Syrian people do not understand why the ongoing Syrian humanitarian and medical crises are being ignored by the world and why nothing is being done to protect civilians in Syria.”<sup>11</sup> His declaration underscores the disparities between the moral and humanitarian posturing typical in political discourse and the world’s failure to act decisively to prevent further human suffering in this conflict. Though the dismantling of Syria’s chemical weapons program is counted as a success in a conflict plagued by failure and pessimism, it has done nothing to curtail the soaring mortality statistics that have resulted from continuous violence and a gutted health care system.

Before the crisis, Syria boasted a sturdy health system which provided free health services and subsidized drugs.<sup>12</sup> Inhabitants received constant care for the chronic conditions that now threaten their lives on a daily basis. The country had its own pharmaceutical industry, which provided 90% of its medicines and exported to over 50 countries. Furthermore, Syria’s health indicators, such as life-expectancy, were on par with those of wealthier, developed countries.<sup>2</sup> With the ensuing civil war and chaos, however, local drug production has fallen 90%, medical supplies are low and remaining clinics are drastically understaffed, while patient numbers have escalated dramatically.<sup>1</sup> The decline of vaccination campaigns has led to the reintroduction of polio into a country which had previously been free of the virus since 1999.<sup>13</sup> Heavy contributors to this deterioration are the targeted destruction of medical facilities and the kidnapping and harassment of health workers: 469 workers have been imprisoned and 15,000 doctors forced to flee. Of the 5,000 physicians practicing in Aleppo prior to the conflict, only 36 remain.<sup>14</sup>

This situation is affecting the region’s ability to provide adequate medical education, as well. In an e-mail exchange, Dr. Al-Khaled explained the deteriorating state of medical education: “After the revolution started, the regime bomb[ed] hospitals in the cities where a conflict between rebels and the Assad regime is going on because protesters and rebels received treatment.”<sup>5</sup> He noted that the institutions of health care and related services have more-or-less collapsed in Aleppo, Deir ez-Sor, Homs and Daraa, but there are still doctors working clandestinely out of their homes or hiding places. However, medical students from opposition-controlled cities do not dare go to university for fear of being arrested. According to him, medical students from the University of Damascus were arrested during a lecture in June for holding views that went against the regime (Personal communication, June 30, 2013). Thus, even physicians-in-training are not being spared from the illegal repression that fully fledged clinicians experience during attacks on hospitals.

The involvement of medical students extends beyond detention, however. During a panel discussion on the medical crisis in Syria at

the Center for Strategic and International Studies (CSIS), Dr. Sahloul, a critical care physician, lamented the ruined health infrastructure and relayed observations of first-year medical students performing surgeries in Aleppo due to the mass exodus of physicians fearing persecution.<sup>15</sup> In June of 2012, Amnesty International reported on the murder of three junior medical workers, two of whom were Syrian medical students; the other was an English literature student and first-aid medic.<sup>16</sup> They had been working with a team of doctors and nurses in provisional “field hospitals” set up to treat injured demonstrators.

The absence of polity and economic vitality has also contributed to disastrous consequences for patients. Dr. Tarek Kteleh, vice-president of SAMS, has been involved with the medical relief effort for over two years. He noted that “half of Syria is now liberated to the opposition and there is no government in liberated areas” (Personal communication, June 24, 2013). Furthermore, “the hospitals are not really hospitals because only two of them have labs. You can’t say they are hospitals if they do not have labs.” The services provided by clinical laboratories, such as blood work and infectious disease screening, are critical for basic patient care. Additionally, since the electricity is down most of the time, hospitals require fuel to run ventilators, refrigerators, and other machines. He explained how essential this fuel is: “At one point, one doctor went to a hospital in Aleppo which ran out of fuel and at least 10 patients who were on ventilators died.” However, fuel is very expensive and thus difficult to come by.

## Principles of Medical Neutrality and Solidarity

The danger that health professionals face in Syria is one of the most alarming features of the conflict. The estimates vary given the chaotic conditions in the region, but the New York Times reported that more than 100 physicians have been killed and as many as 600 have been imprisoned.<sup>17</sup> As described in the previous section, it has also become clear that medical students, too, have been affected. Nevertheless, the cause is one that the international community can rally around in an act of solidarity.

Leonard Rubenstein, Senior Scholar at the Center for Public Health and Human Rights at Johns Hopkins Bloomberg School of Public Health and former president of PHR, discussed the significance of health worker solidarity and the principle of medical neutrality in a conversation over the phone. Medical neutrality and upholding it as a global norm have been the focus of his scholarly activities for many years. According to him, it is important for students of medicine and nursing to reaffirm the values and norms of the medical profession internationally by recognizing colleagues doing similar work under very difficult circumstances (Personal communication, July 2, 2013). Furthermore, professional solidarity demands “reinforcing these values by supporting those who are being punished for adhering to those values.” He noted that the value most at risk is impartiality (i.e. taking no sides in a conflict) due to the punishing of those providing care for those who need it most, irrespective of their political division. It is important to note that this definition encompasses those practicing in non-conflict regions, such as the U.S. or Europe. Selecting patients based on creed or race violates the most basic principles of medical ethics, which are commonly taken for granted in the West.

Beyond the situation in Syria, he cited the arrest of doctors treating demonstrators in Turkey and Bahrain to further illustrate the worldwide threat to medical neutrality. Left uninvestigated and without condemnation, such actions have consequences both for the profession and for patients, as they discourage medical practitioners in conflict zones from adhering to ethical duties out of fear of being targets of violence or persecution. The inability of physicians and nurses to perform their function has an amplified effect across sick populations that depend on medical care. Underscoring this point, Rubenstein asked, “How many women die because a hospital is too damaged to provide emergency obstetric services or the staff has fled? How many children succumb to disease because insecurity precluded visits from vaccinators?”<sup>18</sup> Stephen Cornish, executive director of Médecins Sans Frontières Canada, who was also present at the CSIS panel, used the term “silent casualties” to describe these indirect and unregistered casualties of war: “People with treatable diseases such as diabetes or cancer can no longer get the treatment they need... Children, especially babies under two years old, cannot access vaccinations and are particularly vulnerable to disease.”<sup>19</sup> As

It is critical that the rights of both wounded soldiers and civilians be respected in order to duly apply the principle of medical neutrality, with regard to impartiality.

academics and public figures, Rubenstein and Cornish are able to make clear and explicit just how important it is to protect health workers by upholding the principle of medical neutrality. In doing so, they do a service to humanitarian efforts worldwide by staying informed and engaging with the media in expressions of solidarity.

The International Committee of the Red Cross (ICRC) uses the term “the knock-on effect” to describe this phenomenon of downstream sequelae. The Committee notes that “a single violent incident against health-care infrastructure or workers can have immeasurable longer-term repercussions on entire communities with war-related or chronic health-care problems.”<sup>20</sup> With this description, they make clear that the principle of medical neutrality extends beyond just a political concept grounded in ideology: it has tangible social value in terms of health outcomes in communities. For this reason, it is important to de-incentivize the targeting of health facilities and the exploitation of the desire for medical care, though admittedly they have strategic value, as they undermine and demoralize wounded enemies. These cruel tactics inherently disregard the well-being of innocent civilians, particularly in the context of the “knock-on effect”. In Syria’s civil war, the civilians and their communities are simply collateral damage in the pursuit of weakening the enemy: their survival, on the other hand, has no immediate strategic value in the battle for political power.

In the most comprehensive report to date on the assault on medical care in Syria, published in September of 2013, investigators from the UNCHR documented, in detail, discrete occurrences of attacks on hospitals and medical units, the use of hospitals for war purposes, the targeting of medical and humanitarian personnel and transport and ill-treatment of the sick and wounded.<sup>21</sup> The report, presented at the Council’s 24th session in Geneva, further characterizes the phenomenon of “knock-on” casualties: “Violence against healthcare has significant compound effects, causing dramatic increases in mortality among the sick and wounded. The breakdown of medical services in wartime disproportionately affects vulnerable segments of the population, such as children under the age of five, nursing mothers, the disabled and elderly. In Syria, their suffering is exacerbated by the conduct of the parties to the conflict.” Furthermore, in a nod to the Geneva Conventions, the authors note that the “first efforts to humanize warfare focused on the protection of sick and wounded and those providing them with care. The incidents and patterns recorded reveal that the actions of the Syrian government from 2011 to date have been a cynical betrayal of this fundamental principle.”<sup>21</sup>

This investigation and subsequent compilation of crimes by the UNHCR along with their statement is a significant event that extends well beyond the report itself. The investigation symbolizes the official recognition and serious consideration of grassroots-level efforts led by humanitarian groups and scholars such as MSF, SAMS, and Rubenstein. In other words, solidarity and activism can make a difference. Furthermore, these impacts have a snowball effect: the official broadcast institution of the U.S. federal government, Voice of America, very recently published an editorial describing the reaction of Ambassador Samantha Power, U.S. permanent representative to the United Nations, to the UN inquiry into the assault on medical care in Syria.<sup>22</sup> She reiterated the importance of medical neutrality, condemned the destruction of health infrastructure and called for diplomatic pressure to bring about respect for medical neutrality: “This conflict is going to be remembered even 100 years from now for the obliteration of this core principle.”<sup>23</sup>

These pronouncements and reports are recent developments, but, unfortunately, Dr. Al-Khaled’s sentiments in the *Lancet* are still valid. Talking is not what he had in mind when he urged the world to take action. Meaningful engagement, as will be discussed in what follows, will have to occur through the judicial processes of the world’s regulatory organs.

### The Relevance of International Law

Confronted with the problem of incentivizing combatants to respect the health rights of the groups they seek to injure, both Rubenstein and PHR have advocated calling on the UN Security Council (UNSC) to refer these crimes to the International Criminal Court (ICC).<sup>24</sup> At present, it cannot intervene independently, due to Syria having never ratified the Rome Statute, the agreement that would authorize the ICC to involve itself without UNSC consent.<sup>25</sup> Upon referral of the crimes, those found responsible would stand trial for war crimes or crimes against humanity and, if convicted, be punished accordingly.

Many have acknowledged the difficulty of a UNSC referral, given the veto power possessed by Russia and China, which have been the Assad regime’s leading diplomatic supporters throughout the conflict. In response, Aryeh Neier, former director of Human Rights Watch, suggested the formation of a specialized Arab League tribunal to deal specifically with Syrian war crimes in a manner analogous to the ad hoc Balkan court established after the Bosnian war 20 years ago.<sup>26</sup> This strategy would circumvent the vetoes and bureaucratic obstacles within the UNSC. Due to the urgent need to stop the daily atrocities, he notes that the Arab League could stipulate that crimes committed after such an implementation would have prosecutorial priority, incentivizing a stop to the crimes.

Meanwhile, Betsy Jose, international law scholar and assistant professor of political science at the University of Colorado-Denver, advises caution and restraint in pursuing a referral for judicial intervention by the ICC.<sup>27</sup> She uses the UNSC referral for the Libyan conflict in 2011 to illustrate that restrictions imposed on an ICC investigation by veto-carrying members of the Security Council can delegitimize claims to impartiality and equality before the law. In the case of Libya, the court was barred from considering violations committed by non-parties to the ICC, which included some groups participating in the North Atlantic Treaty Organization (NATO) intervention. In other words, the states with the most power, i.e. NATO, immunized themselves from criminal investigation ex post facto. Such actions politicize processes that are supposed to embody neutrality and impartiality. Jose expresses concern that similar restrictions could be imposed by veto-carrying members of the UNSC (i.e. the U.S., the UK, France, China and Russia) which have independent, complex political interests that would conflict with the judicial process. Historical justification for her concern predates the Libyan conflict of 2011 as well as the ICC itself, which was established in 2002. The most prominent example of this situation occurred in 1999, when the (former) Federal Republic of Yugoslavia (FRY) instituted proceedings before the International Court of Justice (ICJ) against the U.S. in *Yugoslavia v. United States of America*.<sup>28</sup> The U.S. was charged with violating the Convention on the Prevention and Punishment of Genocide of 1948 due to its involvement in the NATO bombing of Yugoslav territory. Though the ICJ expressed “profound concern with the use of force in the Yugoslav territories,” it could not rule on the issue due to a reservation made to the genocide convention by the U.S. mandating that “specific consent” is needed from the U.S. before any dispute is submitted to the ICJ. As it turned out, the U.S. only signed the genocide convention after the inclusion of a provision that requires U.S. permission to investigate charges of genocide brought against it.

Another example of politicizing the ICC’s function was Hilary Clinton’s claim that though investigating war crimes might be warranted in Syria, it could “complicate a resolution of a difficult, complex situation because it limits options to persuade leaders perhaps to step down from power.”<sup>29</sup> She was apparently alluding to Yemen, where the U.S. traded the outgoing president immunity from prosecution in exchange for stepping down from power: perhaps a similar tactic could be employed with Syrian president Bashar al-Assad. As Jose points out, however, such use of the ICC as

a “bargaining chip” can, broadly speaking, damage the legitimacy of international law. For global health practitioners, the primary aim is to enforce medical neutrality not only in Syria, but in all other armed conflicts both present and future. Thus, it is with this end in mind that any ICC intervention should be evaluated. If the Syrian regime can be convinced to step down by using immunity as a bargaining chip at the expense of the ICC’s legitimacy, future attempts at enforcing medical neutrality could be impeded. It is important that these concerns also be voiced by students and professionals expressing solidarity for their counterparts in the region.

Indeed, undermining international law can have serious consequences for the civilian protections that medical professionals operating in conflict areas depend on. Instilling respect for international law, and—more importantly—the fear of violating it, is precisely the goal behind the codification of medical neutrality and other wartime protections. Though breaches of medical neutrality are being committed regularly in the Syrian conflict, documenting and verifying them are critical to compiling charges against perpetrators. In other words, the most pressing concern at present is to obtain any evidence that could potentially be brought against war criminals in any future tribunal. Any ICC intervention would be irrelevant without evidence and each day that passes without scrutiny is evidence lost. Subsequent prosecution and punishment for war crimes can serve as a warning and a deterrent to future combatants who have an a priori incentive to attack hospitals and personnel suspected of providing care to the enemy.

The mobilization of public opinion is also important for making moves toward criminal proceedings. Even though sick and wounded soldiers are protected under the Geneva Conventions, the protection of non-combatants, i.e. civilians, is a much more important and tenable issue around which the international medical community can assemble in solidarity. The crime of killing civilians has a stronger grip on public opinion than the crime of killing sick and wounded enemies, which predisposes the latter to exclusion or neglect. Moreover, world public opinion in this area could wield significant influence in diplomatic affairs and, consequently, in the application of procedural justice. Regardless, it is critical that the rights of both wounded soldiers and civilians be respected in order to duly apply the principle of medical neutrality, with regard to impartiality. In the effort to support medical neutrality by calling for the enforcement of international law, the two groups should not be separated. Harm to any individual not taking part in the hostilities of armed conflict should be prosecuted to the full extent of the law.

Revealing breaches of medical neutrality to a global audience is, at present, a top priority, given the numerous occurrences in recent years despite establishments like the Geneva Conventions. A recent report published by the ICRC documented 921 violent acts committed against medical personnel, facilities, and sick and wounded civilians in 22 countries (unnamed due to ICRC’s commitment to impartiality) during the year 2012.<sup>30</sup> Efforts by the UN or national governments to meaningfully address these violations have been absent. Though the Syrian conflict has been heavily covered in print and television media, violations of medical neutrality have similarly passed largely without official or mainstream acknowledgement. Although the above-referenced UNHCR report on the assault on medical care in Syria and statements by Samantha Power are exceptional developments, they are late: hundreds of thousands are dead and the violence has not abated. Furthermore, due to the rarity of these types of reports, such conduct is often not discussed at all. Reversing the “knock-on effect” will require bolstering the importance of medical neutrality in the public sphere. Only with public pressure on government and judicial bodies backing the effort of humanitarian groups will demands for legal accountability in this context carry any weight in the UN and its member states. Though the law is in place, it must be enforced, whether by UNSC-authorized intervention by the ICC, an ad hoc tribunal, or any other legislative concoction that the world community can agree upon. Adherence and compliance may follow accordingly.

### Conclusion

Setting aside jurisdictional obstacles, condemnation and calls for accountability have important symbolic value, by publicly

reaffirming universally accepted mores and by laying the groundwork for organized, meaningful action. For example, the governments of Norway and Switzerland, along with HRW and Physicians for Human Rights (PHR), another humanitarian group, recently sponsored an event in Geneva featuring prominent speakers and medical professionals. They urged the UNCHR to collaborate with other international agencies and develop strategies which facilitate the availability and safety of health personnel in conflict zones.<sup>31</sup> Dr. Vincent Iacopino, senior medical adviser at PHR, stated that “Medical staff and facilities provide crucial services, and should never become targets or battlegrounds. We have to put mechanisms in place to document attacks, and hold those responsible accountable so that courageous doctors, nurses, ambulance drivers, and others are never again attacked for doing their job of caring for vulnerable people.”<sup>31</sup>

Representative Jim McDermott of Washington has twice introduced a bill to elevate the protection of medical professionals abroad in times of war and civil unrest as a policy priority for the U.S. government. McDermott was “concerned that the United States was not doing enough to stop government forces from harming medical workers, who are some of the only unbiased eyewitnesses that we have on the ground.” Unfortunately, the Medical Neutrality Protection Acts of 2011 and 2013 have not made it through the House of Representatives.<sup>32,33</sup> If implemented, the bills would make it a policy of the U.S. government to “use its voice, vote, and influence in international fora to further define and codify the principle of medical neutrality and to establish accountability for violations of the principle of medical neutrality.” His efforts need public awareness and support.

At the CSIS panel, Rubenstein addressed potential objections to the tactic of condemnation from the belief that it has no influence on state conduct: “All that means is that it’s a guarantee that there will be no response. We know that if you say nothing, nobody will respond. If you say something, you don’t know what the outcome will be.”<sup>16</sup> He is giving voice to the elegance of a simple truth: you do not know until you try. For Western students and physicians observing the conflict from the periphery, the risks are negligible, while the stakes are dire.

Furthermore, discourse and condemnation are two of the few channels through which the international medical community can express solidarity and recognition of the work done by colleagues in Syria during the conflict. Dr. Kteleh, in our personal correspondence, agreed that political solutions to bring an end to the violence and displacement of refugees are necessary. When on the ground, however, the most pressing concern in what he refers to as “war medicine” is the availability of tangible supplies: “For now, what is needed is fuel to run the hospitals because electricity is down most of the time, materials used in hospitals on a daily basis such as cotton and gauze, medical devices, machines, and tools needed to diagnose medical conditions” (Personal communication, June 24, 2013). His assessment was strikingly earthly and underscored the reality behind the lofty rhetoric of international law and academic discourse: the volunteer physicians, nurses, and students that are already working courageously and at great personal risk to prevent further silent casualties are too busy to condemn crimes or pressure politicians. These are responsibilities that should continue to be assumed by fellow health workers around the world as a meaningful way to get involved with the humanitarian effort in this global health emergency. With a death toll exceeding 200,000 and a refugee population of over 6 million spilling into the heart of the Middle East, this war, “the worst humanitarian crisis since the end of the Cold War,” has dramatically shifted the trajectory of international affairs and has ripple-effects that will be felt for generations to come.<sup>34</sup> In the world’s frenzied push to restore equilibrium, it is imperative that respect for human dignity, powerfully symbolized by the Geneva Conventions, not be discarded in the process.

References available at  
JGH Online,  
[www.gjournal.org](http://www.gjournal.org)



# A Look into the Realities and Complexities of Tuberculosis as Observed Amongst Zulu Populations of Durban, South Africa

Margaret Variano  
Tulane University, New Orleans, LA, USA

In the global health field we place particular emphasis on infectious diseases, which have challenged the health of societies across the globe for much of history. Infectious diseases—most notably HIV, tuberculosis (TB) and malaria—have reached alarming levels and become a public health priority. While most infectious diseases are fundamentally similar in the fact that they can spread quickly, they affect different populations in a variety of ways. It is a global health necessity to understand both the cultures of the countries in which infectious diseases are common as well as the ways in which these infectious diseases affect the individual cultures in order to address effectively the challenges that people are facing. This paper focuses on TB, specifically drug-resistant tuberculosis (DR-TB). I have used my experiences with TB and Zulu populations in Durban, South Africa, to compile some of the most notable challenges the disease is posing to the population and KwaZulu-Natal health system today.

According to the Center for Disease Control and Prevention, one third of the world's population is infected with TB, and in 2012 alone there were 8.6 million incident cases and 1.3 million deaths due to the disease.<sup>1</sup> Globally, 3.6% of new cases and 20.2% of previously treated cases are multi-drug resistant. Additionally, South Africa is one of six countries detecting nearly 100% of diagnosed TB cases as drug-resistant.<sup>1</sup> Understanding the symptoms of TB is crucial for detection and diagnosis of the disease. Symptoms depend on the location of active TB bacteria in the body, but inactive TB does not produce symptoms.<sup>2</sup> The most common symptoms associated with TB of the lung include a chronic, sputum-producing cough (more than 2 weeks), dull chest pain, night sweats, weight loss and a low-grade fever.<sup>3</sup> A skin test is encouraged if symptoms persist for more than two weeks. After a positive skin test, diagnosis can be completed through chest x-rays or sputum tests.<sup>3</sup> TB can be diagnosed as either sensitive or drug-resistant. Once a patient is diagnosed with TB, the patient is tested for resistance to various TB drugs in order to create an individualized treatment regimen. Patients are usually started on a two-month regimen of a combination oral chemotherapeutic drug called Rifampin, whose components interact to induce and inhibit the metabolic activity of certain enzymes in the body. Those who are resistant to any drug in this combination are considered to have multi-drug resistant (MDR) TB. MDR-TB patients are instead given some combination of aminoglycoside, or antibiotic, treatment. If the patient is also resistant to these drugs, the patient is diagnosed as an extreme-drug resistant (XDR) case.

As early as 460 BCE, there have been accounts of tuberculosis fatally impacting large portions of populations around the world.<sup>3</sup> Prior to European colonization in the mid-17th century, however, TB was not a large problem in South Africa. After colonization, the disease spread rapidly because of drought, war, mining, recession and the use of South Africa as a health resort for Europeans' TB

treatments created ideal conditions for spreading TB and restricted the country's resources to counter it.<sup>3</sup> Despite having dealt with TB for so long, health professionals are still struggling to reduce the burden of this disease both in South Africa and on a global scale. Currently, South Africa has the third highest TB burden behind China and India, countries with much larger populations,<sup>4</sup> and has the fifth highest drug-resistant TB rate globally. To put this in perspective, in KwaZulu-Natal in 2010, there were 2,032 MDR cases and 201 XDR cases.<sup>4</sup>

The burden tuberculosis places on the healthcare system has proven crippling to South Africa. The high number of patients who need treatment and attention is straining the workforce, and the economic burden of paying for treatments is also considerable. Despite DR-TB forming only a small proportion of the total case burden, it consumes a significant and disproportionate amount of the country's annual TB budget.<sup>5</sup> Although DR-TB only accounted for 2.2% of the disease burden, it drained 32% of the approximate US\$218 million budget.<sup>5</sup> A large portion of the budget is spent on XDR-TB cases because each case of XDR-TB costs US\$26,000, compared with less than US\$7,000 per MDR-TB case and less than US\$300 per sensitive TB case.<sup>5</sup> This expenditure can and should be reduced using proper promotion and control methods, such as the creation of a decentralized treatment model in which smaller institutions are responsible for the planning and implementation of DR-TB treatment, and hospitalizations are reduced by providing more TB treatment in local clinics. South Africa has attempted this structure with their referral system, which requires a referral slip from a clinic in order to be treated at a hospital or specialized healthcare center. Despite its efforts to relieve the burden on higher institutions and localize treatment, this method has not shown consistent efficacy. Local clinics, especially in rural areas, do not always have the resources or staffing needed to support their catchment area, leading to long lines, lack of access to medication and overall patient frustration. As a result, patients do not seek treatment until they develop urgent cases and need to be hospitalized, thus undermining the original purpose of the decentralized system.

During the spring of 2013, I completed a medical internship in which I studied the prevention and treatment methods used to address DR-TB in the KwaZulu-Natal province of South Africa. Throughout the internship I learned about the disease burden of TB and the various challenges health professionals are facing while combating the disease within the context of the Zulu population of Durban, South Africa. These experiences and observations amongst Zulu populations of South Africa can be generalized to understand and address the TB burden on other South African populations and even other populations being affected by TB around the world. The facility in which I conducted my internship was Friends of the Sick Association (FOSA) TB Hospital in Newlands West, just

outside the city of Durban, South Africa. FOSA TB Hospital is an MDR and XDR specialized step-down facility, meaning that it lies somewhere between an emergency hospital facility and a normally staffed in-patient facility. Since its establishment, FOSA TB Hospital has worked hard to understand and help combat the TB epidemic, which has become a mainstay in KwaZulu-Natal. The daily challenges associated with this epidemic include insufficient diagnosis, HIV co-infection, treatment of side effects, defaulting from treatment and the emergence of pediatric TB.

## Insufficient diagnosis

Insufficient preventative and diagnostic practices have contributed to the increase of the disease burden to its current level and severity. Poor prevention strategy and control of drug-sensitive TB has allowed for the spread of drug-resistant TB, as individual sensitive cases can mutate into drug-resistant cases if not treated. The overall level of TB bacteria remaining in the population without treatment has increased the likelihood of mutation, therefore allowing an increase in drug-resistance. While the Department of Health establishes prevention as the key to effective control of DR-TB, there have not been enough changes made to enact actual prevention strategies.<sup>4</sup> In the words of one of the doctors at FOSA Hospital, "It's like the horse has bolted and now you want to go catch it. What you should have done is closed the stable door." The implementation of preventative policy is necessary for addressing the rapid spread of TB in South Africa. In the United States, each state government is responsible for establishing and regulating TB control laws and programs effective for their state.<sup>6</sup> If South African provinces were to adopt similar responsibility, the country could be more successful in addressing TB control and prevention. At the least, it would be held legally responsible if the province continued to fall short of necessary TB management policies.

Many people are not being diagnosed soon enough, causing the initiation of treatment to be delayed. The more the disease is able to progress and multiply in the body, the more rigorous the treatment process needs to be. The TB treatment regimen is already extremely demanding, and delaying the initiation of treatment will further complicate the treatment. Diagnosis accuracy is also a problem for developing a treatment regimen. If the presence or resistance of TB is not properly diagnosed, treatment will be improperly supplied or simply not supplied. During my experience in the hospital, many patients admitted to the hospital had diseases that had already progressed to a dangerous state. Had these patients received treatment earlier, the prospect of their improvement would have been much better. More active public health surveillance, with active community level diagnostic and treatment techniques by local healthcare providers and community health workers, could improve early diagnosis and more prompt initiation of treatment. It is clear that diagnosis alone is insufficient to motivate patients to seek treatment. Therefore, if we put the responsibility on local health professionals, there may be hope for improvement.

One possible explanation for the insufficient diagnosis could be a tendency of many Zulu people to use traditional healers, known as sangomas, when they become ill. This is particularly common among more rural Zulu populations, whose access to healthcare is limited. These sangomas are a major part of the Zulu tradition, but they may be unable to diagnose and treat TB successfully. Traditional healing practices are inadequate for treating infectious diseases such as TB and therefore would only delay the implementation of proper treatment. While sangomas are instructed by the state to refer any suspected TB patients to a local clinic, there are no guarantees, as there is no follow-up on the patients regarding whether they actually go to an alternative provider. While this traditional practice is problematic, South African health professionals have made some efforts to intervene and utilize traditional healers as a promotional or educational tool, rather than a detriment. When visiting one sangoma in KwaZulu-Natal, I noticed she was wearing a "STOP TB" health promotion shirt. This shirt could imply that this sangoma had been educated about TB care and promotion, suggesting a certain level of communication and coordination between local traditional healers and national organizations in the

fight against TB. Another sangoma admitted she does not try to treat any patient displaying symptoms of TB, although she had been educated about the signs and symptoms of TB by a local health worker. While these cases do not prove the presence of improvements in TB diagnosis or treatment, further coordination between state health institutions and traditional healers could improve both the control and diagnostics of TB among Zulu populations. Encouraging sangomas to keep in contact with patients could help determine if those patients are taking their advice and going to clinics for proper treatment. Similar to the referral system, sangomas could require a proof of TB treatment from a clinic before seeing a patient. If the problem persists, South Africa could consider providing TB treatment and medication schedules to sangomas. If health professionals are more educated in treating the disease, they may be able to provide more useful information to patients rather than just turning them away. While hospital treatment is the ideal, educating sangomas and providing them with treatment resources could be a useful compromise. Though a diagnosis would have to be done at a clinic or hospital, allowing sangomas to distribute medication to already diagnosed patients would allow patients to use their preferred healer while simultaneously receiving the most effective care.

## HIV co-infection

The TB epidemic is further complicated by the high comorbidity rate with other infectious diseases, particularly HIV. National data from 2006 stated that there is a 70% TB/HIV co-infection rate among all recorded TB patients.<sup>7</sup> In Sub-Saharan Africa 40-60% of children treated for TB are HIV positive<sup>8</sup> and over 50% of new TB cases in South Africa are in patients who are co-infected with HIV.<sup>7</sup> In 2005, KwaZulu-Natal experienced over 25% prevalence of HIV in addition to more than 50,000 TB cases.<sup>7</sup> Ayesha Kharsany, research associate at the University of KwaZulu-Natal, noted the corresponding trend of HIV and TB, stating, "As antenatal prevalence [of HIV] started rising...what we started seeing was a parallel increase in the caseload of tuberculosis as well."<sup>9</sup> This co-infection likely occurs because immunosuppressed HIV victims more easily contract active tuberculosis than otherwise healthy individuals. This leads to a high HIV prevalence among all patients in TB clinics.<sup>9</sup>

At FOSA Hospital, the doctors estimate the TB/HIV co-infection rate among their patients to be 75-80%. Co-infection hinders treatment because it makes the healing process more complex and extensive. The FOSA Hospital has a policy that all patients be assessed at their HIV Counseling and Testing (HCT) Department. South African national policy says that any HIV-positive person is eligible to start lifelong antiretroviral (ARV) treatment if they have a CD4 count less than or equal to 350.<sup>10</sup> However, should a patient test positive for TB, he/she will immediately begin treatment, regardless of their CD4 count. Because HIV attacks the immune system, the TB symptoms will not improve unless the HIV is addressed. Therefore, FOSA has made it a priority to test and counsel for HIV as a first step to treatment of TB. Frequent tests of CD4 count and Viral Load are conducted, and the results are recorded in the patient's file every week during doctors' rounds. These results tell the doctors the severity of HIV in the patient's body and therefore the level of disease that they face. The concurrency of HIV and TB is a noteworthy challenge that will need to be addressed in the coming years to reduce the burden of both diseases.

This concurrent epidemic is a particular problem among Zulu populations: due to the stigma associated with HIV, HIV patients may not be getting tested for HIV, or may not be open about their illness and treatment should they be diagnosed. While living in the Cato Manor Township in Durban, for example, I noticed there was a significant lack of communication regarding HIV. My Zulu friends and host family members were very willing to discuss health topics with me, with the exception of HIV. My fellow researchers noted a similar occurrence within their host families, which became a notable obstacle to completing health research surveys. The HIV stigma worsens not only the HIV epidemic, but also the TB epidemic

indirectly. Improvement of this complicated relationship between these two illnesses unfortunately relies heavily on social change, which is very difficult to enact. Organizations such as the Southern Africa HIV/AIDS Information Dissemination Service (SAfAIDS) have worked to understand and suggest solutions to the extensive HIV stigma in Southern Africa.<sup>11</sup> Some suggestions include educating religious leaders about HIV/AIDS and encouraging them to facilitate discussions in their services. I witnessed this when attending church with my host family, where the pastor spoke at length about HIV and had a patient share his story as well. Religion is a big part of the Zulu culture, so religious leaders are well respected. This makes them an effective outlet for HIV education and reducing stigma. Additionally, the media has been used to reduce stigma, particularly with health edutainment programs like *Soul City*.<sup>12</sup> This television soap opera series is popular amongst Zulu populations and displays HIV/AIDS information through popular characters, thereby raising awareness and reducing stigma. With continuing efforts like these, social change is possible, and the rippling effects can reduce the concurrent HIV-TB epidemics.

### Side effects and patient response

Another major barrier to TB treatment as observed in Durban is the complexity of the treatment regimen, specifically with regard to treating side effects. National policy guidelines establish that “treatment spans must be determined based on individual culture date conversions, and must be a minimum of six months.”<sup>4</sup> This lengthy treatment requires numerous pills and frequent injections of a combination of various medications, which can be toxic and detrimental to the patient’s body. There are a number of side effects that can occur as a result of the TB medications, ranging from diarrhea to psychosis. The majority of cases suffer from side effects no more severe than nausea and diarrhea, which can be treated with counter-effect drugs. However, aminoglycosides, used to treat MDR-TB, can cause hearing and vision problems, sometimes to the point of deafness and blindness. In addition, many of the hospital’s HIV-positive patients also develop AIDS-related cancer, called Kaposi sarcoma. Epidemic, or “AIDS-defining,” Kaposi sarcoma is a cancer of the cells around the lymph and/or blood vessels and presents itself as tumors on the skin or mucosal surfaces.<sup>13</sup> The cancer can be crippling and requires chemotherapy treatment, which is not only taxing on the body, but further complicates treatment for FOSA patients; as FOSA does not have the necessary resources, they must be brought to a neighboring hospital for this treatment.

Some of the patients experience side effects so disconcerting that they stop taking their medications, choosing their vision or hearing over curing their TB. One Kenyan study of TB treatment defaulters showed 10.8% of observed cases reported not completing treatment due to side effects.<sup>14</sup> A similar study done in Uganda reported a statistically significant correlation between side effects and defaulting from treatment.<sup>15</sup> Though they can still transmit TB to the rest of their community, it is ultimately the patient’s choice whether or not they want to suffer from these side effects. The treatment process for TB is inevitably complex, and the existence of side effects is an unfortunate reality that further complicates the process. Dealing with this phenomenon was a significant stressor observed amongst the doctors at FOSA, who were discouraged by their inability provide effective clinical treatment to patients due to the lack of adequate treatment of side effects and policies regarding patients who refuse treatment due to their side effects. This frustration places stress on the provider and, in turn, on the hospital and system as a whole.

### Defaulting from treatment

Refusing TB treatment poses an immediate threat to medication compliance. Lack of adherence to treatment is a major problem because it leads to MDR and XDR strains of TB. The bacterium *Mycobacterium tuberculosis* that survived the previous treatment undergoes slow but constant and spontaneous mutations that give rise to increasingly drug-resistant organisms. The chance of spontaneous resistance to each first-line TB drug used in South Africa is about 1 in every 100 cell-divisions.<sup>4</sup> With this rate of

resistance across all first-line anti-TB drugs, the problem of drug-resistance is extensive. Additionally, a 2002 survey showed that 6.7% of patients who had previously undergone treatment for TB were now undergoing treatment for MDR-TB.<sup>16</sup> Interestingly, a 2010 study published in *The Lancet* showed that 72% of current XDR-TB patients in their cohort had previously been diagnosed and started on a treatment regimen for MDR-TB.<sup>17</sup> This shows that a significant number of treatments of MDR-TB are also failing, as patient conditions are only getting worse. In early February, the Center for Disease Control and Prevention published a report that warned readers that the first cases of totally drug-resistant, and “virtually untreatable,” TB were reported in South Africa.<sup>18</sup> While it is unknown as to how long these strains of completely resistant TB bacteria have been in South Africa, nine cases discovered in one small area suggest that they have not developed recently.<sup>19</sup> This is something that the healthcare system of South Africa will have to deal with in coming years.

A typical MDR-TB patient takes an average of six medications, while an XDR-TB patient takes eleven—without considering medications for countering side effects and HIV antiretroviral medications. The sheer number of medications makes it difficult and uncomfortable for patients to keep track of taking them all, especially when many are bitter or hard to swallow. It is particularly difficult for patients who must travel to clinics or hospitals for medication who are not being constantly monitored by health professionals because they take the medication at home. Treatment at home relies heavily on the patient’s own active participation in the healing process, which makes it harder to ensure treatment than at an in-patient facility like FOSA. While staying in the rural area of Impendle, I spoke at length with my host family about the main difficulties of daily rural life. One of their main concerns included the lack of convenient transportation and access to health care facilities. For example, walking to town becomes dangerous when it rains, as people have to cross difficult terrain such as engorged rivers. This showed me that it would be difficult for a TB patient to access a clinic, and the difficulty of the trip may discourage patients from keeping up with their treatment.

Efforts such as Community Care Givers and tracer teams are used to help encourage medication compliance but have faced some problems in practice. In South Africa, there are many people employed as Community Care Givers (CCGs) who are not trained health professionals but rather are community members who have taken certain training courses that qualify them to distribute medication and make in-home visits to patients in their given neighborhood jurisdiction. These CCGs are key players in controlling TB outside of the hospital setting because they can visit TB patients and ensure they are taking their medications. However, it can still be difficult for CCGs to monitor patients at home because the patients are not always home when the CCG comes to check on them. When I was working with a CCG in the Newlands West Township, three out of four patients who we were trying to visit in one day were not home. This complicates the process of monitoring treatment regimens, as unmonitored patients and those defaulting from medication cannot be checked. Tracer teams, mobile units that travel to communities in order to track patients and assess whether or not they are receiving and taking their medication, play a similar role. While tracer teams are known to be effective, I was unable to find many teams that were doing this kind of work for TB patients. FOSA once had a tracer team that dissolved about six years ago, most likely due to a lack of funding. Thus, FOSA loses track of patients after they are released, and these patients may default from treatment without any health professional knowing.

FOSA Hospital also faces its own difficulties with keeping in-patients adhered to medication at times. Sometimes patients refuse treatment or run away from the facility because they want to return home. When this happens they are no longer under the medical supervision of the doctors and nurses, decreasing the likelihood of medication regimen adherence. Additionally, patients are sometimes granted pass outs for the weekend or holidays. During my time at FOSA, for example, many patients were going home for the Easter holiday. However, many patients did not return on time after the holiday pass out was over. There is nothing the staff can

do to make these patients come back, and the longer they are gone, the more likely they are to run out of medication or stop taking it. The doctors also informed me that many of the XDR-TB patients now in the facility previously had MDR-TB and refused treatment. They have now returned to the facility with a worsened case of XDR-TB because they did not stay on their treatments initially. Defaulting from treatment is a serious problem and allows the epidemic of XDR-TB to worsen.

Facilities like FOSA now have to try to combat very fatal forms of XDR-TB, which has proved to be a difficult task. The doctors at FOSA estimated that of 160 patients in the hospital, one third are XDR and only five to ten percent of those XDR patients will respond to treatment and recover. There is no policy in place for the 90–95% of patients who do not improve after nine months of treatment. One FOSA doctor phoned his superior in front of me to ask him what he should do with one of his patients who was failing treatment. As the doctor predicted, there was no answer. This policy gap is a problem because while doctors cannot tell patients that they must stay in the hospital away from their families at the end of their lives, it is a public health risk to send an XDR patient freely into the community. Though public health experts may argue that the patient must stay in the hospital, the lack of policy means it is up to the patient whether they want to stay or go home. While any patient who chooses to go home is still required to take medication at a local clinic, they are more likely to default from medication and spread the disease than if they were to remain in the facility. One FOSA doctor referred to this problem as a “revolving door” which is allowing XDR-TB to increase exponentially. There is no treatment for these patients and their release back into the community is allowing the rapid transmission and exponential growth of XDR-TB throughout South Africa.

In order to address the rising level of drug-resistant TB, the World Health Organization suggests starting with improved and more comprehensive surveillance data in order to gain a better understanding of the overall burden—not only in KwaZulu-Natal, South Africa, but also around the world. In 2012 there were 70 countries with continuous surveillance based on drug susceptibility testing (DST) of all diagnosed TB patients, and 66 countries based on testing of select representative samples.<sup>1</sup> With improved surveillance could come improved coverage of DST and improved understanding, which will allow for more focused and effective intervention. In response to the release of infectious XDR-TB patients back into their communities, a policy intervention would be the most plausible solution. Clinically, there is not yet a way to improve these patients, so a societal level intervention will be necessary. By creating a policy that restricts the release of infectious XDR-TB patients and limits their interactions with healthy individuals, we will be able to limit the rapid spread of XDR-TB after failed treatment. However, the prospect of such a policy forbidding the patients’ release is controversial because it could simply discourage patients from seeking treatment in the first place, for fear of being taken away from their families or communities. These conflicting views on policy intervention for failing patients will create interesting debates in the coming years in South Africa’s fight against TB.

### Pediatric tuberculosis

Another emerging challenge in the South African TB epidemic is the increasing prevalence of pediatric TB. TB is generally considered a disease that affects adults, but recently its widespread infection of children has been more difficult to treat than TB in adults. Children comprise over 16% of all TB cases in South Africa, and Dr. Anneke Hesselting of Desmond Tutu TB Centre in South Africa even claims that with better detection we would find that 15–20% of cases worldwide are children.<sup>20</sup> Pediatric TB is a significant issue because children develop the disease more quickly and severely since they have less developed immune systems.<sup>20</sup> It is estimated that 70,000 children die each year from TB, a disease which is preventable and curable with effective prevention and treatment.<sup>21</sup> Children frequently develop the most severe forms of TB, such as miliary TB, or TB with very small lesions but wide dissemination, and TB meningitis.<sup>8</sup> This severity shows that an increased emphasis

needs to be put on pediatric TB, not just TB in adults. “Young children usually become infected after household exposure to an adult or adolescent with sputum smear-positive TB.”<sup>28</sup> This could be prevented if the proper steps were taken to combat the disease and protect children. If health professionals ask TB patients if they have children in their home, it could help protect these children before they become infected.<sup>20</sup> For example, the doctors at FOSA recorded the number and ages of children whom each patient had so that they would be aware of potential infection should that patient be granted a weekend or holiday pass out. I also witnessed doctors speaking with any patient leaving the hospital campus about the potential they had to pass the disease to their families and children if they did not follow the doctors’ precautionary orders. Greater awareness from parents and health professionals like these could help significantly reduce the incidence of TB amongst children.

According to Hesselting, the problem of TB among children is worsening due to insufficient diagnostic efforts from the health care system. One problem is that children are often unable to produce sputum for testing; when they can, it is often a false negative because children often carry a lower, and therefore less detectable, level of TB bacteria.<sup>21</sup> This is a major barrier to diagnosis and, subsequently, control of the disease. Additionally, children with diagnosed cases of TB do not receive proper treatment regimens. Since there is no recognized dose for children, children are given either adult dosages or approximated dosages with broken or crushed pills.<sup>21</sup> Pediatric TB researcher Simon Schaaf admits that the proper dosage for children is actually unknown, and will remain so until funding for pediatric TB research is available.<sup>21</sup> It is important to emphasize that TB can affect anyone of any age in any part of the world.

Based on my findings and the aforementioned challenges characteristic of the South African TB epidemic, there is much progress to be made in the fight against this epidemic. In the coming years health professionals need to take a number of steps in order to control the spread of disease and limit further effects of current epidemics. In sum, these steps include but are not limited to:

- Focus on primary prevention, with efforts such as health education that can raise awareness and prevent transmission altogether.
- Invest in TB research, and ensure that research efforts align with needs observed by health professionals on the ground.
- Coordinate with local and traditional healers to facilitate a wider health effort against infectious disease.
- Facilitate a parallel public health intervention that will concurrently address the HIV and TB epidemics.
- Invest in programs that will help reduce the number of patients defaulting from medication, perhaps by increasing community-level surveillance.
- Acknowledge the severity of and participate in research concerning pediatric TB.

Based on my experiences with drug-resistant tuberculosis amongst Zulu populations, I have seen that the KwaZulu-Natal province is facing a serious epidemic. The abovementioned challenges are barriers to successful healthcare and have created burdens for the Zulu population, health care professionals and the health care system alike. These challenges are by no means unique to South Africa; they can be seen in similar severity and spread in other populations worldwide as well. As we begin to unravel the epidemic’s challenges in one population, we can take lessons learned and apply them to combat these same challenges in other parts of the world. The Zulu population and their struggle with drug-resistant TB is just one example of how crippling communicable diseases can be on different populations around the world. The combat against infectious diseases will require a global effort based on the experiences and hardships of several populations, but with continued global progress we will be able to create a healthier planet.

References available at  
JGH Online,  
[www.ghjournal.org](http://www.ghjournal.org)





*The Journal of Global Health*  
(JGH)

[info@ghjournal.org](mailto:info@ghjournal.org)

5464 Lerner Hall

2920 Broadway

New York, NY 10027, USA

[www.ghjournal.org](http://www.ghjournal.org)

JOGH