Fighting back against mosquito-borne disease epidemics in Latin America and the Caribbean

Dr Anna M Stewart-Ibarra leads a team of researchers based in Ecuador, to deepen our knowledge of mosquito-borne viral diseases. Countries throughout the tropics and subtropics currently face an alarming situation with concurrent epidemics of dengue fever, Zika fever and chikungunya. Conventional vector control and surveillance methods against these viruses have failed to effectively control outbreaks and there is a lack of preventative vaccines readily available. Dr Stewart-Ibarra is using a social-ecological systems (SES) approach to understand how the biophysical and social systems interact to influence the complex dynamics behind these disease epidemics.

Dr Stewart-Ibarra is Director of the Latin America Research Program of The Center for Global Health & Translational Science (CGHATS), at the State University of New York, Upstate Medical University. She is a founding member and director of The Global Health Research Platform, a CGHATS programme based in Machala, Ecuador, that supports research, educational and clinical initiatives to overcome and understand mosquito-borne diseases. Dr Stewart-Ibarra's interdisciplinary team is currently studying dengue fever and other tropical infectious diseases in the area.

Dr Stewart-Ibarra first embarked on her work a decade ago when she began her PhD research on mosquito larval habitat, and climate and social-ecological drivers of dengue fever transmission in the region. Her initial studies in Machala provided the first evidence regarding the effect of climate and social drivers on dengue fever epidemics in the region. Dengue fever, a virus transmitted by the *Aedes aegypti* mosquito, has emerged as one of the top public health concerns worldwide. Her novel approach to the investigation of dengue fever led her and her colleagues to uncover vital information on how social vulnerability interacts with climatic factors to influence the risk of vector borne diseases.

URBAN MOSQUITOES SPREAD EMERGING VIRUSES

Dengue fever, Zika fever, and chikungunya are diseases caused by viruses that are transmitted to people primarily by two species of mosquito vectors: the female *Aedes aegypti* and *Aedes albopictus*. *Aedes aegypti* have adapted specifically to urban environments, breeding in containers with standing water around the home, and biting throughout the day. *Aedes aegypti* are a highly invasive species, and today, they are common across the tropics and subtropics, posing a major public health threat with the emergence of new outbreaks of viral diseases that are spread by the mosquito.

Due to Zika virus rapidly emerging as a major threat to public health, the National Science Foundation (NSF) recently funded $1.7 million worth of rapid response (RAPID)

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A young mother in Machala, Ecuador, is concerned about the health of her newborn daughter. The first cases of Zika fever were reported two weeks before this photo was taken at the end of February 2016. In May 2017, Ecuador reported the first babies born with congenital problems associated with the Zika virus.

Right and above: © Dany Krom

Top: A nurse from the study team in Machala takes a blood sample from a girl. The sample will be tested for dengue, chikungunya and Zika fever. Her neighbour has been hospitalised with severe dengue fever, and the team is looking for other people who may also be ill in nearby homes.

Left: Just some of the devastation caused by the flooding in Machala during the 2016 El Niño event.

grants. Dr Stewart-Ibarra's current research, supported by one of these grants awarded to Upstate Medical University, involves the study of Zika virus transmission in people and mosquito vectors, in relation to climatic and social-ecological factors in southern coastal Ecuador. Findings from the project will help public health officials develop an early warning system that incorporates climate and non-climate information on Zika and dengue transmission.

Dr Stewart-Ibarra's work is exploring a multitude of factors related to Zika and Zika/dengue virus co-infections, including: the prevalence of infections and co-infections in people and mosquitoes, the role of household microclimate on disease transmission, and the economic burden of these diseases on families in affected areas. Her team's work is based in several cities in Ecuador, including Machala, Huaquillas, Portovuelo, and Zaruma. These localities vary in their elevation, climate and socioeconomic conditions, allowing the researchers to investigate how these factors influence the numbers of mosquitoes and disease transmission rates. The results they are obtaining are providing crucial information for establishing effective measures to control the spread of Zika and other mosquito-borne diseases worldwide

Dr Stewart-Ibarra's initial studies provided the first evidence regarding the role of climate and social risk factors in the transmission of dengue fever in this region

KNOWLEDGE ON A LOCAL SCALE

Currently, there are no vaccines available for Zika or chikungunya, and people have limited access to the dengue fever vaccine, licensed recently by Sanofi Pasteur. The need to find effective alternative strategies for management of these diseases is therefore all the more pressing. The only way to control the spread at present is by controlling mosquito populations, which depend on a complex interplay of social and environmental factors. Dr Stewart-Ibarra's research findings are helping to inform public health officials about how to best develop strategies, particularly in high-risk communities.

Through a grant from the US Department of Defense to Upstate, she and her colleagues have developed a prototype for a new, low-cost portable device to specifically attract and exterminate *Aedes aegypti* mosquitoes.

In the urban areas where Dr Stewart-Ibarra is conducting research, many people are living in suboptimal housing conditions. This leaves them far more exposed to bites and vulnerable to acquiring a febrile infection. Her studies have also shown that the economic burden of controlling the mosquitoes is significant for low-income households.

On a community level, the researchers have found that mosquito breeding and dengue risk is surprisingly clustered to specific households. A high prevalence of disease was found to be associated with risk factors that included the condition of the house, amount of shade on the patio, and access to piped water. Any water-bearing container can become a mosquito breeding ground, such as 55 gallon drums, tires and rubbish. Her studies have shown that preventative practices to reduce disease transmission can be as straightforward as covering or cleaning up water receptacles, altering shade on the property, and using mosquito nets. Her studies found that rainfall had affected mosquito abundance in certain communities but not others, due to differences in housing conditions. In areas where the mosquito was found to be breeding in water storage containers filled with tap water due to water

The *Aedes aegypti* mosquito transmits viruses of public health concern such as dengue, chikungunya, Zika, yellow fever, and Mayaro viruses. Mosquitoes collected from homes in Ecuador are tested for these viruses.

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The director of the clinical laboratory in Machala processes blood samples which will be tested for dengue, chikungunya, Zika fever, and other diseases.

scarcity, rainfall did not have an effect. In areas where the mosquito was found breeding in discarded outdoor containers filled with rainwater, rainfall did have an effect on mosquito abundance.

She and her colleagues also discovered how natural disasters, such as the 7.8 magnitude earthquake that devastated Ecuadorian coastal regions in 2016, impact emerging epidemics. The earthquake occurred during the heart of the Zika epidemic, leaving thousands of newly homeless people vulnerable to infections. Following the earthquake, she supported a grass-roots effort that has evolved into the NGO, Walking Palms, that provides integrated health care and, with Ecuadorian institutions and universities, is creating research and training collaborations to address issues related to emerging infectious diseases and natural disasters.

OPTIMUM CLIMATE CONDITIONS FOR EPIDEMICS

Understanding the optimum temperature for vector-borne disease transmission is critically important for predicting future disease outbreaks and is highly relevant across the globe. Stewart-Ibarra and her colleagues have integrated climate data with data obtained from several laboratory experiments investigating temperature-dependent transmission into a mathematical model. This, and other studies focused on climate forecasting, has enabled them to predict the risk of mosquito-borne diseases across Latin America and the Caribbean. For dengue, Dr Stewart-Ibarra and her team have found that transmission increases when temperatures are between 18–34°C, with the highest transmission rates occurring at 26–29°C. When air temperature is outside of this range, the risk of infection is dramatically reduced. They also found that Zika risk across the Americas was greater in 2016, due to warming temperatures across the region, which could have been predicted using seasonal climate forecasts.

Dr Stewart-Ibarra and her team have also discovered that extreme climate events are intrinsically linked to dengue outbreaks. They looked at data from El Niño events, which resulted in unusually warm sea surface temperatures, leading to an increase in air temperature and rainfall. These events also

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Top: A nurse takes the temperature of a woman with a suspected dengue fever infection, while a student researcher records vital signs on an iPad.

Right: A woman is admitted to the Teofilo Davila Hospital in Machala with a diagnosis of severe dengue fever, a potentially life-threatening disease. This case triggered an investigation of additional cases in the community.

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have another devastating effect on Machala, with the city experiencing major flooding during the 2016 El Niño event. This creates the ideal conditions for the proliferation of *Ae. aegypti*, and the recent El Niño event coincided with the first cases of Zika virus reported in the city. This hazardous epidemic trigger unfortunately looks set to increase in frequency, as temperatures continue to rise due to global warming. Therefore, it is even more imperative that researchers partner with the health and climate sectors to develop early warning systems and other tools to predict and prevent epidemics.

DEVELOPMENT OF EPIDEMIC EARLY WARNING SYSTEMS

A major success of their work so far is to have gathered enough information to provide the foundation for the development of a dengue early warning system (EWS) that incorporates climate and non-climate information. In a recent study led by Dr Rachel Lowe from the London School of Hygiene and Tropical Medicine, the team was able to successful predict dengue transmission in 2016, using seasonal climate forecasts and newly developed El Niño forecasts. This new study provides the first forecasts of dengue incidence 11 months ahead of time. Implementation of such a system will allow pre-emptive steps to be taken by the public health sector to decrease the severity of future outbreaks. Dr Stewart-Ibarra and her team's findings are also being used by decision makers to create targeted public health programmes to promote community engagement in dengue control as well as control methods for other mosquito-borne diseases. This work is now being expanded to other regions, such as the Caribbean.

It is imperative that researchers learn all they can about the climate events that trigger vector-borne outbreaks to better predict and prevent epidemics

Q&A

What analysis do you carry out in your laboratories in Ecuador?

We have clinical and entomology laboratories set up in Machala, Ecuador, in partnership with the Ministry of Health and the local university, the Universidad Tecnica de Machala. In the clinical laboratory, we enroll patients with suspected dengue fever, chikungunya or Zika fever in the study, then collect demographic information and a blood sample. The samples are tested for DENV, CHIKV, or ZIKV. They are then sent for further analysis, including the identification of other co-infections. For example, we've also screened our samples for the presence of Chagas disease (transmitted by the kissing bug) and Rickettsial diseases (transmitted by ticks).

In our entomology laboratory, we have basic mosquito rearing capabilities, and we have two experimental huts. These are replicas of local houses which are fully screened in, so that mosquitoes we release into the hut won't escape. In the lab, we rear *Aedes aegypti* mosquitoes for different experiments, such as testing new mosquito control devices in the experimental huts, or testing for insecticide resistance. We also collect adult mosquitoes from homes in the community, and bring them back to the laboratory to sort by species and sex. These mosquitoes are later analysed for the presence of DENV, CHIKV, ZIKV and other viruses.

How have the local communities responded to your research?

Local communities have been very receptive to our research. The work began as a grassroots research initiative, supported by Ecuadorian institutions and Ecuadorian researchers, and our research focus is driven by public health priorities in Ecuador. When I started working with urban communities in Machala during my PhD, I developed a close relationship with the community leaders. They were very receptive and were glad that we were paying attention to the broader social-ecological problems associated with dengue fever, which include access to potable water, garbage collection, housing conditions, etc.

At that time, my role as a researcher was to create a space where community leaders could have a dialogue with public health leaders, to identify their needs and develop joint solutions. Today, my role is to ensure that our research stimulates the development of new interventions that can reduce the risk of these mosquito-borne diseases. This is the nature of translational science – to move from the bench to real world solutions.

What have been the most challenging aspects in carrying out your fieldwork?

One of the greatest challenges we faced was when the earthquake occurred in April 2016. My role changed dramatically from researcher to emergency responder. A 7.8 magnitude earthquake devastated the north-central coast of Ecuador, resulting in the worst natural disaster in many decades. We immediately stopped all research and relocated to the disaster area. We raised funds from the US and worked with local organisations to set up a primary care clinic and medical brigades to attend to people from the most affected communities. This required close coordination with the local Ministry of Health, the National Secretary of Risk, local religious organisations, and the Sathya Sai School.

The earthquake occurred as the Zika epidemic was sweeping through the region. Tens of thousands of people were sleeping outdoors for weeks and months, exposed to infectious mosquito bites. Water supply systems were damaged, resulting in water storage in buckets and drums, and an increase in mosquito larval habitat. People's immune systems were suppressed because they were experiencing posttraumatic stress and losing sleep due to the recurrent aftershocks. We found that women who reported a greater number of posttraumatic stress symptoms were also more likely to report arbovirus (DENV/CHIKV/ZIKV) symptoms.

This experience fundamentally changed the way that I understood the intersection of social vulnerability, natural disasters and emerging epidemics; and the role of the scientist in times of emergency. Over one year later, this work has evolved into the NGO, Walking Palms, which is led by local volunteers David Madden and Avriel Diaz. Walking Palms continues to provide integrated health care to six communities in the city of Bahia de Caraquez. They are the only non-governmental group that has provided continuous post-earthquake health care to the communities. It will be many years before these communities recover, and long-term support is imperative.

Are there any other mosquito-borne diseases that pose a threat to Latin America at the moment?

There is a major risk that malaria will re-emerge in the region. Historically, malaria was endemic and caused the greatest burden of mosquito-borne disease in southern coastal Ecuador. It was completely eliminated from the region in 2011, and in the bordering province in northern Peru in 2012. However, in 2015 we began to see a resurgence of malaria in nearby areas. As often happens, investment in malaria control and surveillance has been dramatically reduced following the reduction of transmission. Unless we are careful, the same thing will happen to malaria as happened with dengue fever, which was eradicated throughout the region in the 1950s, and re-emerged in the 1980s following the decline in vector control.

What have you enjoyed most about your work in Ecuador?

I have strong personal connections to Ecuador, as I am a US-Ecuadorian citizen. This work has allowed me to bridge my passion for ecology and social justice, and to conduct research that directly addresses some of the most significant public health issues today. One of the most rewarding aspects of my work has been to see the growth and development of the research programme, from a grassroots pilot project ten years ago, to a vibrant interdisciplinary research programme. The research platform has also provided important international training opportunities for US and Ecuadorian students, researchers, and international practitioners. Our success is due to the fact that US and Ecuadorian partners share the vision that this is a long-term partnership, with all partners contributing important roles.

Detail

RESEARCH OBJECTIVES

Dr Stewart-Ibarra aims to understand the role of climate and social vulnerability in the emergence and persistence of dengue fever, Zika and other mosquito-borne infectious diseases.

FUNDING

Clinical Research Management (CRM); U.S. Centers for Disease Control (CDC); NSF EEID; NSF Zika Rapid; Prometeo Fellowship of the National Secretary of Higher Education, Science, Technology and Innovation (SENESCYT) of Ecuador

COLLABORATORS

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BIO

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