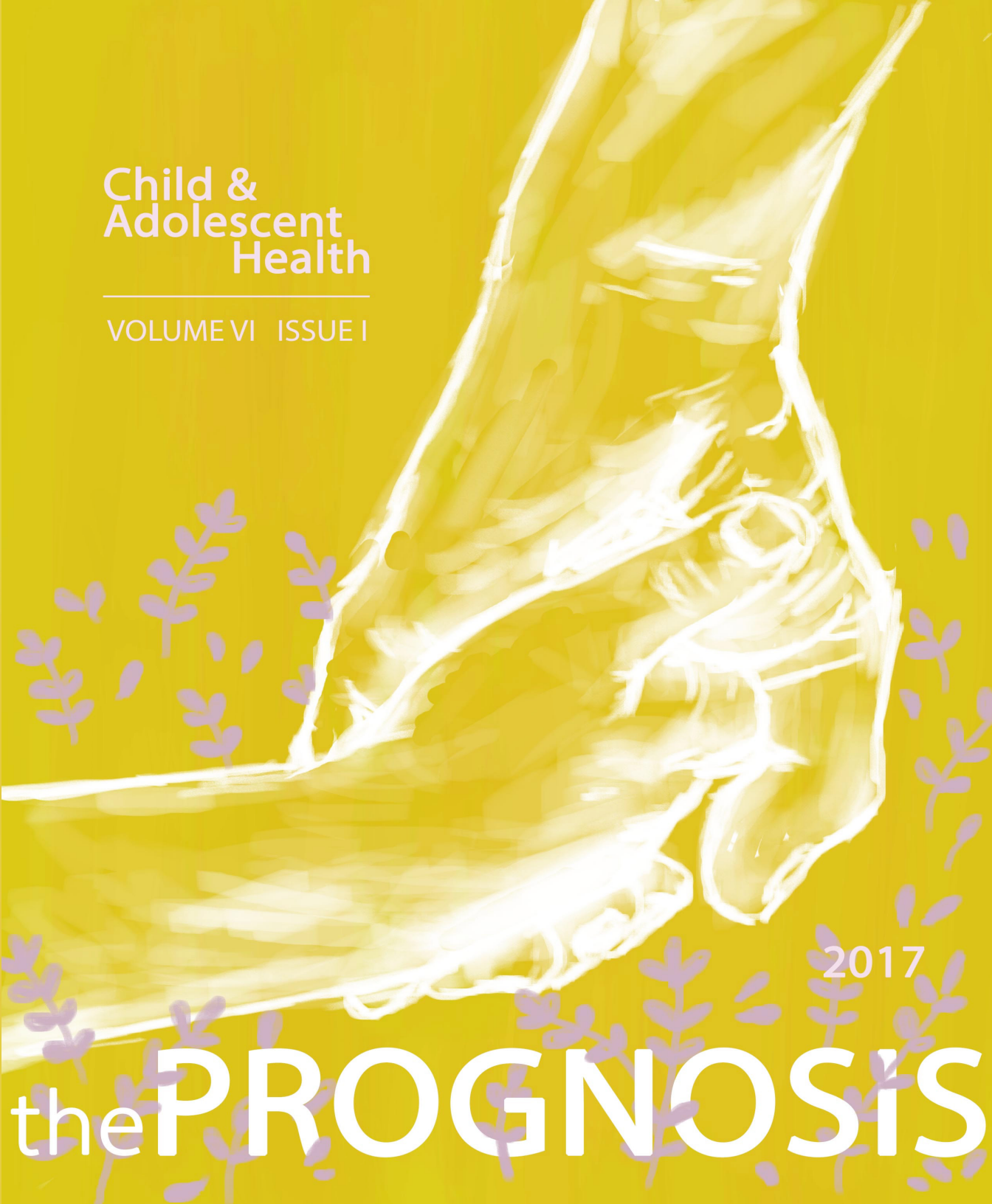

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The Prognosis is supported by McGill Global Health Programs (GHP) and the Institute for Health and Social Policy (IHSP). In keeping with the journal's focus on research at the intersection of social, biomedical, global, and local perspectives on health, these organizations are uniquely placed to support the ongoing work of this student-run publication.

GHP partners with various departments at McGill to promote human well-being, productivity and economic development, and is actively involved in research and training around the world. Committed to collaborative projects that improve health through educational, clinical, developmental and research programs, McGill Global Health Programs is excited about new avenues to enrich the education of students interested in global health. The IHSP conducts interdisciplinary research on the impact of social conditions on health and welfare. The IHSP aims to translate findings from research in social inequalities and health outcomes into concrete provincial, national and international policies. The IHSP is keen to develop additional opportunities to spread research findings that improve population level wellbeing.

From the Editor-in-Chief

Dear Reader,

The Prognosis, McGill's student journal of global health, was founded in 2011 by a group of students dedicated to highlighting interdisciplinary scholarship in the emerging field of global health. With each new editorial board, the journal has evolved, though we strive to maintain our initial mandate of promoting research at the intersection of social, biomedical, global and local perspectives on health.

For the second year in a row, Volume six of the Prognosis has a theme: Child & Adolescent Health. As we witness the epidemiological transition from infectious to chronic diseases as the leading cause of mortality worldwide, there is an increasing need for research on the global health issues specific to young people. This publication seeks to highlight both challenges and triumphs in the field of child and adolescent health worldwide.

In this volume, we feature five exceptional research papers from students at McGill University. The topics covered range from suicide awareness in Indigenous communities in Manitoba to radio-based mental health initiatives in Malawi and Tanzania. We feature an article exploring the efficacy of a ban on marketing junk food to children in Taiwan, and two case studies looking, respectively, at the development of the dengue vaccine and India's impressive campaign to eliminate Polio. The student authors hail from a wide variety of academic backgrounds, including Anthropology, Medicine and Microbiology and represent undergraduate, graduate and PhD programs.

The 2016-2017 Editorial Board is proud to present to you this edition of the Prognosis, on a topic deserving far more attention than it currently receives. We hope you enjoy reading this compilation of student work and we thank you for supporting the next generation of global health leaders.

Jessica Farber
Editor-in-Chief

Editor-in-Chief

Jessica Farber - Hon. B.A., International Development

Jessica is in her final year of a B.A. in Honours International Development. Her research interests lie in issues of forced migration & refugees, human rights, and global health equity. She currently works as a research assistant on corruption and governance reform in the Southern Cone of Latin America. She has previously worked as a Research Associate for the Council on Hemispheric Affairs, publishing several pieces on human rights in Central America, and she was a 2015 McBurney Fellow for the McGill Institute for Health & Social Policy, working with an NGO in El Salvador. Throughout her time at McGill, Jessica has been a proud member of Universities Allied for Essential Medicines, a non-profit organization working to expand global access to affordable medicines.

Editorial Board

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Madlen is in the final year of her Honours Bachelor's Degree at McGill University. Stemming from her educational background in microbiology, her global health interests are infectious disease prevention and diagnosis in high-burden, low-resource settings. She currently works as a research assistant at the McGill International TB Centre where her most recent project focused on evaluating a new molecular HIV-1 viral load test in India. As a passionate advocate for health and social justice, she is also involved with Universities Allied for Essential Medicines, working to improve the accessibility and affordability of medicines and diagnostics. Starting in Fall 2017, she will be pursuing an MSc in Epidemiology at McGill University under the supervision of Dr. Madhu Pai.

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Vaidehi is in her last semester of her BSc. in Pharmacology at McGill. Her involvement with global health stems from her experiences in healthcare settings in Canada and India. Currently working in pharmacological research, she is interested in infectious disease epidemiology and antimicrobial resistance. She admires global health research for its interdisciplinary nature, and hopes that this edition of The Prognosis will serve to integrate diverse student perspectives in the field.

Anna de Waal - B.A., Psychology

Anna de Waal is a second year student majoring in Psychology, with minors in Political Science and the Social Studies of Medicine. She is passionate about human rights, social stratification, and Indigenous health, with previous research focusing on HIV self-testing in South Africa. She currently holds a junior research assistant position with Dr. Nitika Pant Pai's lab in Clinical Epidemiology and Infectious Diseases. She is excited to be part of the Prognosis team to explore the intersection of society, politics, and the environment in shaping global health challenges.

Nousin Hussain - Hon. BSc., Microbiology and Immunology

Nousin Hussain is currently a fourth-year Microbiology and Immunology Honours student. She is excited to be amongst a group of equally passionate editors, keen on bringing global health research and concerns to the greater university community. Growing up in a marginalized neighbourhood in Toronto, she understood at a young age the disparities that are present in healthcare services and accessibility. She has since then developed a passion for community development and medicine both in the local and global context. This drives her to find innovative solutions and research strategies that empower those that are most burdened by disease. She hopes that the compelling case studies and articles presented in Prognosis will shed light on these key global health issues.

Clare Fogarty - Hon. BSc., Microbiology and Immunology

Clare Fogarty is in the final year of her undergraduate degree in Honours Microbiology & Immunology with a minor in the History & Philosophy of Science. Through her academic interestes in biomedicine and bioethics, she discovered her ultimate passion for global health research and policy. She presently works as a research student at the McGill AIDS Centre, investigating potential antivirals for emerging infectious diseases. As Clare continues her studies in public heath, she hopes to pursue work in neglected and emerging infectious disease control, as well as issues in health and social justice

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Tessa is in the final semester of her undergraduate degree. She has a keen interest in entrepreneurship, writing, and editing. She is currently honing her layout and design skills as an intern at Drawn & Quarterly publishing house. After graduation, Tessa will work full-time on her silkscreen print apparel company, Asset Designs.

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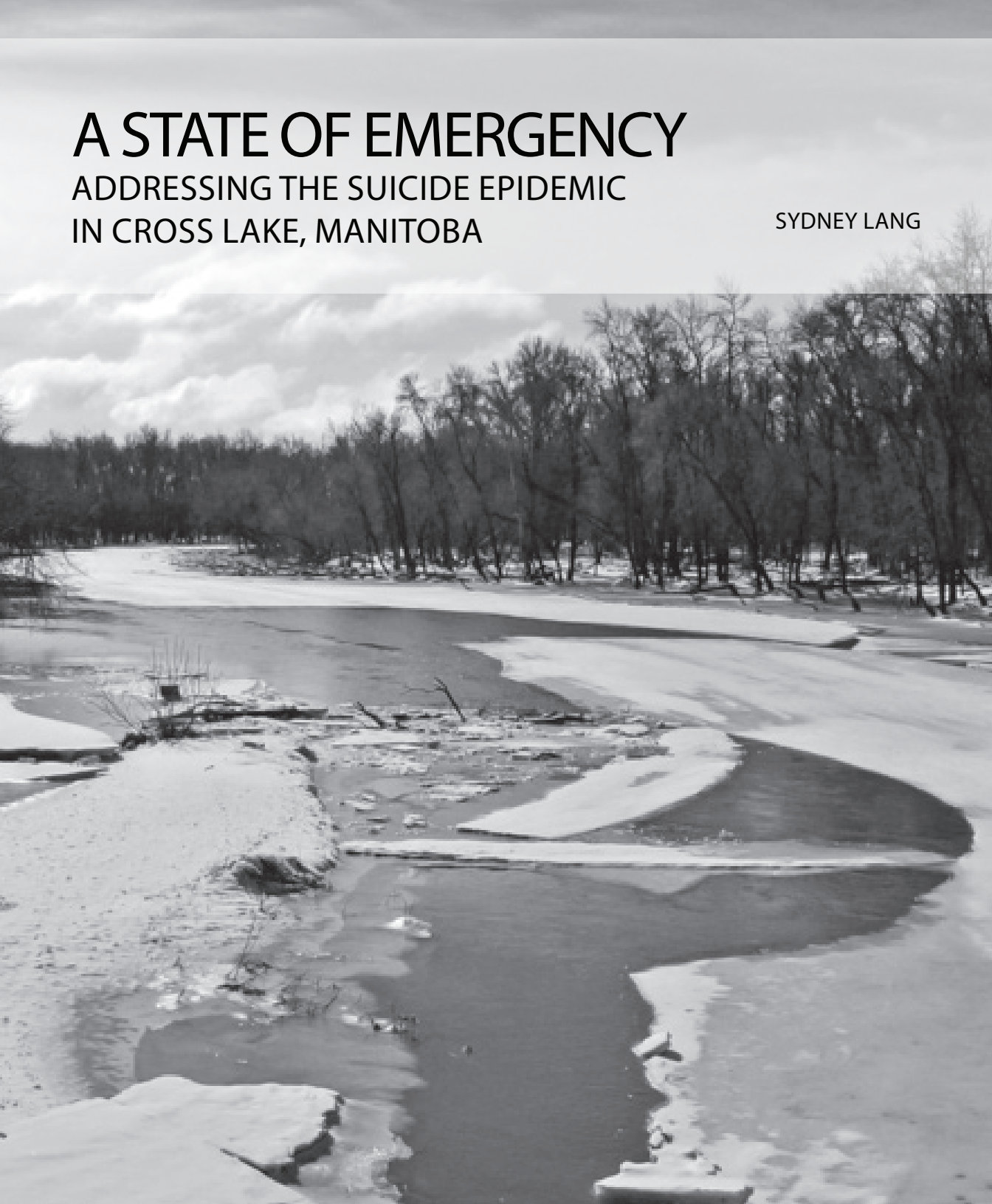
A STATE OF EMERGENCY

ADDRESSING THE SUICIDE EPIDEMIC IN CROSS LAKE, MANITOBA

SYDNEY LANG



"What if staying alive has something to do with witnessing the death in life? What if dying and being borne along by those who love you, is also a way of being alive? How might we come to care for life that is constitutively beside itself, life that could never be fully itself?"

-Lisa Stevenson, Life Beside Itself (page 18)

Pimicikamak Cree First Nation has recently declared a state of emergency, after a sixth suicide within the past two months, in addition to 140 suicide attempts within the past two weeks (1). The extremely high suicide rate in Pimicikamak exists as a disproportionate and persistent reality in many Indigenous communities across Canada and around the world (2). Mental health and well-being in Indigenous communities are often informed by, and contribute to, the settler colonial project and its effects, including poverty, trauma, and structural violence (3-5). Although government resources and services have been implemented to address suicide amongst Indigenous youth in Canada, these responses are often insufficient. While sometimes culturally relevant, the treatment facilities in Winnipeg that DeVerteuil and Wilson explore in their research, for example, are not always the most effective solution (6). The use of government interventions in Indigenous communities through biomedical healthcare systems has further been theorized as a contemporary realization of settler colonialism.

Pimicikamak Cree First Nation, a reserve of only 8,300 people, is not unaccustomed to trauma (6). For the past year, the community has relied on an understaffed crisis line and overworked service personnel to address the recent rise in mental health concerns and suicide attempts (1,7). The community experiences poverty and overcrowded housing and suffers from an 80% unemployment rate (1). The reserve is also located near a Manitoba Hydro generating station, which has since destroyed surrounding land (including land on the reserve) and failed to produce the promised economic development in the community. The provincial government acknowledged the extent of the destruction in 2013, calling attention to the damage caused by hydro development on "traditional land, way of life and cultural identity" (7). These state and corporate-led developments have contributed to the everyday challenges faced by the community (1,7).

I endeavour to use the situation in Pimicikamak as an entry point into a larger, more systemic discussion of youth suicide in First Nations communities. It should be mentioned that I have not done first-hand research in this community; my analysis is informed by media coverage of the crisis in Pimicikamak, along with a theoretical analysis of academic literature. Furthermore, Pimicikamak is only one of many First Nations communities experiencing such a suicide epidemic (2). I will critique a variety of assumptions that underlie the suicide epidemic in Pimicikamak, including the biopolitical logic of care, and call into question previous understandings of mental illness in Indigenous communities, such as historical trauma and cultural continuity. I will then explore notions of agency and affect, through the concept of cosubstantiality – mutually indwelling, or coexistence in and of the same nature – to provide a more cohesive and holistic understanding of the situation in Pimicikamak. I will argue that the understanding of suicide in Indigenous communities is complex and often contradictory, but that we must engage with the uncertainties expressed and felt by these communities in order to create

spaces in which meaninful responses to suicide can emerge.

Finally, this analysis acknowledges and respects Indigenous sovereignty and urges against the essentialization of indigeneity. Such a topic should not be explored solely through a scientific or prescriptive lens, but through one that recognizes individual and community agency in parallel with the deeply traumatic effects of colonialism on mental health and well-being.

Rethinking Historical Trauma & Cultural Continuity

The portrayal of the "state of emergency" in Pimicikamak in mainstream media conveys the idea that suicide is a current and novel phenomenon that must be urgently addressed. However, we must critique notions of temporality within popular (and academic) discourses on Indigenous suicide (8). To start, these discourses fail to consider that suicide could have existed prior to settler colonialism (8: p.169). As Fiddler and Stevens describe, and as was clearly depicted in Killing the Shamen, there are pre-existing justifications for and understandings of suicide and death (8: p.170). However, it was not until colonial contact that these experiences were pathologized and feared. Today, most discourses surrounding Indigenous suicide are informed by understandings of historical trauma and cultural continuity.

Historical trauma acknowledges that collective trauma in one generation has implications on future generations; that stressors and trauma accumulate and increase the risk for both negative health and social well-being for Indigenous peoples today (9: p.321). Cross Lake Residential School, also known as St. Joseph's Residential School, operated in Cross Lake from 1908 to 1948 (8). Although infrequent, when mainstream media acknowledges this history, it fails to show the ways in which settler colonial institutions persist today despite the closing of residential schools. Historical trauma is a concept that may be used to make sense of the ongoing, intergenerational hardships within Indigenous communities, as Bombay, et al. (9) explore in their paper, The Intergenerational Effects of Indian Residential Schools. However, there are several risks of using historical trauma as an overarching framework of analysis.

Maxwell (10) critiques the use of historical trauma as a framework for analysis, and states that it legitimizes individual suffering while obscuring colonialism. Historical trauma, as it is reproduced through colonial professional discourse, focuses the blame of trauma on Indigenous families and child-raising, suggesting that trauma passes through generations and pathologizes the Indigenous family (10: p.408). She argues that trauma is a social construct, mobilized in specific contexts for specific purposes (10: p.411). As previously mentioned, Pimicikamak is situated next to large hydro development projects. These critiques of historical trauma may reveal the ways in which suffering from environmental destruction and land dispossession have been depoliticized. They further explore how discourse on suffering and trauma is mobilized to both control the Indigenous family and allow physical control of and within the reserve by healthcare professionals, especially when biomedicine is prioritized and programs are not culturally appropriate. Furthermore, the pathologization of Indigenous families works to legitimize assimilative and intrusive educational and clinical practices that perpetuate colonial state control of Indigenous communities (10: p.408). This reveals that the emphasis and response to certain

forms of trauma in Indigenous communities simultaneously leads to ignorance of others and perpetuates manifestations of settler colonialism.

Chandler and Lalonde (11) also look to historical understandings of culture to argue that suicide amongst Indigenous communities results from a lack of cultural continuity. Cultural continuity, as understood by Chandler and Lalonde, is an Indigenous community's ability to preserve their cultural past in the context of their imagined future, or to control their future lives; their research indicates a link between cultural continuity and reduced rates of suicide (11: p.221.) However, most of the factors they used to determine cultural continuity, including health services, police services, fire services, and community control of education, are all general markers of healthy communities. Kirmayer, Tait, and Simpson question whether these factors are truly representative of cultural continuity, as many factors, such as involvement in land claims and involvement in municipal government and school systems, cannot be viewed as "cultural traditionalism," but rather as local control (12: p.19). Notions of cultural continuity also place culture in the past as something that remains in isolation, carried through each generation without negotiating or interacting with outside cultures and systems (12: p.20). In the media's representation of Pimicikamak, the reserve is framed as traditionally isolated, which contributes to the notions that cultural continuity is important and present (1). Such representations may serve to normalize the violence within these communities, framing suicide as an "Aboriginal problem." This allows the public to accept the suicide epidemic as an inherent reality on the reserve, as exhibited by media portrayals of the "state of emergency" in many Indigenous communities (1,2).

Logic in Contention: Resisting Biopolitics and Respecting Cosubstantiality

The complicated situation in Pimicikamak illustrates the limitations of concepts such as historical trauma and cultural continuity. As mentioned previously, the reserve has recently relied on a suicide crisis line; this is a common response from the Canadian government. Both the existence of the crisis line and media representation of the crisis in Pimicikamak indicate that the government's predominant response is to implement more preventative resources and services. Lisa Stevenson refers to biopolitics to explain this phenomenon: "... I use the term "biopolitical" to describe a form of care and governance that is primarily concerned with the maintenance of life itself, and is directed at populations rather than individuals" (5: p.3). Stevenson argues that the logic of biopolitics not only shapes the ways in which Indigenous peoples are governed through biomedicine and care, but also how individuals both come to see themselves and engage with others (5: p.4). Stevenson's research depicts the violence that is perpetuated through this regime of care.

Stevenson questions the representation of a regime of care "in which it doesn't matter who you are, just that you stay alive" (5: p.7). Evidently, this is the representation of Pimicikamak that mainstream media has chosen to portray. This kind of representation is also common in other media portrayals of Indigenous suffering, including those of Missing and Murdered Indigenous Women (MMIW), in which neither the women's stories nor their individuality are depicted in mainstream media; they are simply a part of the MMIW campaign. When discussing and reporting on Indigenous communities, a focus on community problems tends to obscure the media's accountability to the individual in need (13).

The concept of cosubstantiality, as experienced within Indigenous communities, is a more productive lens through which to approach Indigenous suicide. Although it could be argued that biopolitical regimes of care do focus on community well-being over the individual, cosubstantiality recognizes the value of the individual within the community. Cosubstantiality unveils the connection between the individual and the community, where the individual's body belongs to the collective (14: p.513). As Povinelli (14) explores, this creates a coexistence of sovereignty and biopolitics. However, we must question the implications of these understandings; in Pimicikamak, the death of a community member is felt by everyone in the community, yet the community's understandings of suffering have also been influenced by biopolitical logic and the biomedical regime of care. Although they may coexist, they do so in tension, and often complicate the relationship of the individual to himself, his community, and the care he receives. High rates of suicide and depression cannot be addressed by treating the community as a homogenous group, but rather by recognizing the individual's situation in and connection to the community.

Concluding Remarks: Taking Control

Suicide in Pimicikamak is not simply a topic to be studied and researched, but an evolving state of affairs and an urgent reality. I have critiqued the government's response as embedded within biopolitical logics of care, and I have challenged notions of cultural continuity and historical trauma that have informed academic understandings of Indigenous suicide. We must move beyond these reductive understandings and recognize the ways in which understandings of life and death are also a product of settler colonialism. What does it mean to question those conceptions? To start, we must challenge the dichotomies that structure our understanding of suicide in Indigenous communities, where one state of being is prioritized over the other: life and death, individual and community, past and present. As Lisa Stevenson posits: "What if staying alive has something to do with witnessing the death in life? What if dying and being born alongside those who love you is also a way of being alive? How might we come to care for life that is constitutively beside itself, life that could never be fully itself?" (5: p.18) To better understand the epidemic of Indigenous suicide, we should move beyond our own conceptions of life and death, and explore how their meanings may differ for a population that has spent its existence resisting an oppressive set of institutions, ideologies, and individual actors.

Suicide in Indigenous communities addresses a contradiction in the settler colonial logic, whereby the promotion of mental health and the prevention of suicide exist in contention with colonial narratives of elimination and a dying nation (14). Stevenson states: "...the ultimate irony of such forms of anonymous care in the colonial/post-colonial context is that caregivers exhort Inuit to live while simultaneously expecting them to die" (5: p.7). Mary-Ellen Kelm suggests that children in residential schools may have "committed suicide to assert control over their bodies" (3: p.154). Do self-destruction and self-harm contribute to the elimination of Indigenous peoples, or do they challenge structural genocide and the "letting die" of these communities? Can these contradicting notions exist at the same time? How do notions of cosubstantiality play into the narrative of suicide as a form of self-control and resistance? Stevenson argues that ethnographers should move beyond the desire for truth and certainty, and begin to embrace the uncertainties that permeate the commu-

nities we study. Perhaps if we begin to embrace the uncertainties of the meanings of life and death, as well as the contradictions between resisting biopolitics and understanding cosubstantiality, then it is possible to create a space in which meaningful responses to the suicide crisis can emerge. Larger and more systemic challenges to settler colonialism, including the reallocation of land, will be crucial components of a sustainable and community-based response to this crisis.

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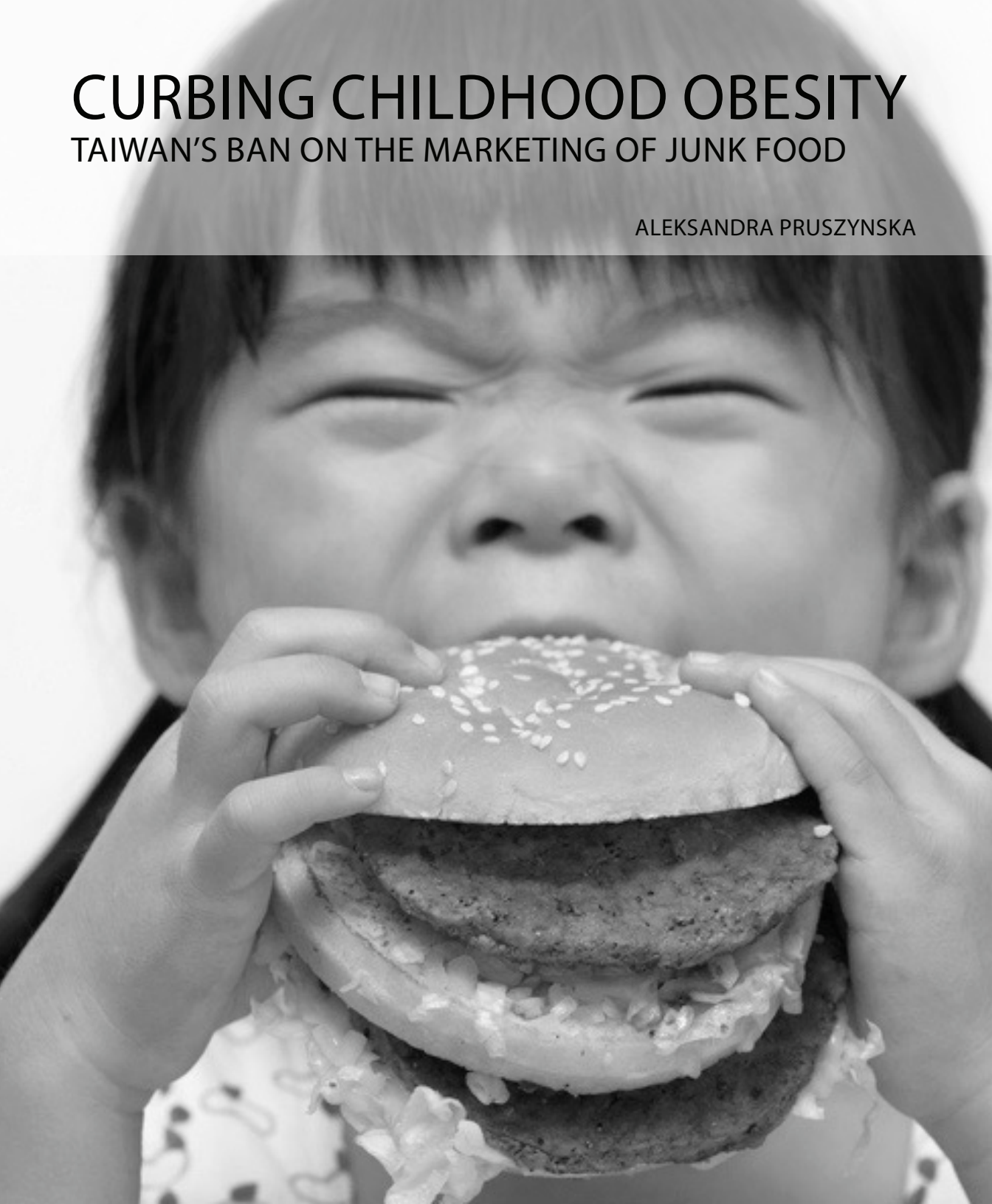
CURBING CHILDHOOD OBESITY

TAIWAN'S BAN ON THE MARKETING OF JUNK FOOD

ALEKSANDRA PRUSZYNSKA



Childhood obesity in Taiwan, as in Canada and many other countries, has been steadily increasing in recent years (1,2). To address this problem, Taiwan's Ministry of Health banned the marketing of junk food on television to children in January 2016. This paper examines the implementation of Taiwan's law, and offers observations on the food industry's response to the law. Three distinct behaviors of the food industry in Taiwan were observed. First, in May 2016, fast-food corporations marketed few food groups. Second, McDonald's adapted their marketing strategy. Third, McDonalds improved the nutritional content of the Happy Meal.

Background

Globally, non-communicable diseases (NCDs) were the leading cause of premature mortality in 2015 (3). The four main types of NCDs are cardiovascular diseases (e.g. heart attacks and stroke), cancer, chronic respiratory diseases (e.g. chronic obstructive pulmonary disease and asthma), and diabetes. A common risk factor for three of these four NCDs is obesity. Based on the emerging problem of childhood obesity, scholars predict that NCDs will start to affect populations at a younger age, which means that the number of deaths due to NCDs will continue to rise. Consequently, public healthcare professionals advocate for interventions that target childhood obesity. One strategy to decrease childhood obesity is to ban the marketing of junk food to children. In January 2016, Taiwan implemented a ban to address childhood obesity, and the reaction of the Taiwanese food industry reveals valuable insights about this health policy.

In Taiwan, the primary advocacy for this policy came from the Child Welfare League Foundation, a non-governmental organization (NGO) devoted to improving child welfare services. One of the issues for which they advocated was the ban on the marketing of junk food to children. The organization achieved three advocacy milestones. First, they conducted a nationwide survey of 1,351 elementary and middle school students assessing their TV viewing habits (4). Second, the Foundation's Research and Development Director, Chiu Ching-hui, stated publicly that "even adults would be tempted by the ads to buy junk food, let alone young children" (5). Third, Alicia Wang, a former CEO of the Child Welfare League Foundation, became a legislator of the Chinese Nationalist Party (KMT) and strongly supported the ban. Additionally, Dr. Nain-Feng Chu, a researcher working for the Ministry of Health on the topic of childhood obesity, explained that this ban was implemented one year after Taiwan's health ministry began a campaign to inform the Taiwanese population about the dangers of trans and saturated fats (6). These types of fats are often used in the preparation of the deep-fried products sold in the popular Taiwanese night markets. Creating an awareness about the negative health consequences of the consumption of trans and saturated fats made it easier for the general public to understand the rationale behind the ban of marketing junk food to children.

The policy to ban the marketing of junk food during children's TV programming in Taiwan defined junk food as foods with fat exceeding 30 percent of the total calorie count, foods with saturated fat exceeding ten percent of the total calorie count, foods with an excess of 400 milligrams of sodium per serving, and foods where added sugars make up over ten percent of the total calorie count (7).

The ban prohibits the marketing of junk food on five children's TV channels between 5:00pm and 9:00pm, the most popular viewing hours. During restricted advertising times, ads cannot be aired on television channels that target children and should not include certain phrases or representations that market unhealthy food as a substitute for a healthy meal. However, such ads can still be aired in other time slots, or on channels not targeting children, such as news channels. There is also a complete ban on the promotion of complimentary toys given out with meals, a common marketing technique among fast food chains which are becoming increasingly popular in the big cities in Taiwan. Additional promotions, such as offering a toy or gift for an additional price wi–––th the purchase of a product, are similarly banned.

Moreover, any company marketing junk food on children's TV channels faces a penalty between NT$40,000 (US$1,189) and NT$4 million (US$118,917). Advertisers can also be asked to correct the content of the ad if it is deemed a serious violation, and can be fined up to NT$600,000 (US$ 19,104) if they refuse to stop airing the ads. Health departments are tasked with supervising companies which includes increasing inspections (5). The government also established a phone line, which anyone can call to report illegal activities, thereby allowing parents and those concerned about children's health to help enforce the law.

Methods

A three-day sample (two weekdays and one weekend day) was collected by watching the children's TV channel, YOYO TV, within the time specified by the policy between May 20th and May 31st 2016. Short videos and pictures of the food advertisements were taken, and the type of each food advertisement was recorded. Additionally, a McDonald's advertisement and Happy Meal menu were analyzed.

Results

Overall, this study observed three reactions of the food industry. First, few categories of food were marketed to children. Second, McDonald's promoted their brand without breaking the law. Third, the children's menu at McDonald's in Taiwan became more nutritious.

The marketing after the implementation of the ban included four main types of foods. First, foods high in sugar were still advertised, though it is uncertain whether these foods meet the criteria of junk food, or whether the industry was trying to advertise these products despite the risk of a fine. The foods advertised included ice-cream and a snack made of a mix of juice and dried fruits. Second, ready-to-eat vegetables, tofu, sausages and eggs sold in 7/11 stores were frequently advertised. Third, an ad featuring nutritional supplements for children who have low appetite was featured.

Additionally, outside of the three-day sample, an advertisement for McDonald's was analyzed. In this TV advertisement, McDonald's encourages children to read books, and in a subtle way, promotes its brand. In the ad, parents concerned about the noise coming from their child's bedroom are relieved to find their child engaged in reading a pop-up book.

Later in the ad, the book that the boy is holding appears to be magical, with sparks and playful music accompanying it. A monkey then places the book among other books and a McDonald's Happy Meal Box.

During the entire 25-second advertisement, no images of food sold by McDonald's appear; only a symbol of McDonald's, a Happy Meal box, and a McDonald's logo are present. McDonald's is using a clever strategy to promote their brand to children without advertising junk food.

Moreover, in anticipation of the future law, McDonald's improved the nutritional content of its Happy Meal two months before the implementation of the ban (9). In May 2016, the MacDonald's Happy Meal in Taiwan replaced French fries with a choice of a corn cup, a small salad, or a fruit bag, and replaced pop with a choice of orange juice or milk . The fast food giant has continued to improve the nutritional content of its menu, and in January 2017, McDonald's added protein-rich chicken bites to the menu.

Discussion

The ban on the marketing of junk food in Taiwan may have prompted some changes in the behavior of the food industry. While it is not clear whether it is a direct result of the ban, in May 2016, junk food advertisements were rare, whereas advertisements for healthy food choices, such as for seasoned vegetables and milk were common. Additionally, nutrient-poor foods such as American sliced cheese, common in the western diet, were advertised as a healthy food. This type of advertisement reflects a dangerous tendency of the food industry – aiming to replace the traditional diet with low quality food.

While not all fast food corporations are alike, McDonald's can be used as a fair representation of the junk food industry in Taiwan. McDonald's reaction was strong, although it is unclear whether it was a reaction to the ban, or simply an adaptation to the increasing public awareness of the negative consequences of junk food. First, to advertise their products without breaking the law, McDonald's adopted new marketing strategies. McDonald's aired the previously-mentioned ad on adult TV stations, rather than on children's stations restricted by the ban. Additionally, McDonald's provided customers of Happy Meals with books. Dr. Nain-Feng Chu clarified that the ban restricts the promotion of junk food, but it cannot stop the food industry from providing gifts, especially if they have an educational purpose (6). McDonald's behavior highlights the fact that implementation of the ban is just a first step in the efforts to stop the marketing of less healthy products to children. This type of law requires constant improvement as new marketing techniques continue to evolve. Secondly, McDonald's improved the nutritional content of its menu two months before the law was implemented. Overall, creating public awareness about the importance of nutrition has been highly successful for Taiwan's Ministry of Health. It is reasonable to expect that other fast food chains will follow McDonald's lead.

Conclusion

The analysis of Taiwan's ban on the marketing of junk food to children provides insight into the components required to successfully implement such a law. First, before advocating for a specific intervention, it is important to analyze the food culture of the society to which it is applied. Second, to establish the legislation, political will is essential. Third, the public must understand the rationale for an intervention before the law is implemented. Fourth, while a punishment for non-compliance to the law might not be sufficient to stop the marketing practices of a company, it emphasizes the importance of the law. In addition, establishing a phone line or

other form of communication to report illegal actions allows citizens to engage with the law. Finally, public awareness can encourage the food industry to improve the nutritional content of foods, which can help curb the childhood obesity epidemic.

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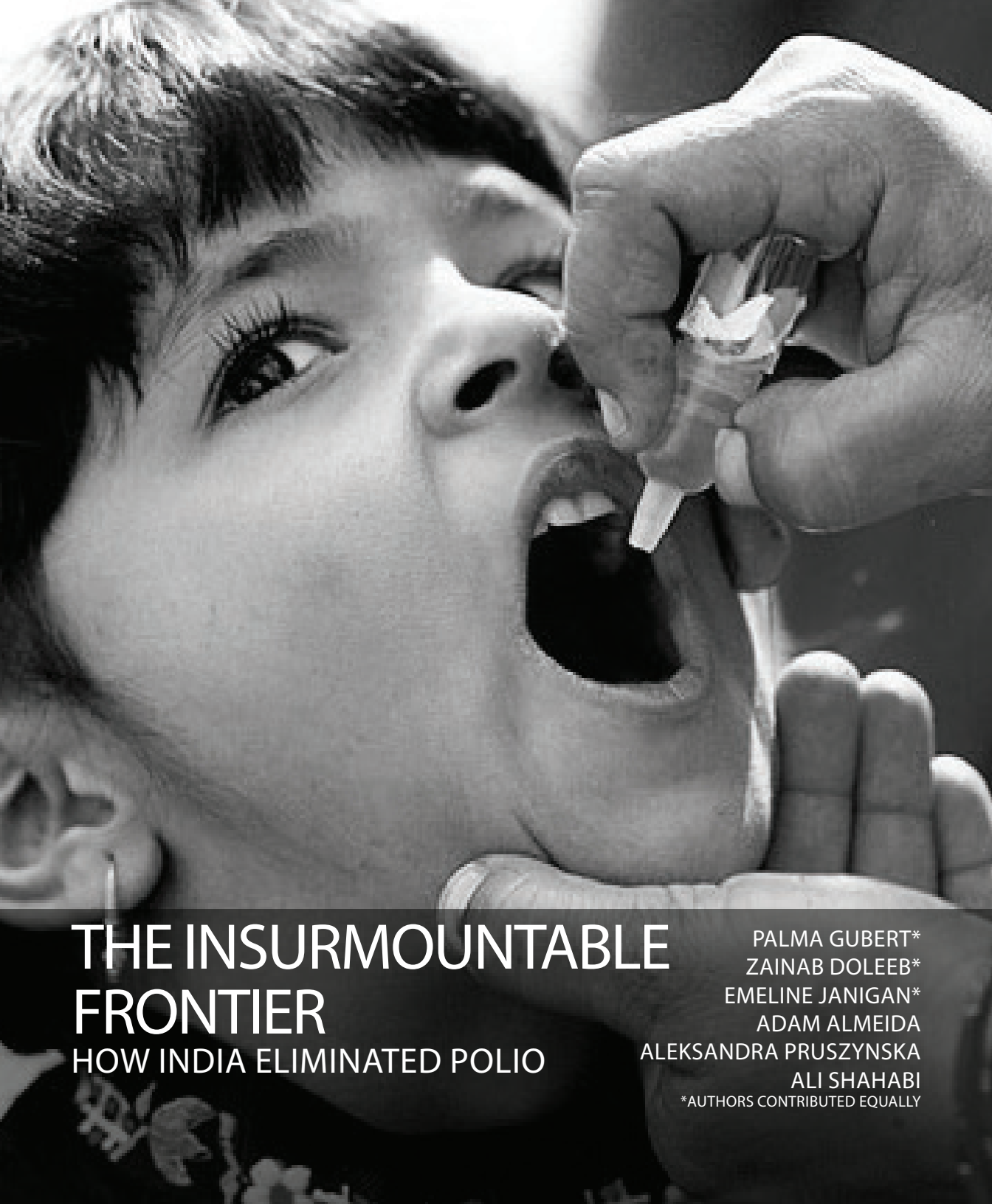

THE INSURMOUNTABLE FRONTIER

HOW INDIA ELIMINATED POLIO

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This case study evaluates India's efforts to eliminate all poliovirus strains in the country. This was done through massive immunization campaigns that targeted specific and marginalized groups, public awareness campaigns, and an emphasis on nation-wide surveillance. Ultimately, polio was successfully eliminated in India and the country averted 1.48 billion disability-adjusted life years. The number of cases declined from 200,000 in the 1970s to 400,000 in the 1980s, and finally to zero cases in 2012. This case owes its success to political will, coordinated inter-sectoral collaboration, significant funding (over US$2.4 billion from multiple contributors), and persistent efforts to immunize all children.

Background

Poliomyelitis ("polio") is an infectious virus that can lead to paralysis or death. There are three serotypes of the wild poliovirus (WPV): WPV1, WPV2, and WPV3. Although polio is incurable, vaccines have helped to eliminate the virus in most countries around the world. In 1953, when 35,000 children per year in the United States were being disabled by polio, Jonas Salk developed the inactivated poliovirus vaccine (IPV). As a result, incidence of polio in the United States fell by 85 to 90% between 1955 and 1957. In 1962, another breakthrough occurred when Albert Sabin produced the oral poliovirus vaccine (OPV), which was less expensive and logistically easier to administer (1).

The global success of polio vaccination quickly became evident. By 1988, polio had disappeared from the United States, the United Kingdom, Australia and much of Europe, but remained prevalent in more than 125 countries. The World Health Organization (WHO) certified Latin America polio free in 1994, the Western Pacific region (including China) by 1997, and all of Europe by 2002 (2). India officially eliminated polio in 2014. As of 2016, Nigeria, Pakistan and Afghanistan are the only remaining countries that are not polio-free (3).

Eliminating polio in India was once seen as an insurmountable challenge due to its large and mobile population, extreme poverty, and poor sanitation, among other impediments (4). The elimination of polio was considered of secondary importance to that of other diseases such as malaria, leprosy, tuberculosis, and visceral leishmaniasis (kala azar). This further hindered efforts to stop its transmission (5). Once the Indian government prioritized polio, it provoked multilateral collaboration from non-governmental organizations and public and private parties from within and beyond the country. Ultimately, in 2011, India detected its last case of polio (6).

The Strategy: Pre-2000

In 1974, the WHO launched the Expanded Programme on Immunization (EPI) with the aim of reaching all children with necessary vaccines. In 1978, the EPI was adopted by India, which accounted for at least 50% of the world's polio burden at the time (4, 7).

In 1979, the trivalent oral poliovirus vaccine (tOPV) was introduced in India (7). The tOPV protects against all three serotypes of poliovirus, and is administered orally, without the need for trained health professionals, sterile settings, or syringes (8).

Between 1978 and 1982, 104 million children were immunized with DPT (a combination vaccine against diphtheria, tetanus, and polio), and 4.1 million with three doses of tOPV. Despite these efforts, in 1981 India experienced a nationwide polio epidemic (7). From the 1970s and into the early 1990s, polio was still hyper-endemic in India, with 200 to 400,000 cases annually. In 1985, Rotary International introduced tOPV as part of its Universal Immunization Programme with the aim of reaching all Indian districts (5). Due to the low immunogenic efficacy of tOPV during the 1970s and 1980s, the number of polio cases reported in vaccinated children skyrocketed (7).

By 1988, polio was finally on the decline in India, which John and Vashishtha, in a 2013 study, attribute to increasing vaccine coverage and growing herd immunity (7). That same year, the World Health Assembly resolved to target polio for global eradication by the year 2000, a decision which India supported. The WHO promoted four strategic components to accomplish this task: achieve and maintain high OPV coverage, augment regular immunization with supplementary doses of OPV (Supplementary Immunization Activities, or SIAs), increase systematic polio surveillance with support from virology laboratories, and use local OPV campaigns to interrupt any remaining clusters of WPV transmission (7).

In 1995, the Global Polio Eradication Initiative (GPEI), together with the WHO, UNICEF, the Centers for Disease Control USA (CDC), and Rotary International, designed the National Polio Surveillance Project (NPSP), a joint initiative by the WHO and the government of India (7). NPSP supported the Indian government by providing technical assistance and monitoring for routine OPV immunization, acute flaccid paralysis (caused by polio) surveillance, and SIAs (9). At the time, roughly 50,000 individuals were still contracting polio each year in India (6).

In the same year, Pulse Polio Immunization (or PPI, formerly SIAs) was launched by the Indian government. The program consists of two annual National Immunization Days (NIDs) on which children were vaccinated at fixed booths (10). There were over 700,000 vaccination booths in each campaign, staffed by 2.5 million vaccinators (11). Approximately 172 million children received vaccinations on each NID (12). Local community mobilizers encouraged members of the community to immunize their children on NIDs, and the program was publicly supported by religious leaders and celebrities. By 1991, 53% of Indian babies had received OPV, and 73% by 1997 (5). By 1999, after nationwide PPI campaigns, WPV2 was eliminated from India, but WPV1 and WPV3 continued to circulate (10).

Post-2000

Since the objective of eradicating polio before the turn of the century was not met, efforts in India began to intensify in the year 2000. Four rounds of PPI took place nationally in the fall and winter, with two additional rounds occurring sub-nationally in eight states with low EPI coverage. In the same year, the WHO and NPSP strengthened virology laboratories to intensify virological surveillance of WPV transmission (10). WPV transmission could not be interrupted in the states Uttar Pradesh (UP) and Bihar, despite PPI campaigns reaching 94-95% of targeted children (7). As a result, PPI began house-to-house vaccinations in addition to booth immunization. By 2001, WPV transmission exclusively took place in these high-risk states (10).

To combat lack of access to tOPV, the 'under-served' strategy was launched in 2003 to target specific marginalized communities in UP, including Muslims, migrants, and other socioeconomically disadvantaged groups who were often missed in routine tOPV immunization campaigns and National Immunization Days (NIDs) (5). It became clear in 2004 that the migrant population that travelled for seasonal work needed to be prioritized, and thus the 'transit vaccination' strategy was implemented, with vaccination teams working out of bus stands, railway stations, markets, and other points of transit (7).

In 2005, the monovalent OPVs type 1 and 3 (mOPV1 and mOPV3) were licensed in India. These monovalent vaccines only confer immunity to their respective virus serotype and demonstrate increased efficacy compared to tOPV (7). Uttar Pradesh and Bihar began to use mOPV1 and mOPV3 later that year, and continued to invest in the under-served and transit vaccination strategies (13). After 2005, PPI campaigns were increased to ten times per year to compensate for low routine coverage. The quality of polio surveillance was also bolstered such that poliovirus transmission could be quickly detected anywhere in India (7).

In 2006, the inactivated poliovirus vaccine (IPV), which provides immunity against all three polio strains, was licensed in India. The India Expert Advisory Group (IEAG) began limited use of supplemental IPV dosing in Uttar Pradesh, in addition to mOPV1 and mOPV3, and focused efforts began to specifically eliminate WPV1 (7, 9).

In 2009, the IEAG announced their 107-block plan to focus on high-risk areas of Uttar Pradesh and Bihar (9). The IEAG recommended combining mOPV1 and mOPV3 to create the bivalent oral poliovirus vaccine (bOPV). By the end of 2009, WPV1 had nearly disappeared and thus WPV3 elimination was prioritized (10). In January 2010, bOPV was added to PPI campaigns. In 2010, 42 cases of WPV were detected, and in 2011, only one case was detected. In 2011, the average rate of unvaccinated children under two years old was 1.8% in Uttar Pradesh and 0.3% in Bihar (6).

Since its initiation in India in 1995, through collaboration with the government-run PPI and the WHO, the National Polio Surveillance Project provided 12.1 billion doses of OPV to India (11). In 2012, no WPV was detected and India was deemed polio-free. The WHO declared that India had successfully eliminated polio in March of 2014 (6).

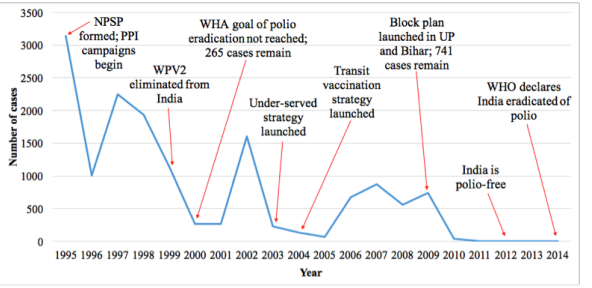

Figure 1. Total number of wild poliovirus cases in India, 1995 to 2014 (7, 14-16).

Health Impact

A study by Nandi et al. analyzed India's elimination initiative from 1982 to 2012 by calculating the variation in paralytic polio cases, polio-related deaths, and disability-adjusted life years (DALYs) (12). The authors chose 1982 as a start date for their analysis, as OPV was only introduced in India sporadically between 1978 and 1982. They created a hypothetical counterfactual model in which the polio campaign did not occur, through which

it was determined that the polio campaign prevented 3.94 million paralytic polio cases, 394,000 deaths, and 1.48 billion DALYs from 1982 to 2012.

Furthermore, as a consequence of the polio elimination campaign, improvement of routine immunization (RI) and primary healthcare have been observed in India. India's 107-block plan concentrated its efforts on upgrading RI, decreasing rheal rates, increasing breastfeeding, and improving sanitation. Encompassed in this strategy was an attempt to attack multiple issues rather than solely focusing on polio vaccination. A mass education campaign took place to spread information about the aforementioned issues, and this multifaceted approach was a contributor to the success of the eradication initiative. The campaign effected change in multiple areas of health by strengthening several programs, and ultimately enhanced routine immunization and primary healthcare while simultaneously helping to eradicate polio (17).

Financing & Cost-Effectiveness

As the possibility of worldwide polio eradication increases, the list of polio-endemic countries shrinks; polio eradication is no longer a region-specific issue, but rather a global fight. Most countries and organizations that have contributed funds to fighting polio have done so towards the global eradication effort as opposed to funding specific countries, creating difficulty in determining India-specific polio funding. Additionally, the timeline of funding is not straightforward due to the length of the polio eradication campaign. However, a general, though not absolute, understanding of the stakeholders in this initiative may be deduced from the existing literature.

Several donors have contributed specifically to India to combat polio, including the Global Alliance for Vaccines and Immunization (GAVI), Rotary International, Germany (via the GPEI), and the government of India. According to the WHO, the Indian government is one of the biggest contributors to the polio campaign. India's initiative was mostly self-funded; as of 2013 the Indian government had contributed US$2 billion towards polio elimination (18). GAVI, the public-private partnership devoted to increasing vaccination rates in developing countries, provided US$16,531,545 to India for IPV support between 2000 and 2016 (19). In addition, in 1985, Rotary International, an international service organization, introduced their PolioPlus program with the goal of immunizing all children against polio. Since its inception, PolioPlus has contributed US$176.5 million towards polio efforts in India (D. Green, December 8, 2016). Germany has provided approximately $275 to $314 million to India since 2005 (20-26).

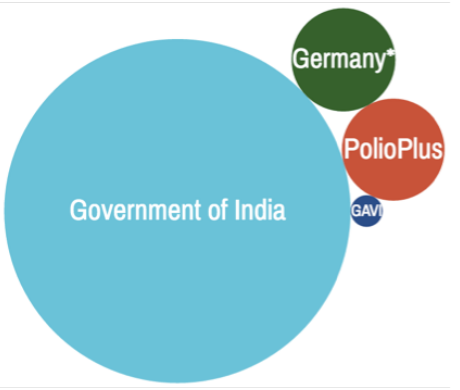

Figure 2. Approximate proportional spending by the government of India, Germany, PolioPlus, and GAVI towards polio elimination in India up to 2016.

*This is an estimated value because Germany's donations towards polio in 2007 and 2008 were split between India and Nigeria. It is not stated how much each country received from the donations. We estimated the funds were split evenly between the two countries.

Nandi et al. estimated the overall growth in productivity in India as a result of the polio campaign at US$1.71 trillion from 1982 to 2012 (12). If polio is eradicated globally, it is predicted that the net benefits will range from US$40 to 50 billion in the twenty years post-eradication, almost 85% of which will directly accrue to low-income countries (27). Although these benefits in productivity and health are profound, they must be evaluated in the context of the costs of vaccination. Prinja et al. determined the cost of vaccination for polio as US$28 per child (28).

Challenges & Reasons for Success

The GPEI accurately anticipated that India would be one of the most difficult countries in the world in which to eliminate polio. India faced several challenges such as a weak civic infrastructure for distributing vaccines, an inadequate public healthcare system, and a large mobile population prone to missing routine immunizations. In a nation with a population of more than 1.2 billion, a sizeable portion of India's inhabitants live in remote mountainous areas that are difficult to reach for vaccination. Poor sanitation and endemic diarrhea in Uttar Pradesh and Bihar, the two most populous northern states, intensified WPV transmission (10). Further exacerbating the problem, tOPV did not provide adequate immunity, leading to a rise in polio cases among already-vaccinated children throughout the late 1970s and early 1980s (7). Many communities also resisted immunization out of fear that vaccines were a covert sterilization effort from the Indian government, among other misconceptions (10). A feasible approach to elimination in India had to address each of these challenges.

Ultimately, the commitment of the Indian government toward its goal of eliminating polio was the key to success for this initiative. India's government was highly involved in the elimination process, taking ownership of the effort throughout. This included direct supervision and regular review of the GPEI program by the Prime Minister's office, as well as chief ministers taking control of elimination in their own endemic states (10).

However, the Indian government did not achieve polio elimination on its own. Collaboration between the government, non-governmental organizations, the public and private health sectors, and the general public was paramount to India's success. Organizations such as Rotary International, WHO, UNICEF, CDC USA, and the Bill and Melinda Gates Foundation contributed to the finances and labour that allowed for the realization of this enormous goal (29).

The polio elimination campaign relied on involvement of leaders from various societal spheres. Academic bodies, including the Indian Academy of Pediatrics, helped build community awareness by debunking the misconceptions surrounding polio vaccination (10). The use of religious leaders, iconic film personalities like Amitabh Bachchan, cricket players, and radio and television to support polio vaccination influenced the public to have their children immunized on NIDs (30). These combined efforts helped communicate the campaign to the public.

To address the shortage of healthcare workers needed to immunize all targeted children, the Indian government recruited more public health nurses and social workers. They also trained volunteers from all backgrounds - mothers, students, community leaders, and religious clerics - to work at vaccination booths and speak to families about upcoming immunization dates. Schoolchildren also organized and participated in large rallies to raise awareness about polio immunization (30).

There were two pervasive myths hindering the polio elimination effort. The first was the belief among certain Muslim communities that the polio vaccine was part of the Indian government's effort to sterilize Muslims again just as it had in 1975-1977 (36). The second was a misconception that a previously immunized child did not require further dosage. In fact, many parents believed that more than one dose was harmful to the child. To address the first myth, the Indian government enlisted the help of the Ulema, a council of Muslim clerics, who led public campaigns to dispel fears about sterilization. They made announcements at mosques and distributed signed letters ensuring the safety of the vaccines. To counter misinformation regarding the safety of additional vaccinations, the anti-polio campaign produced public service announcements on television educating parents as to why supplemental doses of the polio vaccine were not harmful, and were in fact essential for full immunity. The government also trained volunteer immunizers on how to persuade reluctant parents to vaccinate their children (30).

With an enormous population and lack of comprehensive health surveillance infrastructure, efficient management of the campaign was essential. Through the house-to-house strategy, for example, health workers used a house-marking system to indicate the vaccination status of each residence (30). Simple innovations, such as tracking newborns and mapping missed children, also helped facilitate widespread OPV delivery. (10).

Future Directions

Although India has eliminated wild poliovirus, the threat of vaccine-derived poliovirus (VDPV) remains. This can occur in the rare instance when the attenuated form of the virus from OPV mutates into a virulent strain. Poor sewage and contaminated water sources facilitate transmission of VDPV (31). To avoid a large VDPV outbreak, India should transition towards IPV while simultaneously strengthening its health and sewage infrastructure.

IPV, which avoids the risk of VDPV, is also more efficacious compared to OPV, though it must be injected rather than administered orally. GPEI and GAVI have been working to introduce IPV into routine immunization in India since November 2015. However, a full switch from the OPV to the IPV has not yet taken place due to shortage of supplies and difficulties with storing IPV which requires cold-chain management (32). Today, India's vaccination of infants against polio involves either a single dose of intramuscular IPV at fourteen weeks of age, or two fractional doses of intradermal IPV at six and fourteen weeks of age. Primarily as a result of cost restraints, no IPV will be given to children above this age group (A.S. Bandyopadhyay, December 10, 2016).

Furthermore, given that India shares a border with Pakistan, a nation which still has active polio cases, there is concern regarding the possible reintroduction of polio into India. The Indian government has thus mandated polio vaccine requirements for

travelers moving to and from polio-endemic countries in order to mitigate this threat (33). India continues to utilize the NPSP, a system which Dr. Nata Menabde, WHO Representative to India, claims "surpasses all quality performance indicators and standards that are recommended globally for such a system" (34). Such a program could be adapted to track the elimination of other communicable diseases, like malaria and visceral leishmaniasis.

The NPSP is the hallmark of India's current prevention strategy. It was set up by the WHO in 1997 to help support the government with early detection. As part of this large initiative, the program enrolled more than 40,000 health facilities from the private, public and informal sector to report on paralytic cases. As part of protocol, stool specimens are gathered and sent to one of eight WHO-accredited labs in the country to test for polio. Presently, this data is instrumental in identifying targeted populations to prevent future outbreaks (34). The NPSP has also expanded to monitoring for measles, Japanese Encephalitis and other immunization campaigns (35).

The challenges and successes encountered by India in this long process may serve as a guide for other countries still battling polio. By following India's example of consistent effort, supplemented with political will and international support, Nigeria, Afghanistan and Pakistan may soon eliminate polio, thus bringing the world closer to the goal of global eradication.

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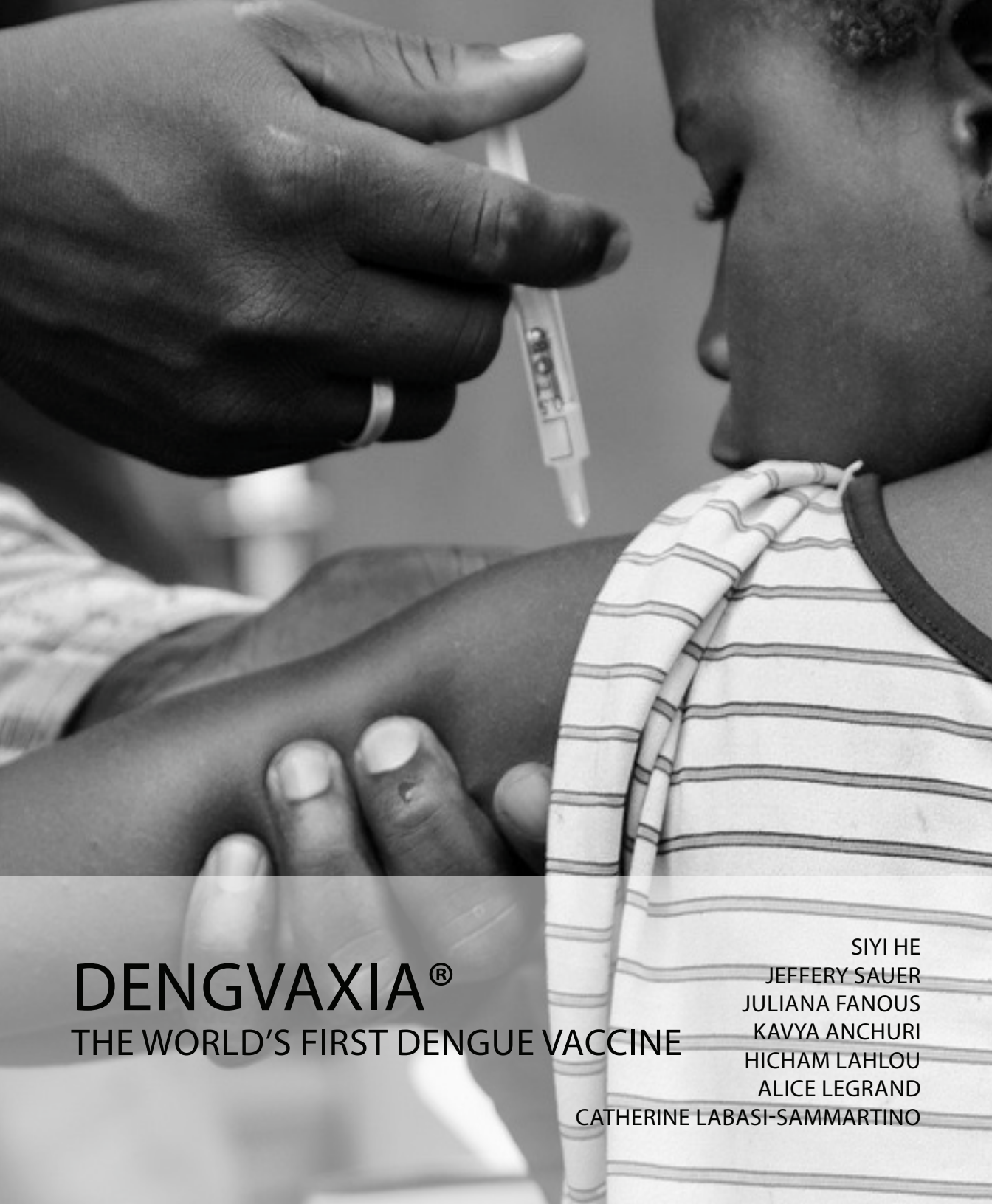
Appendix

bOPV: bivalent oral poliovirus vaccine
CDC: Centers for Disease Control
DALYs: disability-adjusted life years
DPT: diphtheria, polio, and tetanus vaccine
EPI: Expanded Programme on Immunization
GAVI: Global Alliance for Vaccines and Immunization
GPEI: Global Polio Eradication Initiative
IEAG: India Expert Advisory Group
IPV: inactivated poliovirus vaccine
NIDs: National Immunization Days
NPSP: National Polio Surveillance Project
OPV: oral poliovirus vaccine
PPI: Pulse Polio Immunization
RI: routine immunization
SIA: Supplementary Immunization Activities
tOPV: trivalent oral poliovirus vaccine
UP: Uttar Pradesh
VDPV: vaccine-derived poliovirus
WHO: World Health Organization
WPV: wild poliovirus



DENGVAXIA®

THE WORLD'S FIRST DENGUE VACCINE

SIYI HE
JEFFERY SAUER
JULIANA FANOUS
KAVYA ANCHURI
HICHAM LAHLOU
ALICE LEGRAND
CATHERINE LABASI-SAMMARTINO

Dengue fever is considered a Neglected Tropical Disease (NTD), as it both affects predominantly resource-limited countries and highlights the need for increased research and development (R&D) (1). The situation has become critical given that transmission of dengue has increased in both frequency and magnitude, and has expanded to new areas. However, over the last two decades, dengue R&D has grown extensively, particularly in the vaccine division of the pharmaceutical company Sanofi, which has led to the development of the world's first dengue vaccine: Dengvaxia®. Concerns have now surfaced regarding the vaccine's efficiency, specifically amongst children younger than 9 years of age, and in low-transmission areas. Therefore, the creation of Dengvaxia® is not the final step towards the eradication of dengue. R&D must not only continuously seek an improved version of Dengvaxia®, but should also consider other dengue vaccine candidates, and improve distribution of the vaccine in all affected countries.

Background

Dengue fever is a viral disease, transmitted predominantly by the Aedes aegypti mosquito vector. It is characterized by a multitude of clinical manifestations, including symptoms such as headache, muscle/joint pain, nausea, sore throat, and rash (2). While dengue fever is self-limiting in the majority of cases, secondary infections can lead to more severe presentations, notably dengue hemorrhagic fever (DHF) (3). There are four distinct strains (or 'serotypes') of the dengue virus, all members of the Flaviviridae virus family: DENV-1, DENV-2, DENV-3, and DENV-4, each capable of giving rise to an epidemic. Regions labeled as 'hyperendemic' show infection from multiple strains, while 'hypoendemic' areas only show infection from one strain (4).

Descriptions of symptoms consistent with dengue fever have been found in a Chinese medical encyclopedia dating back to 265-420 AD, while epidemics of dengue in what is now considered the West Indies and Central America were reported in the 17th century. The A. aegypti mosquito had spread to urban coastal areas worldwide by 1800 due to rapid industrialization and increased far-range transportation. By the end of World War II, hyperendemicity and DHF had emerged in Southeast Asia. Following decades of mosquito control efforts attempting to suppress A. aegypti in the Americas, many eradication programs initiated by the Pan-American Health Organization (PAHO) were discontinued in the 1970s (3). By 1995, dengue incidence had reverted to pre-intervention levels in the Americas and Pacific regions. Global incidence of dengue has since increased rapidly, particularly in the last fifty years (3).

Efforts to estimate global disease incidence yield a figure of 50-200 million clinically observable infections per year worldwide, though the risk of contracting dengue is greatest in the Americas and Asia (5). The year 2015 saw outbreaks of dengue worldwide, most notably in Brazil, Malaysia, the Philippines, India, Hawaii, and the Pacific Islands. Approximately 500,000 people are thought to require hospitalization due to DHF each year, of which approximately 20,000 cases are fatal (3). Together, both fatal and non-fatal presentations of dengue account for 1.14 million disability-adjusted life-years (DALYs) lost in 2013 (6).

Stanaway et al. (2016) show the percent increase in DALYs lost due to dengue from 1990-2013 in various regions of the world, demonstrating a robust, progressive escalation of the global burden of dengue (6). However, the true incidence of dengue may be larger than reported, as 3.9 billion people across 128 countries are thought to be at risk of dengue infection (2).

From a biomedical standpoint, there are several obstacles to the development of a successful dengue vaccine. Firstly, the most challenging obstacle to recognize is that secretion of neutralizing antibodies in response to a weakened dose of dengue does not alone signify acquired immunity from natural infection or the next encounter with the dengue virus (13). As vaccine trials which assess the efficacy of a vaccine usually rely on the host's seroprevalence of antibodies mounted against the pathogen in question, this particular obstacle renders such an approach unviable. Rather, longitudinal studies of vaccine efficacy need to be performed in the field --in regions where dengue is endemic --with long-term follow-up of vaccine recipients to observe their resistance (or lack thereof) to subsequent exposure to dengue. As a result, any new vaccine to be developed for dengue prevention will be far more expensive in the R&D stages than for other diseases for which a simpler, more rapid marker of acquired immunity exists.

Secondly, non-human primates do not develop overt dengue fever, which poses a challenge for testing potential treatments in non-human models. Thirdly, each of the four dengue virus strains is antigenically distinct, such that the immunological response mounted by an infected patient is different against each strain. The lifelong immunity conferred via infection by one serotype does not protect from the other three serotypes, leaving the patient susceptible to secondary infection. Thus, an effective vaccine would have to be multivalent, providing immunity against all four serotypes, in order to prevent both primary and subsequent infections. However, multivalent live vaccines can cause interference between serotypes (7), meaning that the vaccine recipient will only mount a robust immune response to one or two of the serotypes. Fourthly, there is a risk that dengue vaccination could result in antibody-dependent enhancement (ADE). ADE occurs when non-neutralising antiviral proteins facilitate virus entry into host cells, leading to increased infectivity in the cells. It is an important risk to take into consideration because a partially effective vaccine as Dengvaxia® may increase the severity of natural infections, as secondary infections are more severe in some cases. Finally, the dengue vaccine, when co-administered with previously established vaccines, should not have undesirable effects. This is a complicated issue to consider, given that different countries have diverse immunization programs and schedules (8).

Before 1970, only nine low-and-middle-income countries (LMICs) had experienced severe dengue epidemics (3). Yet, while low-income countries (LICs) were financially incapable of investing in a vaccine, high-income countries (HICs) did not support the project because dengue neither affected their populations nor threatened their security. However, the burden of disease has shifted geographically, as the disease is now endemic in more than 100 countries and cases have been identified in France (in 2010) and in Florida (in 2013), among others. In fact, "threat of a possible outbreak of Dengue fever now exists in Europe" (2). In HICs, dengue and the mosquito vector accompany travelers returning from dengue-endemic countries.

Furthermore, endemic areas of the mosquito vector are expanding as the range of suitable environmental conditions for its reproduction is increasing due to climate change (10). Indeed, Monaghan et al. posit that by 2061-2080, A. aegypti habitat "would increase by 8% under moderate emissions pathways" (11). Evidently, the spread of the disease has prompted a call for intervention.

The Call for Intervention

Despite efforts to control dengue, based primarily on vector control and case-management, both the costs and burden of disease have continued to grow. Prevention of dengue by vaccination has become necessary to cope with these concerns (12). Historically, the development of a safe and effective dengue vaccine has faced many challenges (13, 14). In the last decade, vaccine development efforts have increased dramatically due to a heightened awareness of the dengue pandemic (15). Sanofi Pasteur, the vaccines division of Sanofi, has developed a recombinant, live-attenuated tetravalent dengue vaccine. A live-attenuated viral vaccine actively replicates in the host, resulting in an array of wild virus-like antigens, which could potentially provoke a response similar to natural immunity (16). CYD-TDV, branded Dengvaxia®, was licensed in 2015 as the first dengue vaccine. To date, eleven countries have approved the vaccine (17). In April 2016, the World Health Organization (WHO) recommended that dengue-endemic countries consider using Sanofi Pasteur's Dengvaxia® "to immunize populations with high levels of dengue endemicity, aged between 9 and 45 years old" (18).

Vaccine Development and Implementation

Phase I clinical trials: small-scale trials conducted to assess vaccine safety in humans.
Phase II clinical trials: larger trials that mainly assess the efficacy of the vaccine against artificial infection and clinical disease. Vaccine safety and side-effects are also studied.
Phase III clinical trials: conducted in a large pool of subjects across several sites to evaluate efficacy under natural disease conditions. If the vaccine retains safety and efficacy over a defined period, the manufacturer can request the regulatory authorities for a license to market the product for human use.

Results of Clinical Trials: Phases I, II, III

Ten years of Dengvaxia® clinical trials were conducted prior to the successful completion of Phases I-III in 2014, involving 25 clinical studies in 15 countries worldwide. More than 40,000 volunteers were enrolled in the clinical studies, and 29,000 of them received Dengvaxia®. The vaccine demonstrated protection of 67% of these participants against dengue (15).

A Phase IIb study (CYD23) – observer-masked, randomized trials – was conducted in healthy Thai schoolchildren aged 4–11 years. In Ratchaburi, Thailand, 2669 children were randomly assigned to receive three injections of CYD-TDV, and 1333 were assigned control injections, consisting of the rabies vaccine or placebo. Overall, 3673 participants were included in the primary analysis (vaccine, n = 2452; control, n = 1221). The vaccine efficacy was 30.2% (95% Confidence Interval [CI]: −13.4 to 56.6), but differed by serotype. In the intent-to-treat population (all children who were enrolled and randomly allocated to treatment), the efficacy observed for

for DENV-1 was 61.2% [95% CI: 17.4–82.1], for DENV- 3 was 81.9% [95% CI: 38.8–95.8], and 90.0% [95% CI: 10.6–99.8] for DENV-4 (15). However, for DENV-2, which is the predominant serotype, efficacy was only 3.5% (95%CI: –59.8 to 40.5). The lack of observed efficacy against DENV-2 occurred again in phase III studies.

Two pivotal phase III studies, CYD14 and CYD15, were respectively carried out in children aged 2–14 years in Asia, and in children and adolescents aged 9–16 years in Central and South America. Each of the studies included five endemic countries, consisting of 11 sites in Asia and 22 sites in Latin America. Both trials (CYD14&CYD15) successfully met their primary end-point. During the active phase of the disease, both trials showed higher efficacy against severe disease and hospitalization for dengue (in CYD14, 56.5% overall efficacy against dengue disease vs. 67.2% against hospitalization; in CYD15, 60.8% overall efficacy against dengue disease vs. 80.3% against hospitalization) (15). Secondary analyses showed that all four dengue serotypes contributed to the overall efficacy, although the efficacy against serotype 2 was inconclusive, which is considered a weak point of Dengvaxia® and is still under research.

In total, six vaccines are in clinical development, but to date only Dengvaxia® has completed phase III trials (48). Dengvaxia® has a three-dose schedule, each six months apart, with its durability not yet established. The vaccine was well tolerated, with no safety signals after 2 years of active follow-up after the first dose. In both trials, there were no marked differences in the rates of adverse events (49), which is a key to Dengvaxia®'s success since other dengue vaccine candidates failed to avoid adverse events. Moreover, no cases of acute viscerotropic or neurotropic diseases were recorded, and no vaccine-related deaths were reported (15). In addition to the surveillance during clinical trials, there is a four-year long follow-up phase called LTFU, which is in line with the WHO guidelines. During the first year of LFTU, there were no significant differences in symptoms and signs between vaccine and control groups. These results, which include data from 10 countries with different populations in age and ethnicity, have demonstrated the efficacy and safety of Dengvaxia®.

Moreover, Dengvaxia® also takes the risk of resulting in antibody-dependent-enhancement (ADE) into consideration. No, or only minimal, ADE activity in vitro was observed. In particular, there was no in vitro ADE in the presence of broad neutralizing responses against all four DENV serotypes (50). More research is ongoing and will continue to be addressed by long-term follow-up and future post-licensure studies.

So far, the vaccine is approved in eleven countries: Mexico, The Philippines, Brazil, El Salvador, Costa Rica, Paraguay, Guatemala, Peru, Indonesia, Thailand, and Singapore, and the distribution process differs in each (19). Dengvaxia® is now available in certain private healthcare clinics in Costa Rica, Mexico and the Philippines for immunization of individuals 9 to 45 years of age. In El Salvador, the vaccine is now considered the first public dengue prevention, and can be administered by healthcare professionals. In Brazil, Paraná State has launched the first public dengue immunization program in the Americas, targeting vaccination of 500,000 of the state's residents this year. The first public dengue immunization program has also begun in the Philippines, where the country planned to give one million public school children their first dose

by June 2016. For many of these implementations, Dengvaxia® has received endorsements from key medical societies at national and regional levels.

Reasons for Success

During the last century, the dengue virus rapidly expanded from its tropical origins to subtropical and temperate climates. In the early 2000s, both the WHO and the U.S. military classified dengue as "the most important and rapidly spreading mosquito-borne viral disease in the world", which resulted in the classification of the disease as a major international concern (20). One of the key events prompting the successful development of Sanofi's dengue vaccine was the emergence of the Dengue Vaccine Initiative (DVI) in 2010 (47), a non-profit organization that seeks to promote further awareness of the urgent need to support both the development and use of the dengue vaccine (17). To assist this initiative, the International Vaccine Institute (IVI) advocated for international research and partnerships, as well as knowledge-sharing between the WHO, the Sabin Vaccine Institute, and the International Vaccine Access Center through the John Hopkins School of Public Health (47). This resulted in the formation of a Global Product Development Partnership wherein multinational partners could contribute expertise in vaccine development and production, demand forecasting, budget impact planning, economic aspects analysis, as well as vaccine advocacy (47).

Since the development of the vaccine, Sanofi Pasteur, the current manufacturer of Dengvaxia®, has partnered with several international institutions. For instance, the vaccine division has partnered with the University of Mahidol in Bangkok, where a previous version of the vaccine had been researched, as well as the Pediatric Dengue Vaccine Initiative (PDVI) in 2006 to accelerate R&D for a dengue vaccine (22). Finally, Sanofi conducted its R&D in nations with robust R&D infrastructure (USA, France), which led to accelerated testing and manufacturing of the vaccine.

The DVI has managed to attract massive sources of financing since the emergence of the Global Product Development Partnership. In 2011, the DVI received grants from vaccine developers to facilitate discussion between the major stakeholders in order to ensure the vaccine is widely available in countries where dengue is prevalent (21). The Bill & Melinda Gates Foundation committed to a US$55 million grant in 2003 to the International Vaccine Institute to accelerate the development of a safe and protective dengue vaccine (32). In 2011, the foundation allocated an additional US$6.9 million grant to further promote this agenda (23). Since then, it has continued to support DVI (21).

Assessing the Evidence

Sanofi Pasteur has alleged that developing the vaccine required nearly 20 years of research and approximately US$1.7 billion in investment (24). Although early agreements between Sanofi and other players extend from 1994, the previously mentioned global health funds accounted for the sustained financial commitment that enabled the vaccine's development. Western news outlets have reported on the large market for Dengvaxia®, suggesting that the rapid approval of the vaccine in different countries could lead to a US$1.4 billion market by 2020 (25). Sanofi Pasteur increased sales by 15% to US$5.1 billion (from 2015) and has seen consistent growth in recent years despite the er revenue streams, such as Sanofi's diabetes franchise (26).

Pricing for Dengvaxia® is likely to change over time. Early pricing reports from the government-subsidized school children vaccination plan in the Philippines reported that Dengvaxia® would cost the government around US$70 per child (3,500 Philippine Pesos), although other early immunization campaigns in the Philippines were reported to cost approximately US$22 per injection (27). Early estimates from Brazil place the cost of the vaccine between US$46-55 (29), which make it much more expensive than other mosquito-borne infectious disease medications; for example, the price of chloroquine tablets to treat malaria, depending on the place of procurement and available subsidies, can be as low as US$0.10 (51).

Challenges for the Future

The WHO Strategic Advisory Group of Experts on Immunization (SAGE) met in April of 2016 to make recommendations based on mathematical modelling evaluations. These evaluations demonstrated that in high-transmission settings, the introduction of routine Dengvaxia® vaccinations in early adolescence could reduce dengue hospitalizations by 10-30% over a period of 30 years. Accordingly, the SAGE suggested that countries consider introducing Dengvaxia® "only in geographic settings [with a] seroprevalence of approximately 70% or greater in the age group targeted for vaccination [and stated that Dengvaxia®] is not recommended for use in children under 9 years of age, consistent with current labelling" (30).

The primary limitation of Dengvaxia® is mixed vaccine efficacy in specific subpopulations. A modeling study found that in high-transmission areas, vaccination is associated with a 20 to 30% reduction in both symptomatic disease and hospitalization (31). There is evidence that Dengvaxia® can produce infection-enhancing antibodies in vaccinated seronegative individuals (32), leading to higher hospital admission rates, notably among children younger than 9 years (33). A potential solution to this issue would be immunological screening before vaccination in order to identify seropositive individuals, such that they would be the only group to receive the vaccine. However, this would significantly reduce the prospective vaccination population (34).

Moreover, recent evidence suggests that dengue virus antibodies can significantly increase the Zika outbreak peak, speed up the Zika outbreak peak timing and therefore enhance the Zika virus infection by driving greater Zika replication. Using a selection of human monoclonal antibodies, researchers have demonstrated that plasma immune to the dengue virus produced antibody-dependent enhancement (ADE) of a Zika virus infection (35, 36). Although the sequence of the envelope protein for each virus differs by 41-46%, the dengue virus antibodies, rather than neutralizing it, bind to the Zika virus and promote ADE (35). The Zika virus could potentially be considered an additional member of the dengue serocomplex (35). Overall, the enhancement of Zika by dengue antibodies could lead to particularly devastating outcomes since the highest prevalence of Zika occurs in areas where dengue is currently endemic. Further investigations are thus necessary to better understand these processes that must be considered in the development of an effective dengue or Zika vaccine (36).

A fifth serotype of the dengue virus, dubbed DENV-5, was discovered after genome sequencing of a viral sample from a patient in the Sarawak region of Malaysia during an outbreak in 2007, though the

infection was initially attributed to DEN-4 (37). Primates infected with the isolated DENV-5 strain-mounted distinct immune responses from those elicited by either of the first four viral strains, indicating that the fifth serotype was indeed a distinct pathogen (38).

The public health consequences of this new serotype remain to be seen, though most cases in the Sarawak outbreak –-some of which, presumably, can be attributed to DENV-5-– were deemed mild (38). However, the discovery of a new viral strain further complicates the multivalent vaccine-development process, as a fully effective dengue vaccine must address all existing dengue serotypes in order to prevent a more severe secondary infection.

Keys to Lasting Success

Funding for the development of Dengvaxia® is attributed to corporate, philanthropic, and governmental benefactors, namely, Sanofi Pasteur, the Bill & Melinda Gates Foundation, and the Australian government. This multilateral financial support was a pivotal factor in the completion of the clinical trials, exemplifying the importance of global cooperation and the coordination of private and public partnerships. Furthermore, the vaccine's approval by the WHO provided all member-states with a trusted certification of Dengvaxia® safety and effectiveness. There are three key principles to ensure Dengvaxia's success going forward: (1) advanced trials leading to full WHO approval, (2) a commitment by Sanofi Pasteur to prioritize better health over increased profits, and (3) continued innovation in product development, and implementation of global partnerships.

A key challenge will be recognizing heterogeneity across the different countries affected by dengue, in regards to each nation's unique supply constraints, potential vaccine demand, and existing health policy. Country-to-country differences have complicated Dengvaxia® rollout strategies. International Vaccine Access Center researchers have identified key differences, including unequal availability of resources, constrained national budgets, insufficient health care coverage and policies, and diverse political priorities (39).

Implications for Global Heath

While Dengvaxia® offers a promising model for vaccine development, perhaps equally important are other initiatives such as DVI. Dr. In-Kyu Yoon, the director of the DVI, has stated that "there is a need for more than one vaccine and more than one vaccine manufacturer" (41). Currently there are five dengue vaccine candidates in clinical development. The two most advanced candidates, now in Phase II trials, were respectively developed by the U.S. National Institutes of Health (NIH) and the Japanese pharmaceutical company Takeda (WHO, 2016). T003 from the US NIH is based on wild-type strains with specific mutations to weaken the virus. It has been licensed to several manufacturers, such as Butantan, who estimate Phase 3 trial completion by May 2018 (42). Another potential competitor to Sanofi Pasteur is Takeda. They have recently announced their investment of over 100 million euros in a dengue vaccination manufacturing plant in Germany (43).

In the past, Sanofi US decreased the price of a tuberculosis drug, rifapentine, in response to the actions of health equity advocates demanding support for US public health programs (44). This reduction in price demonstrates a willingness from Sanofi to engage with activists; a similar interaction may be important in the future of Dengvaxia®.

Moreover, Sanofi Pasteur purports a long-standing commitment to community involvement: "each year, the Sanofi family of companies [...] – [including] Sanofi Pasteur – strives to maintain and expand a strong Corporate Social Responsibility program by investing in youth, innovation and the community" (45). Shepard et al. (2016) predict Dengvaxia® will participate in the reduction of the current global economic dengue burden of US $8.9 billion, 60% of which is due to productivity loss (46). However, the impact of these vaccines on the market and Sanofi's claim on Dengvaxia® as intellectual property has yet to be fully observed or quantified. Dengvaxia®'s development offers a hopeful example of how a product with decades of dedicated research, sufficient funding, and innovative multinational collaboration can improve the wellbeing of people around the globe.

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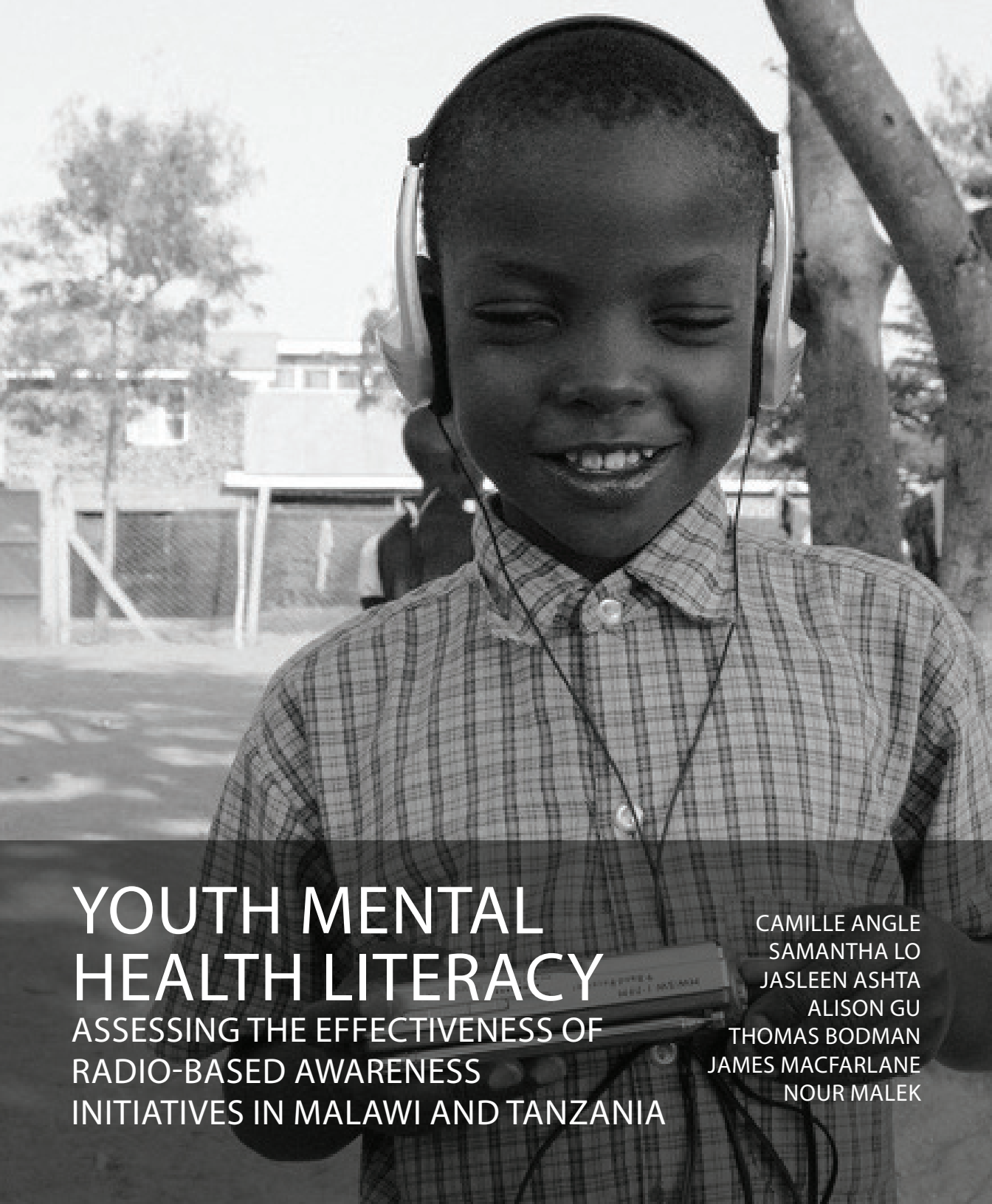

YOUTH MENTAL HEALTH LITERACY

ASSESSING THE EFFECTIVENESS OF RADIO-BASED AWARENESS INITIATIVES IN MALAWI AND TANZANIA

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This paper evaluates the effectiveness of an intervention meant to expand treatment for adolescents with mental illness in Malawi and Tanzania. The researchers developed radio programs addressing mental health for youth and provided training on mental disorders for educators and healthcare workers in Malawi and Tanzania. At a cost of CA$2.7 million, the program treated over 1,000 adolescents for depression and other mental illness.

Introduction

Despite often being left out of the greater discussion on global health, mental health disorders represent a significant burden worldwide. Roughly 5% of any human population is affected by neuropsychiatric illnesses such as psychoses, dementias, drug and alcohol dependence, and depression (1). Approximately 5.9% of total global DALYs lost are due to mental disorders, with the highest burden occurring between the ages of 20 to 30 years old (2). Mental disorders also contribute significantly to global mortality; for example, suicide is reported to be a leading cause of death for youth in China and India (3). Compared to physical and biomedical pathologies, mental illnesses tend to be more difficult to identify and understand, and are thus neglected as a global health concern (4). Depression is projected to soon be responsible for the highest burden of disease in young people worldwide (5).

A large proportion of the population in both high-income countries (HICs) and low and middle income countries (LMICs) are affected by mental illness. People living in LMICs face increased exposure to social and health risk factors for mental illness such as poverty, malnutrition, and violence. LMICs also have a high percentage of youth within their populations. Specifically, 60-70% of people living in Malawi and Tanzania are under age 25, with children between 0-14 years of age comprising 45% of their total populations (5). Over half of the population in Malawi lives in poverty (6, 7). Additionally, in Malawi, 2.1 million adolescents aged 10-19 live with HIV (7). And while the exclusive prevalence of mental disorders among youth in both Malawi and Tanzania is unknown, the prevalence among youth in sub-Saharan Africa is between 13% and 20% (8, 9). Furthermore, these sub-Saharan LMICs also suffer from poor quality of health care. The lack of mental health literacy among the public and training among healthcare workers, coupled with high levels of stigma, result in large treatment gaps for mental illness—especially for youth. In addition, Malawi's youth struggle to receive an education due to the lack of infrastructure and resources. In 2014, 69.4% of Malawi youth aged 15-24 did not progress beyond a primary school-level of education (5, 6).

In Malawi, it could be argued that treatment of mental illness is neglected due to the country's focus on infectious disease treatment and prevention. In 2012, only 0.9% of the country's healthcare budget was allocated to mental health, amounting to US$0.293 per capita (10). Furthermore, tertiary mental health services are only available through three sources in the country: two hospitals associated with the Ministry of Health and a non-governmental organization, Scotland-Malawi Mental Health Education Project (SMMHEP; mostly tailored to graduate students and medical doctors rather than the younger population). In 2012, there were only four registered psychiatrists and psychologists in the entire country. There are simply not enough mental health experts and clinics to meet the needs of Malawi's 16 million inhabitants. This

problem is compounded by the stigma surrounding mental health, causing affected individuals to become isolated from their communities and unable to receive the necessary care. This stigma has also discouraged people from entering into psychology-related fields of study and work, further perpetuating the problem.

The United Republic of Tanzania suffers from a similar lack of mental health resources. Tanzania allocates a greater percentage of its budget to mental health than Malawi (2.4% of their budget or US$0.647 per capita) (11), yet there remains a lack of mental health services. There are only four trained psychiatrists and one or two social workers for every one million Tanzanians. In addition, most clinics do not have protocols to guide the management and treatment of mental health disorders (11).

Studies conducted in Goa and Thirthahalli Taluk, India, as well as Uganda, have shown that groups who undergo interpersonal psychotherapy and/or take antidepressant medications experience a greater decrease in symptoms than a non-treated control group (12, 13, 14). However, such treatments can only be provided and prescribed with appropriate training, thus emphasizing the need for better mental health literacy, training, and funding. As approximately 70% of mental disorders can be diagnosed before the age of 25, investments in these areas must target youth (15). Early diagnosis and treatment will increase life expectancy and participation in the labor force, contributing to an overall improvement in productivity (16).

This case study summarizes and evaluates the implementation of Canada's mental health literacy program, The Guide, in Malawi and Tanzania, with the hopes of assessing the potential for scale-up to other countries in sub-Saharan Africa.

Intervention

Principal Investigator Dr. Stanley Kutcher of the Department of Psychiatry at Dalhousie University (Halifax, Nova Scotia, Canada) and his team put together an initiative to apply a unique, integrated Pathway Through Care program for young people with depression in Malawi (starting in 2012) and the Kilimanjaro region of Tanzania (starting in 2014). With a CA$2.7 million contribution from Grand Challenges Canada (GCC), this initiative was carried out by Farm Radio International, a Canada-based not-for-profit organization dedicated to fighting poverty and food insecurity in Africa (Box 1). Farm Radio International contributed its expertise in radio-based and mobile phone-based communication, which are frequently used by farmers to promote greater collaboration, communication, and sharing of agricultural knowledge.

To pioneer their project, Dr. Kutcher's team worked to create relations with key policymakers in both Malawi and Tanzania. Additionally, the team conducted surveys to assess baseline knowledge of mental health and stigma among youth in Malawi and Tanzania. The survey gathered information about the respondents, their radio-listening habits, as well as their knowledge, attitudes and opinions about depression. The survey revealed that there is no word for "depression" in Chichewa, one of the main languages of Malawi, nor does it exist in other dialects native to sub-Saharan Africa. Victims of depression were stigmatized and labeled as either weak, lazy, or possessed by spirits, and were often punished as a result.

Box 1. Farm Radio

Farm Radio International is a Canadian not-for-profit organization which works with approximately 600 broadcasters in 38 countries across Africa to fight poverty and food insecurity using the medium of radio to provide information (31). Farm Radio International started out as Developing Countries Farm Radio Network (DCFRN) in the late 1970's. It was the brainchild of George Atkins, voice of CBC's noon farm radio program for 25 years. While visiting Africa, George Atkins saw the value in being able to reach farmers with information about affordable, sustainable farming techniques to improve self-reliance, increase food security, gender equality, and reduce poverty. Radio is a particularly efficacious method of reaching farmers in many places in Africa due to the prevalence of radio sets relative to other methods of communication. A 2011 study by Farm Radio International showed that only 2% of farmers had access to a landline, 3% to the internet, and 18% to mobile phones, yet 76% of farmers had access to a radio set (33). This, coupled with the low production cost of radio programs and relatively low cost of maintaining infrastructure, allows Farm Radio International to reach millions with Participatory Radio Campaigns at the cost of "pennies per farmer".

Reflecting these beliefs, health and government officials coined the term, matenda okhumudwa, which roughly translates to "disease of disappointment." Additionally, the survey also revealed that approximately 25% of students reported feeling hopeless on a daily basis. Dr. Kutcher et al. designed a set of unique interventions that: (i) raised mental health awareness through a radio program for youth, (ii) trained teachers with the use of a mental health literacy program adapted from a Canadian mental health curriculum, and (iii) instructed community health care providers on the identification, diagnosis, and treatment of adolescent depression. Together, these programs represent "An Integrated Approach to Addressing the Challenge of Depression Among the Youth in Malawi and Tanzania" (IACD).

The IACD was comprised of four integrated components (17, 18, 19, 20): (i) raise awareness, provide information, and broadcast first-person testimonies through the use of radio programs broadcasting music, a "soap opera" story of youth, and interactive discussion; (ii) decrease stigma through the development of youth listening clubs led by teachers or peer educators to guide discussions on the content; (iii) train teachers to increase mental health literacy through the implementation of a mental health school curriculum; (iv) train community health care providers in the identification, diagnosis, and treatment of youth depression, and encourage the development of a "hub and spoke" model, linking schools to these trained providers.

Raising Awareness and Mental Health Literacy on Air and through Youth Groups

Three radio stations in Malawi and one in Tanzania broadcasted interactive radio programs tailored to youth, including a soap opera that addressed topics of mental health, sexual and reproductive health, and substance abuse (21). The radio program also recruited famous Malawian and Tanzanian personalities as ambassadors to break down stigma associated with mental health. The Diktator—a well-known Malawian rapper—was voted by youth to host the radio program Nkhawa Njee 'Yonse Bo' ("Depression Free, Life is Cool"). Since its debut four years ago, the program has reached over 500,000 youth in both Malawi and Tanzania. The aim of this intervention was to break down

negative stereotypes surrounding mental disorders. Using mobile phones, listeners were able to leave comments and feedback for radio hosts and mental health experts, ask questions, and participate in quizzes and polls.

To guarantee that youth both within and outside schools were tuning in to the radios shows, the IACD trained peer educators to lead radio listening clubs and promote discussions to improve mental health literacy. The in-school youth clubs were comprised of students and teacher mentors. The out-of-school clubs were comprised of school drop-outs as well as unemployed youth that had completed secondary school (aged 20-30 years). Additionally, listeners were given the phone number of an automated, interactive voice response system through which the location of their closest mental health provider could be obtained. These calls were provided free of charge. Over 3,000 youth approached teachers with concerns about mental health and more than 1,000 reached out to mental health providers to receive treatment.

Surveys, in the form of short questions, were used to assess youth awareness of mental health issues and available care options. Post-implementation surveys indicated that the mental health literacy of youth significantly improved in both Malawi (N≈500) and Tanzania (N≈200) ($p<.001$, paired t test) (22). In addition, attitudes towards mental health issues also improved ($p<.001$) (22). Students reported being more inclined to advise friends and classmates to seek mental health care, suggesting that the program promoted an impactful "pay it forward" effect ($p<.001$; Figure 1) (21, 22).

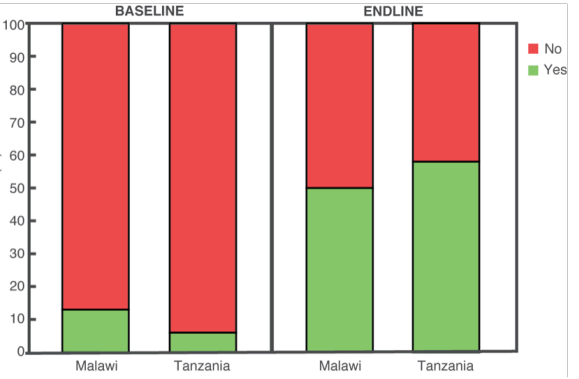

Figure 1.
The percentage of youth who advised a peer to get help from a healthcare professional in Malawi (MW; N≈500) and Tanzania (TZ; N≈200) before (baseline) and after (endline) being exposed to the radio program. Adapted from Kutcher, 2016.

Improving Mental Health Literacy through School Curriculums

Oftentimes, teachers are the first contact to mental health literacy for adolescents through the school curriculum. Teachers provide an opportunity to enhance access to mental healthcare for youth that may have a mental disorder. Thus, it is necessary to train teachers to identify high risk students and refer them to trained health providers. To achieve this, Dr. Kutcher worked with local mental health experts in both countries to adapt a training program he had helped to develop in Canada, the Mental Health and High School Curriculum Guide (The Guide) (Box 2). As a result, the African Guide (AG) was assembled and three-day training workshops were provided to educators that included a module-by-module revision of the AG on mental health literacy and a how-to for integrating basic concepts of mental health and mental disorders into classroom teaching (23). Moreover, the training provided teachers with basic Cognitive Behav-

Therapy (CBT) based interventions to help them talk to students in distress and offered a program that helped them learn how to identify mental health problems in students and appropriately select a clinic for referral. In Malawi, the workshop involved 218 teachers and youth club leaders (121 males, 96 females, and 1 gender not provided) that were selected by Malawi's Ministry of Education from primary and secondary schools (22, 24, 25). In Tanzania, the program was conducted in fewer districts—namely, Arusha and Meru; 61 secondary school teachers (29 males, 29 females, and 3 of anonymous gender) participated (20).

To assess whether teachers' levels of mental health literacy and attitudes changed over the course of their training, they were given pre- and post-intervention questionnaires. These questionnaires assessed general mental health knowledge and consisted of questions with the options "true", "false", and "I don't know". Participants were encouraged to use "I don't know" to avoid guessing. They also answered eight questions about attitudes and stigma on a seven-point Likert Scale that ranged from "strongly agree" to "strongly disagree". Finally, participants responded "yes" or "no" to questions about their experience referring or advising others to seek professional help for a mental health problem, as well as questions about whether or not the teachers themselves personally recognized and/or sought professional help (21).

Prior to the training, educators in Malawi correctly answered an average of 58.3% (Mean (M) = 17.5±4.07) of the 30 questions about mental health, mental illness, and depression. This improved to 76.3% (M= 22.94±2.89) following completion of the workshop (22, 24, 25). A paired t-test indicated this to be a highly significant difference ($p < 0.0001$, paired t-test). Interestingly, this improvement did not differ by gender or region ($p>0.05$). In Tanzania, educators correctly answered 65.9% (M = 19.76±3.57) of the 30 questions prior to training. This improved to 77.8% (M = 23.34±2.63) after training ($p < 0.001$) (20, 22). Moreover, attitudes toward mental health ($p < 0.001$) and comfort levels for addressing mental health needs ($p > 0.05$) significantly improved after the workshop, signifying a decrease in stigma.

Box 2. The Mental Health and High School Curriculum Guide (The Guide)

The Guide* is a web-based mental health literacy curriculum comprising of a teacher self-assessment tool, a teacher self-study module, a student evaluation tool, and 6 classroom ready modules (23). The modules include learning objectives, lesson plans, classroom-based activities, and teaching resources (e.g., written materials, animated videos, and PowerPoint presentations). The 6 modules are as follows: the stigma of mental illness, understanding mental disorders and their treatments, experiences of mental illness, seeking help and finding support, and the importance of positive mental health. The Guide has been certified by Curriculum Services Canada, a pan-Canadian curriculum standards and evaluation agency, and endorsed by the Canadian Association for School Health. The Guide was field tested in numerous schools across Canada, and pilot studies have confirmed its effectiveness in the province of Nova Scotia (34) and in the city of Toronto, Canada's largest metropolitan area (35).

The efficacy of the workshops is further reflected in the percentage of educators that referred students to seek mental health care. 95% of teachers in Malawi and 84% in Tanzania reported that they identified students with mental health problems, and

a subset reported advising the students to reach out for help (Figure 2) (22). During this preliminary analysis of the intervention's impact, the trained educators had taught over 500 classes in 30 Malawian schools and over 300 in 20 Tanzanian schools. A later assessment conducted to measure the one-year impact of improving mental health literacy in Tanzania demonstrated that the number of teachers trained in the guide increased to 159 and the number of students exposed reached about 4657 (M=145.53 per teacher) (26). Interestingly, not only did the same analysis show that teacher referrals increased by a factor of 3 over time, but roughly 400 students (M=13.76 per teacher) said they would approach teachers with a mental health concern. Similar significant improvements were found in Malawi (22).

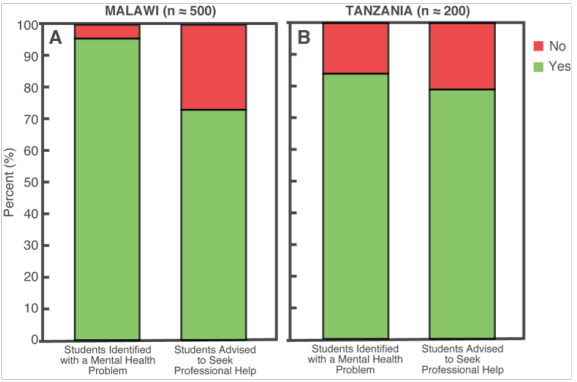

Figure 2. The percentage of students identified by teachers in Malawi (A) and in Tanzania (B) to have a mental health disorder (bar on the left) and referred to seek professional help (bar on the right). Adapted from Kutcher, 2016.

Providing Mental Health Care, Not Just a Rare Service

Finally, utilizing AG training modules similar to those developed for teachers, the IACD program taught frontline healthcare practitioners how to screen for, diagnose, and treat depression, while also emphasizing mental health care provided by community healthcare providers rather than mental health services provided by mental health specialists. These healthcare providers worked in communities near the target schools and served as the resources to which the teachers were instructed to refer students.

A survey was conducted in two sections: the first assessed healthcare professionals' (HCPs) self-reported confidence regarding identification, diagnosis, and treatment of depression in young people; the second was a questionnaire featuring similar questions to those used to assess teachers' mental health literacy before and after training. The confidence self-reports used a 4-point Likert scale that asked HCPs to rate their confidence from "not confident" (1 point), "somewhat confident" (2 points), "very confident" (3 points), to "extremely confident" (4 points). Forty-six HCPs were on average "very confident" in their ability to identify, diagnose, and treat depression in adolescents, yet the average score of the knowledge assessment questionnaire was only 55% correct answers (19). While the sample size was small, the results indicate that training of HCPs in Tanzania is inadequate, and that simply asking them about their competence is not an appropriate metric for assessing capability. In an attempt to compensate for this, Dr. Kutcher trained a group of 4-6 Master Trainers composed of a mix of psychiatrists, psychologists, counselors, and psychiatric nurses. The Master Trainers then trained 20 future trainers, who in turn trained community-based healthcare providers (27). In total, a year after the initial implementation of IACD, 94 HCPs had received training in Malawi, and 75 HCPs had received training in Tanzania (22).

Additionally, fluoxetine—the generic equivalent of Prozac and a relatively cheap medication (~CA$0.78/20 mg capsule)—was made available for the first time by the Ministry of Health in both Malawi and Tanzania as the first-line pharmacological intervention in the treatment of adolescents with depression.

Discussion

The popularity, efficacy, and longevity of the radio-based mental health programs are key indicators of the value of this medium in reaching young people in sub-Saharan Africa. While the cost-effectiveness of these mental health programs has not been specifically assessed, analyzing studies of analogous farm radios in Africa may provide insight into this factor. In 2007, the African Farm Radio Research Initiative (AFRRI) examined the effectiveness and efficiency of radio communications in improving agricultural productivity and food security for rural communities in five countries: Malawi, Tanzania, Uganda, Mali and Ghana (28). The costs associated with installing Farm Radio in these countries are highly variable and depend on the type of station as well as other environmental factors. For example, a 'micro-station' in Mali with a broadcast range of 2.5 km costs US$650 to set up, while a public broadcaster with the signal strength to serve the entirety of Tanzania costs roughly US$8 million. The average cost of setting up a station for AFRRI partners was approximately US$100,000. Indeed, running costs varied widely, as an AFRRI partner survey revealed costs ranging from US$20,330-$541,000 per annum for public broadcasters, US$2,500-$930,000 per annum for commercial stations, and US$2,500-$286,000 for community stations (28).

With GCC's funding coming to an end, constant revenue is essential for the radio initiative to be viable in the long-term. Farm Radio stations typically have two avenues of revenue available to them: 10% internally-generated (advertisements, competitions, subscription fee) and 90% externally-generated (grants and loans from NGOs/IGOs including the Canadian International Development Agency (CIDA), the Bill and Melinda Gates Foundation, Alliance for a Green Revolution in Africa (AGRA)) (29, 30, 31). However, this has led to a "too many cooks in the kitchen" effect causing disagreements over how farm radio in Malawi and Tanzania should be regulated and discouraging continued funding. A recent documentary, "Mental Health on Air," summarizes the impact of the IACD program and shows interviews and clips of children participating in the youth clubs. This documentary may help sway other funders to join the efforts to continue to combat the stigma surrounding depression in sub-Saharan Africa.

Enhancing mental health literacy through a school rather than a non-school curriculum approach has several advantages. For example, it does not require additional program development as it utilizes methods already used by Western educators that have been adapted for sub-Saharan cultures. The IACD approach worked well in both Malawi and Tanzania, appealing to major governmental institutions. For example, Malawi's Ministry of Education is reviewing the AG to incorporate it into the national school curriculum, rather than just the four districts where this case study was implemented. Furthermore, the Ministry of Health is recognizing the IACD as an integral component of the reform of Malawi's mental health policy and plan.

Finally, the potential for the cascade model of training to scale up is considerable. However, due to the lengthy training times, the HCP trainees must have sufficient resources to enable them to train without a drop in frontline care (27).

Unfortunately, the IACD approach has some limitations. The study lacks a control group, which means that it is not feasible to attribute the improvement in referrals made by teachers solely to the influence of the intervention—although other explanations are unlikely since no referrals were made prior to the intervention. In addition, while the number of mental health care referrals significantly increased, there is no data that indicates whether or not the advisees actually sought care. Moreover, data on whether those students continued to seek help and if their conditions improved is difficult to obtain due to the limited duration of the program. Fortunately, an extension phase funded by GCC is examining some of these areas. It is also worth noting that all results in this case study were obtained from the work of Dr. Kutcher and his colleagues; an independent source—ideally within Malawi and Tanzania—would be favorable to validate the data and impact. Finally, considering the positive influence that radio has had on the youth of Malawi and Tanzania, the authors of this case study question whether television could serve as an even more potent medium due to its visual nature. However, televisions are inconsistently available within sub-Saharan communities, which explains the need for the greater coverage achieved by radio.

Conclusion

Radio-based mental health awareness/literacy programs for youth have immense potential to proliferate. In 2014-2015, Farm Radio International worked with more than 600 broadcasters in 38 African countries to reach an estimated 20 million farmers (32). The radio programs may be an effective way to raise awareness, but the capacity of these programs to improve mental health outcomes is limited without the support of the youth radio clubs, school-based mental health literacy programs, and HCP training and treatment availability.

The IACD approach increases mental health awareness among youth and members of their support networks because of its integrative approach and capacity-building initiatives. Further, IACD allows for community-based HCPs to provide treatment through closer training and provision of medications and psychological interventions known to be effective in treating depression.

The results of the studies conducted by Dr. Kutcher and his colleagues suggest that mental healthcare outcomes among youth in sub-Saharan Africa could be substantially improved if the IACD approach were scaled up to cover the entirety of Malawi, Tanzania, or even the full extent of the Farm Radio International coverage area. Unfortunately, cost remains a barrier to the scale-up process. To this end, Farm Radio International and the IACD must strengthen partnerships with major health and aid organizations to ensure sustainability by securing funding, and to maintain accountability for ongoing improvement in training.

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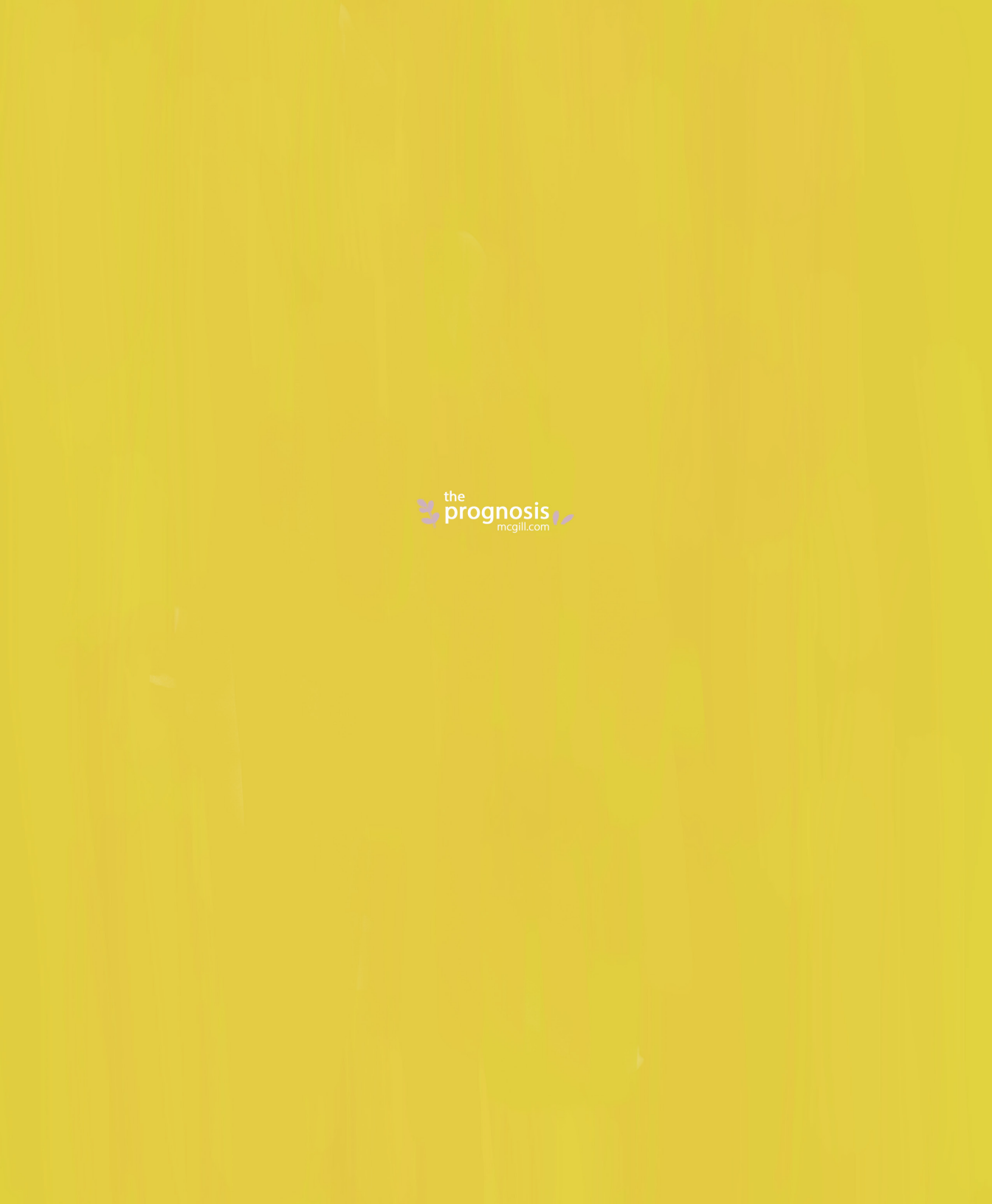
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