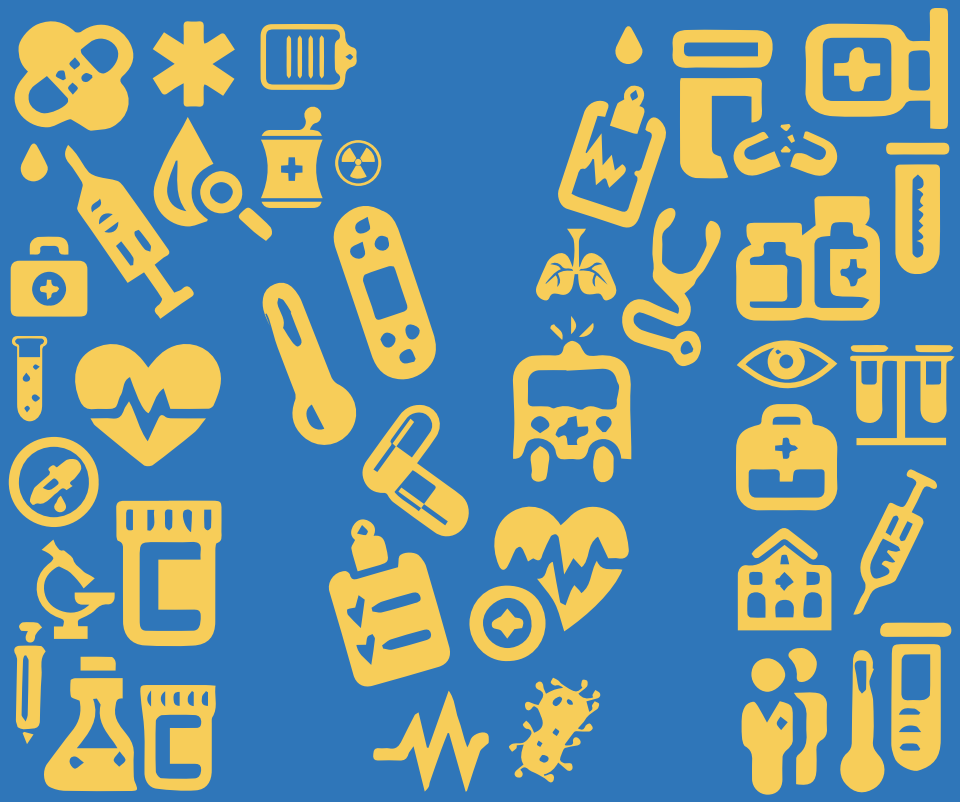
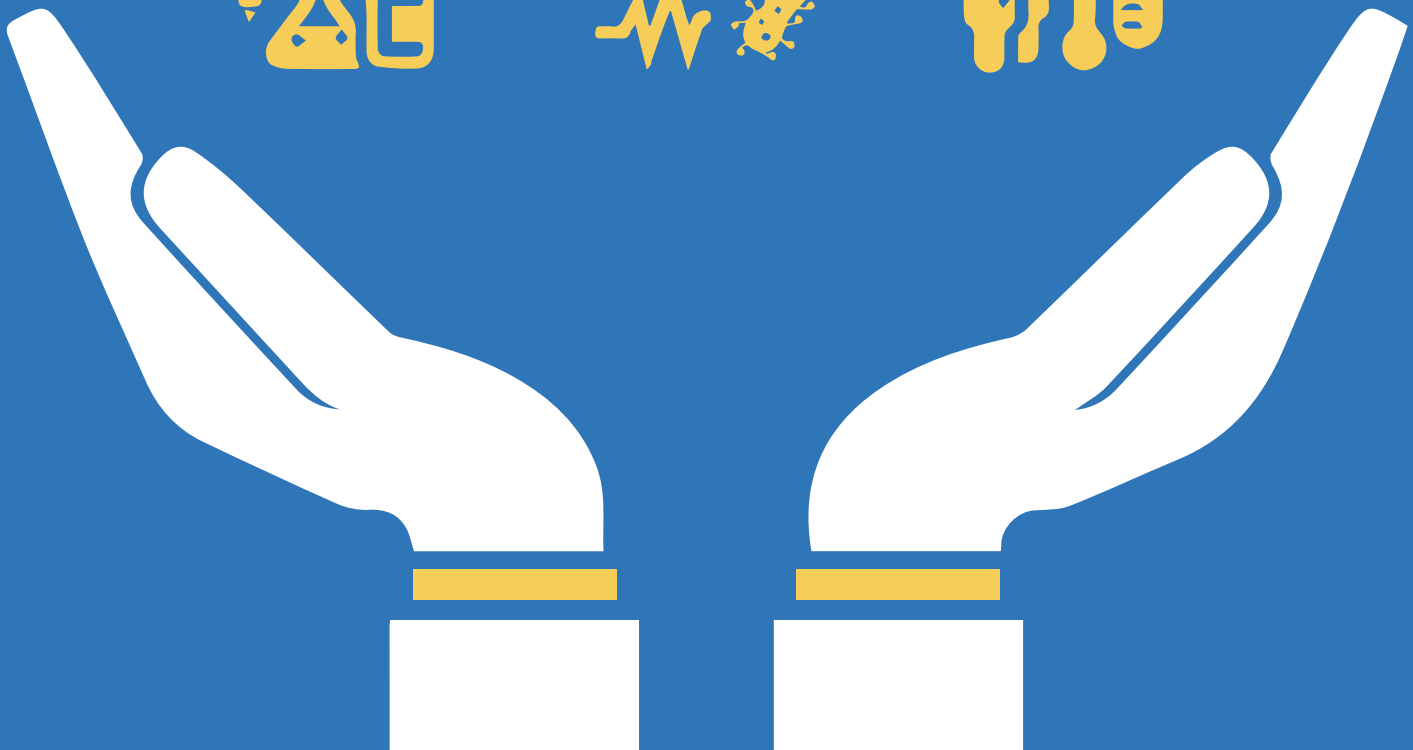
THE UNDERGRADUATE JOURNAL OF PUBLIC HEALTH





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Letter from the Editors

Dear Readers,

It is our pleasure to present to you the inaugural issue of *The Undergraduate Journal of Public Health* at the University of Michigan. Our journey began as a product of passionate conversation in which we both realized there was no forum to independently engage with public health issues. Recognizing this unfulfilled niche on campus, we conceptualized an undergraduate student–run journal, which would create a platform that promotes an active dialogue about relevant issues in public health. We hope to give a voice to a new generation of aspiring physicians, policy makers, and public health professionals.

Although sometimes arduous, this process has been incredibly fulfilling and ultimately humbling. We have been immensely lucky to be surrounded by fellow undergraduates who possess an unparalleled commitment to this publication. The leadership of our executive board, Hannah, Sanjay, and Ajay, has been essential to the establishment of this organization. With their unique perspectives, the five of us were able to refine our vision. Our editorial board is comprised of driven individuals who share our love for public health and are the backbone of the journal. They were vital liaisons between the board and our writers and we couldn't be more grateful for having this particular group of individuals for our inaugural issue. We would also like to thank our PhD student reviewers who took the time to lend their expertise to our editing process. Of course, the journal would not be a reality without the skillful pieces from student writers from Ann Arbor and beyond, which showcase a compelling array of topics.

This process has deepened our understanding of community at the University of Michigan. First and foremost, we would like to thank the School of Public Health for their generous financial support and advice as we crafted this publication. We would also like to thank the Department of Science, Technology, and Society for its contribution to our efforts. Throughout the past year, we formed a close relationship with individuals from Michigan Publishing; the guidance we received from Jason and Allison was integral to the development of this journal. We were also fortunate enough to receive assistance from the informationists at Taubman Health Sciences Library, and resounding support from our undergraduate peers. We hope we can carry this momentum forward for future issues because the creation of this publication is as important as it is timely.

Public health is striking in its pervasiveness; it knows no borders. This allows it to thrive in an increasingly globalized world where societies are an amalgamation of different cultures, races, and identities. Its ability to incorporate perspectives from other fields allows it to transcend conventional ways of understanding health. Therefore, it is increasingly necessary that we, as a community, strengthen our commitment to exploring public health in a global context.

Best Regards,
Krittika Pant and Sonia Ahluwalia
Editors in Chief

FIELD NOTES

Unintended Consequences of the Bangladesh Tubewell Intervention: A Case Study

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Abstract:

The mass poisoning of Bangladesh citizens in the 1970s demonstrates a potent public health disaster. What started as a program to shift from surface water sources to an aquifer water source to combat diarrheal diseases spurred on mass arsenic poisoning across the country for generations. Implementing public health interventions always comes with unanticipated consequences of those purposeful actions. The case study on the Bangladesh tubewell intervention will analyze some of the unintended negative consequences associated with addressing the water sanitation crisis in Bangladesh.

Keywords: Unintended Consequences, Tubewell, Bangladesh, Water Sanitation Intervention

Sometimes, good intentions have negative consequences. A simple solution to save lives might unintentionally cause more damage than even the original problem. Even in the field of public health, policies and health interventions meant to serve a community can lead to disastrous consequences. Examples of this scenario are riddled throughout history. From the disastrous effects of colonial medicine that still persist today, to the recent U.N. debacle of the cholera outbreak in Haiti, caused by U.N. peacekeepers and health personal, public health interventions have had their fair share of historical triumphs and gaffes. A new concept of global health interventions has emerged from these phenomena where the public health community is witnessing a rise in unintended consequences. Whether these consequences are unintended medical side effects, environmental catastrophes, or social injustices brought upon a community, public health officials are now gearing toward trying to implement new solutions to minimize those negative effects. To explore how such consequences arise undetected and unpredicted, take Bangladesh's clean water tubewell initiative as a case study.

The mass poisoning of Bangladesh's citizens in the 1970s demonstrates a potent public health disaster. What started as a program to shift from surface water sources to an aquifer water source to combat diarrheal diseases spurred on mass arsenic poisoning across the country for generations. In the late 1970s, the Bangladesh government, international aid agencies spearheaded by UNICEF, and other nongovernmental organizations (NGOs) came up with an

ambitious solution to bring clean water to the nation's villages. The proposed solution was a tubewell—easy, hardy, hand-operated pumps that sucked water from a shallow underground aquifer to the surface (Water.org, 1990). Approximately, 4 million wells were drilled to replace the traditional surface water source. Those with higher incomes could afford this life-saving public health measure, whereas the poor received loans from nongovernmental agencies to install them in their communal courtyards. By the early 1990s, 95% of Bangladesh's population had access to "safe" drinking water through 10 million tubewells (Mushtaque & Chowdhury, 2004). The project made significant progress and mortality due to water-related diseases declined rapidly. It also improved the lives of women who no longer had to walk long distances to find water or depend on the charity of their neighbors (Mushtaque & Chowdhury, 2004). In all, this intervention was a public health success story and a medical miracle for the impoverished nation.

Unfortunately, all this good did not last. In 1983, dermatologist Kshitish C. Saha in neighboring Calcutta, India, identified the skin lesions on some patients as a symptom of arsenic poisoning. This increase in symptoms of patients, notably immigrants from Bangladesh and the eastern Indian state of West Bengal, was traced back to those who drank mineral water from the tubewells. Over the next few years, environmental scientists Dipankar Chakraborti of Jadavpur University in Calcutta established that many aquifers in West Bengal (that are shared with Bangladesh) were severely contaminated with arsenic (Mushtaque & Chowdhury, 2004). Strangely, although the shift to move away from the arsenic water source occurred in India, it was not until 1993 that any tests were conducted for the Bangladesh water supply; the British Geological Survey (BGS) ran extensive tests on the aquifers and water supplies and deemed it safe—not having tested for arsenic.

Many in the medical community pushed for further testing when a dramatic increase in symptoms related to long-term intake of high concentrations of arsenic began to present in the population. The first sign of poisoning, which may appear as late as 10 years after someone started drinking arsenic-laden water, includes black spots on the upper chest, back, and arms (melanosis). Hands and feet become hard and lose sensation (keratosis). The patient may also suffer from conjunctivitis, bronchitis, and, at very high concentrations of arsenic, diarrhea and abdominal pain. In the second stage, mixed white and black spots appear on the skin (leucomelanosis), legs swell, and the palms and soles crack and bleed (hyperkeratosis). These sores are painful and can become infected; they make working and walking difficult. In the third stage, the sores turn gangrenous, the kidneys or liver may stop functioning. In about 20 years, cancers show up—most notably cancers of the bladder, kidney, liver, and lung. Cardiovascular and neurological complications also occur around this time (Davis, 1996).

Later that year, Abdul W. Khan of the Department of Public Health Engineering in Bangladesh conducted several more tests and discovered arsenic in tubewell water in the western district of Nawabganj. Further testing also raised another concern of ingesting arsenic through a second route: the staple diet of rice eaten two or three times a day. In the dry months, rice fields are irrigated with pumped underground water. Researchers from the University of Aberdeen in Scotland found that the arsenic content of local rice varies from 50 to 180 parts per billion, depending on the rice variety and on where it is grown (Feldmann, Bralatei, Lacan, & Krupp, 2015).

This disaster extends to today's Bangladeshi patients with many cancers being linked back to the tubewell and arsenic exposure. Still, Bangladesh's medical infrastructure is ill equipped to

deal with the influx of patients and the multifaceted health ramifications that come along with a crisis of this magnitude. Health workers can offer ointments to relieve the pain of lesions and to prevent infection, and gangrenous limbs can be amputated, but chronic arsenic poisoning has no real remedy. Drinking safe water can dispel the early symptoms of arsenicosis, but providing such water is not as easy as it sounds (Mushtaque & Chowdhury, 2004).

In response to the crisis, many different solutions have been proposed and implemented. The government created the Bangladesh Arsenic Mitigation and Water Supply Project in 1998. The World Bank provided US$32.5 million loan to this organization, but much of the money remains unspent to date because of the uncertainties of how to proceed (Mushtaque & Chowdhury, 2004). In addition, many governmental branches, NGOs, and international aid groups that originally undertook the project have now begun playing the "blame game," fighting over proposed methods of treatment, who should pay compensation to the victims, and how best to deal with the unsafe drinking water situation. Many have brought their cases up in the legal system and battles are still being fought over compensation and reparations for damages, both physical and emotional, specifically against BGS for neglect and improper testing. However, the international community is also worried that such lawsuits, although justifiable, could deter organizations from working in developing countries that desperately need aid in the future (Clarke, 2001).

Although the situation looks messy, not all groups are embroiled in bitter legal battles. The Bangladesh Rural Advancement Committee (BRAC), an NGO, has been working since 1997 to find an answer to the arsenic dilemma. Their mission is to empower people and communities in situations of poverty, illiteracy, disease, and social injustice. Their interventions have a philosophy of sustainability and large-scale impact and of enabling positive changes through economic and social programs that enable men and women to realize their potential. Unlike other groups previously mentioned, BRAC originated in Bangladesh and emphasizes working with communities to solve issues by incorporating and centralizing them in the implementation of the solution. They recognized the villagers' mistrust in the government and the foreign aid workers who had installed these pumps and provided an easy and "safe" water source only to come back years later and declare them unsafe. Their solution involves training about 160 village women, even some who are illiterate, to test tubewell water using field kits. The volunteers tested more than 50,000 tubewells, painting those that showed more than 50 μg of arsenic per liter (the government specifies no more than 50 μg/L as dangerous levels) red and those that showed lesser green. Later, BRAC would send in experts to confirm the levels and found about 85% to 90% of the wells were correctly labeled by the women. The volunteers also acted as proxy health care workers, learning to identify those with skin lesions and other obvious signs of arsenicosis and to distinguish the three stages of the ailment. The victims were then taken to hospitals and examined by doctors (BRAC, 2001). By observing the volunteers testing tubewells, identifying patients, and reporting cases to the proper authorities, everyone in the targeted villages became aware of the previously unknown problem. The volunteers also worked closely with other community members and BRAC personnel to create maps that showed local sources of water—arsenic-free tubewells, ordinary wells, streams, and ponds—that could possibly replace contaminated tubewells (BRAC, 2001).

There are compelling reasons to return to using surface water as the water source in Bangladesh. Surface water is plentiful and free of arsenic. Unfortunately, the villagers feel

that although they want arsenic-free water, they do not want to feel that they are going back in time to methods they once discarded such as the contaminated ponds and pools of surface water (Mushtaque & Chowdhury, 2004). Fortunately, there exist three solutions to keep the tubewells without poisoning the population. A new filtration method has been invented to help clean contaminants such as arsenic, fecal matter, and bacteria from rainwater and other sources. The three-pitcher system (attached directly to the tubewells) uses stepwise filtration layers such as iron chips, sand, charcoal, and cloth to clean the water collected from the aquifer pumped source. However, drawbacks are that it is expensive on a small scale (installing them on community tubewells) and the sludge from the iron chips is not easy or environmentally safe to dispose of by those not trained to handle the waste. To implement it on the aquifers and on a large scale (centralized filtration of the aquifer), government funding is needed, and aid workers would have to pool resources and ensure that refiltration happened every few months (Mushtaque & Chowdhury, 2004). This method seems the least plausible solution when considering the financial difficulties the country already faces. There is also the option of drilling deeper tubewells to access the arsenic-free water located in deeper aquifers. However, this method is also costly and BRAC feels it could inadvertently repeat the mistakes of the past if those deeper aquifers are not properly tested. A pilot program implemented by BRAC in some areas treated water from a centralized facility that was supplying to some villages. People seem to respond best to this method, but it is not ideal for the more remote areas (Mushtaque & Chowdhury, 2004). Recently, Columbia University estimated that approximately US$290 million would cover an integrated 5-year testing, monitoring, and mitigation program for arsenic all over Bangladesh. This program is sorely needed but it may be more than Bangladesh can afford.

The BRAC solutions implemented are a good stepping-stone for better solutions to the water crisis. The community involvement and routine testing are vital to ensure any community's continued health. However, the US$32 million loan from the World Bank should be used to install filter centers and water treatment plants for the surface water sources. That way, even if it takes time to reach the deeper aquifers and dig deeper tubewells, people would have access to some source of clean water. BRAC's recent US$1 million grant should go toward compensation and covering health care costs of those already suffering from arsenic symptoms (BRAC, 2001). Testing and monitoring are a big factor in ensuring good water quality, and through the BRAC system, it is adequately taken care even if it is on a smaller community scale.

While all these strategies can be implemented to mitigate the effects, for the future, officials should consider a more promising field of solutions centered on community-based interventions. The term *community-based* has a wide range of meanings. The four categories of community-based projects focus on four areas: community as setting, community as target, community as agent, and community as resource. These types are used in combination with the biosocial framework for community interventions and with the use of a theory of community change to implement a more sustainable and positive role of public health values. Community-based interventions employ a broad array of strategies that include education/behavior change, engineering/technology, and legislation/enforcement. Only those interventions that employ multiple tiered programs in addition to targeted community-based interventions are the ones that can truly protect the community from all standpoints. In this instance, for the Bangladesh tubewells, community-based interventions, although a relatively

new topic in the public health field and used in the mitigation process, should have also been integrated in the original intervention design. This consideration could have potentially predicted or cut the negative effects of the original intervention on the population. Although water safety was a pressing issue at the time, implementing an intervention design that worked for one public health concern on another public health issue without closer inspection on logistics and regulations, not running pilot programs to see whether the design could be carried over to another area of public health, or even providing a contingency for the community members in case of negative effects, all contributed to the mass poisoning.

With so many differences in opinions and the bitter legal battle raging, this problem has extended for years without a concrete solution to Bangladesh's water crisis. Thousands of people have suffered and will continue to suffer if nothing is done. The solutions implemented by BRAC on the community level to help mitigate some of the damage are amazing, especially in its multidisciplinary approach and community-wide implementation methods. However, much work has yet to be done to provide better access to a safe water source for more than 150 million people (*World Population Review*, 2015). Although the tubewells were initially meant to save people dying from contaminated water, they led to an even greater fiasco. Labeled as the worst mass poisoning in human history, this success story gone wrong should be viewed as a cautionary tale to public health officials who act before doing a thorough investigation of all aspects of an intervention. Hopefully, the international community will learn from the tragedy in Bangladesh when working on future health care interventions in other communities.

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INDEPENDENT RESEARCH

Indoor Residual Spraying, the AGAMal Program, and Malaria Prevention in Nangodi, Ghana

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Abstract:

Sub-Saharan Africa continues to experience the devastating health and economic consequences of malaria. Although various public health interventions have been evaluated, their indicators do not capture the ground-level experiences of target populations. Taking community-member recommendations for interventions may improve administration and effectiveness of future programs. This study focused on community-member feedback of an indoor residual spraying (IRS) program that took place in Nangodi, Ghana, from 2011 to 2013. IRS involves spraying a residual insecticide onto the walls of a house, and lasts for many months. The study used qualitative methods to document community members' knowledge of malaria prevention, experiences with the IRS program, and factors contributing to their participation in future IRS initiatives. Forty semistructured interviews were conducted, including 35 Nangodi residents, three program sprayers, and two physician assistants. Interviews were conducted from May to December, 2015. All those who had their homes sprayed with IRS (94%, *n* = 33) accepted the program again. Community members were motivated to accept the intervention again because they did not have other means of malaria protection, and the spray improved sleep quality by eliminating mosquitoes and eliminated the nuisance of other household pests. Many community members experienced serious human health consequences and death of livestock, which may have been a result of poor communication of the purpose of IRS and safety protocols. This study revealed that gaps in communication resulted in negative side effects.

Keywords: Indoor Residual Spray, Malaria, Ghana, AGAMal Program

Introduction

In 2015, 214 million cases of malaria were reported globally, and 438,000 deaths resulted from malaria for all ages (World Health Organization [WHO], 2015). The burden of malaria is disproportionately higher for children and pregnant women due to their weaker immune systems (WHO/UNICEF, 2003).

In 2011, the prevalence of malaria parasite in children 6 to 59 months of age in the 10 regions of Ghana ranged from 9.8% in Greater Accra to 77.4% in the Upper East Region (UER) using rapid diagnostic tests (Ghana Statistical Service [GSS], 2011). In addition, in sub-Saharan Africa alone, 25 million pregnant women are at risk of *Plasmodium falciparum* infection annually (Desai et al., 2007).

This high burden of malaria has commonly been addressed with a combination of indoor residual spraying (IRS) and insecticide treated nets (ITNs) or long-lasting insecticidal nets (LLINs), as these methods are cost effective and supported by a growing evidence base (Yakob, Dunning, & Yan, 2011). However, distribution of ITNs and LLINs has been challenging. ITN and LLIN prevalence in the Northern, Upper East, and Upper West regions of Ghana ranged from 51.4% to 67.2% (GSS, 2011). In addition, ITNs and LLINs do not offer complete protection from malaria, as there has been evidence of mosquito resistance to chemicals used in LLINs (Fuseini, Ebsworth, Jones, & Knight, 2011). There is also evidence that shows people sleep outdoors without bednets during the hot, dry months of December to March in northern Ghana (Monroe et al., 2015). IRS has been reintroduced in Ghana because the high rates of malaria have not been adequately reduced by ITN and LLIN distribution.

In 2011, the international mining company AngloGold Ashanti launched an IRS program called AGAMal (AngloGold Ashanti—Malaria Control Programme Ltd; Ghana Statistical Service, Ghana Health Service, & ICF International, 2015). IRS is a vector control intervention that involves spraying an insecticide, which lasts for several months, on the walls of a dwelling. The insecticide kills insects and pests that come into contact with the surface. It is an effective method to reduce malaria transmission that works best when applied to a high percentage of households in a community. AGAMal officials, in conjunction with the Ghana Ministry of Health, identified 63 districts in six regions of Ghana where IRS was to be carried out. However, "as of 2013, it had covered only 33 districts" (Ghana Statistical Service et al., 2015, p. 194). One of the districts where the 2013 spraying program took place was Nabdam District, in the UER. This study focuses on the implementation of the AGAMal Programme in Nangodi, an agricultural and small-scale gold mining town, which is the district capital of Nabdam District (Figure A1).

Several studies on the AGAMal Programme have been reported in Ghana since 2011, although they have focused on mosquito resistance to pyrethroids and organochlorines (Coetzee, Van Wyk, Booman, Koekemoer, & Hunt, 2005; Fuseini et al., 2011; Hunt et al., 2011). Some studies elsewhere in Africa have been conducted on the community acceptance of IRS programs (e.g., Mazigo et al., 2010, in Tanzania; Montgomery, Munguambe, & Pool, 2010, in Mozambique) and on community knowledge and perceptions of IRS (e.g., Ediau et al., 2013, in Uganda; Vundule & Mharakurwa, 1996, in Zimbabwe).

This study fills a gap in the literature with rich, qualitative data that narrate the overall experience of IRS programs from a community perspective. It also describes the experiences of residents after the IRS implementation to better understand how community members perceived the program, problems that arose from its implementation, and recommendations for

Table 1. Characteristics of Respondents (*n* = 35), IRS Questionnaire, Nangodi, Ghana, May–June 2015.

Characteristics	Women	Men	Total
	Age		
20–29	3	1	4
30–39	5	1	6
40–49	4	3	7
50–59	1	2	3
60–69	8	1	9
70–79	4	1	5
80+	0	1	1
Total	25	10	35
	Section of Nangodi		
Guosi	3	2	5
Kalini	6	2	8
Napalik	6	3	9
Napalik Zoa	7	1	8
Soliga	3	2	5
	Education		
No education	22	6	28
Primary	1	1	2
Junior/senior secondary	2	1	3
Postsecondary	0	2	2
	Occupation		
Farmer	24	5	29
Livestock raising	1	0	1
Teacher/student	0	2	2
Public works, highway	0	2	2
Business	0	1	1

future implementation of the IRS program. By identifying and addressing multiple perspectives, positive perception of the IRS program may increase uptake of programs in these communities.

Research Setting and Method

Research for this project took place in Nangodi, Nabdam District, UER, Ghana, from May through June of 2015, with follow-up interviews during December of 2015. Nangodi has a population of 6,911 (Nangodi Community Health Centre Data, 2015) and spans approximately 60 square miles (Hunter, 1967). The majority of residents are involved in farming and livestock/poultry rearing (Destombes, 2006). Some residents are additionally engaged in small-scale gold mining (Renne, 2015).

Researchers selected participants from five of the largest sections within Nangodi: Napalik, Napalik Zoa, Soliga, Guosi, and Kalini. Participants were selected based on convenience sampling. Inclusion criteria for participants were that they were 18 years of age or older and lived in Nangodi during the entirety of the AGAMal IRS campaign (2011–2013). When possible, interviews were conducted with women who were pregnant during the IRS program to collect information on antenatal and postpartum effects of IRS. The primary method of data collection was in-depth, semistructured interviews. Interviews were conducted with 25 women and 10 men from 35 compounds (Table 1).

The interview guides included both directed and open-ended questions on malaria knowledge, malaria prevention, and treatment methods, and the benefits, negative consequences, and recommendations with regard to IRS. Resident interviews were used to gain a better understanding of community experiences with malaria prevention and the IRS program. In addition, key informant interviews were conducted, and included a physician's assistant at the Tongo Hospital (in Tongo, Talensi District, where the regional AGAMal program office was located; Figure A2), a physician's assistant at the Nangodi Health Centre, and three Nangodi health workers who sprayed during the AGAMal IRS campaign. Interview questions with physician's assistants centered around the logistics, spraying process, and issues while implementing the program. They also focused on the physician's assistants' perspectives on how community members received the program, and recommendations for improvement. Questions were asked about the health consequences of spraying, the impact of IRS on reducing malaria cases, and malaria treatment options and prevention methods. Interviews conducted with the sprayers focused on measures taken to protect the health of sprayers, training for the IRS program, logistics of the IRS program, and community members' experiences with the program.

Researchers used semistructured interview guides, which were iteratively improved and expanded throughout data collection. As a result, interviews became longer and more detailed as questions were added. This lack of standardization is signature to qualitative research, and allows for complex and rich data to develop with time. It is not important in this form of research to standardize all questions, as findings do not need to be statistically significant at a population level. Rather, the value of the information collected is that it provides information that is difficult to capture in quantitative data.

Some interviews were conducted in English, including all five health worker's interviews. However, most interviews were conducted in the local language, Nabt. Researchers asked the question in English, and research assistants translated these questions from English into Nabt. As participants answered, research assistants translated participant answers into English for the researchers. All interviews were recorded and transcribed by hand as they were conducted. The interviews were coded in Excel, with three sets of field notes to corroborate the transcripts. Grounded theory was used as a framework for coding, and codes were developed as they emerged in the transcripts (Guest, MacQueen, & Namey, 2012). Codes and themes were reviewed and validated by two researchers to establish interrater reliability.

Officials from the Nangodi Health Centre permitted access to malaria case records at the Nangodi Health Care Centre between 2012 and 2015 (Table 2), which were used to document the changes in confirmed malaria cases before and after the IRS campaign in Nangodi.

Written and oral consent were obtained from participants in this study based on the requirements of the Institutional Review Board (IRB) Health Sciences and Behavioral Sciences (HSBS) at the University of Michigan. All four of the study researchers also completed the University of Michigan–Institutional Review Board: The Program for Education and Evaluation in Responsible Research and Scholarship (UM-IRB PEERSS) Human Subjects courses prior to beginning the project.

Results

Malaria Knowledge

Community members had extensive local knowledge on malaria, its sources, and treatment methods. Twenty participants stated that the elderly, children, or infants were most likely to

Table 2. Nangodi Health Centre—Monthly Outpatient Morbidity Returns: Malaria.

Year	Month											
	Jan	Feb	March	April	May	June	July	Aug	Sept	Oct	Nov	Dec
						2012[a]						
Simple	72	69	89	57	67	187	235	362	192	236	—	223
Lab confirmed	22	17	20	15	—	—	—	—	41	71	—	—
Severe	21	9	23	11	12	47	61	39	40	49	—	39
Lab confirmed	8	5	4	2	—	—	—	—	23	40	—	—
						2013[b]						
Suspected	231	100	71	112	101	134	150	—	—	160	260	135
Tested	—	—	—	—	—	—	—	—	—	—	—	—
Tested positive	—	24	16	7	13	40	141	—	—	144	246	125
						2014						
Suspected	342	356	467	435	498	145	431	385	408	539	471	330
Tested	64	314	435	408	366	118	430	385	408	539	471	330
Tested positive	64	146	149	87	79	44	103	171	161	235	216	103
						2015[c]						
Suspected	258	[203][e]	293	254	208	[201][d]	252	386	609	730	609	254
Tested	258	[203]	293	254	208	[201]	252	386	609	730	609	254
Tested positive	62	85	125	67	42	32	91	151	151	300	360	166

Note. IRS = indoor residual spraying.
[a]Year 2012 was the year before IRS began in Nangodi. Testing for confirmed cases of malaria, either by laboratory analysis of blood samples or through rapid diagnostic testing, was not implemented in 2012.
[b]IRS began in Nangodi in October 2013. There were 246 confirmed cases of malaria in November 2013, which dropped to 125 confirmed cases in December 2013. Data are missing for August and September 2013. In January 2014, there were 342 suspected cases but only 64 cases tested and confirmed. Testing improved in February 2014, and there were fewer confirmed cases through July 2014, when confirmed cases of malaria began to increase.
[c]After the second IRS round in December 2014, the number of confirmed cases dropped in January 2015 and remained low through August 2015, when the number of confirmed cases began to increase.
[d]Figures in brackets are uncertain due to illegibility.

get malaria, and only one participant mentioned pregnant women. Furthermore, all participants noted some common symptoms of malaria such as vomiting, fever, headache, and body weakness/malaise. Twenty-seven participants recognized mosquitoes as the source of malaria, but of these participants, 25 also associated malaria with environmental conditions such as dirty dishes and environments, stagnant water, uncovered food, and rainy or cold weather. Unlike earlier studies conducted in the UER (Adongo, Kirkwood, & Kendall, 2005, p. 369), community members in this study associated malaria with mosquitoes, although the majority cited certain environmental factors.

Malaria Treatments

Throughout the interviews, medical plurality for treating malaria was a prominent theme expressed by participants. Twenty-six community members knew of, and used, neem, papaya, moringa, and mango tree leaves to treat or prevent malaria. This treatment involved boiling the leaves in water, letting them cool, and then bathing in and drinking the water. However, community members differed in whether they thought local remedies or

antimalarials were the most effective method. Twenty-seven participants preferred clinic treatment, whereas three preferred herbs, and five participants believed that both treatments were effective. According to one man,

> They both are important and support each other. When one fails, we will use the other. (Interview 23, Nangodi, May 30, 2015)

Responses also reflected more details on usage depending on their socioeconomic status; five participants stated that if they did not have the money to go to the clinic, local herbs were the next best treatment method.

Malaria Prevention

Participants used multiple techniques for preventing malaria, and knowledge on bednet usage and malaria was extensive. All 17 participants who stated that they used bednets reported using them to prevent either malaria or protect themselves from mosquitoes. Furthermore, all participants who used bednets knew how to hang it by tying the bednet up along four or six corners of the ceiling or walls (Figure A3). Twenty of the 35 participants owned bednets, although only 17 bednet owners stated that they used them regularly. Nine of the 17 participants who regularly used bednets said that they experienced problems with them, such as rashes, itching, eye irritation, and uncomfortable heat. However, these problems were not the most prominent barriers to bednet use. Rather, of the 18 participants who did not own or use a bednet, nine participants reported that they did not have one because it had spoiled and they did not have the money to buy a new one. Thus, economic barriers were the most significant obstacles for bednet use.

Participants suggested various techniques to prevent malaria. The most common prevention method that participants mentioned was to keep the environment or oneself clean (n = 16). Thirteen participants suggested using a bednet could also prevent malaria. Other common themes included the spraying campaign, preventing standing water, wearing protective clothing, and using mosquito coils, insecticides, and neem seed oil. Three participants stated that neem (seeds or leaves) could help prevent malaria. Five participants stated that the spraying program could also help prevent malaria.

IRS Knowledge

Overall, participants' responses to interview questions varied, reflecting different levels of understanding on the AGAMal IRS program. Almost all participants knew that its purpose was to kill mosquitoes and other nuisance insects, as well as to prevent malaria.

Participants gave varied answers to the question of when they were instructed to reenter rooms after the spraying was completed. Some participants were advised that they could not enter their rooms for 1 to 4 hr after spraying was completed, whereas others were told that they could only enter their rooms the next day. Participants also had various explanations for the time period that the sprayed chemical lasted in one's household; some thought 1 week, whereas others thought it would continue to be effective for 6 months, although most reported a 2- to 4-month period of efficacy (n = 14; compare with Montgomery et al., 2010). In addition, some participants reported that once the scent went away, it was no

longer effective and the mosquitoes would then return. One woman stated, "When the scent is gone, the power is gone."

Another woman was not given any information to prepare for the sprayers' arrival. This woman noted, "We were not pre-informed, so we just had to rush and get everything out that same day. We couldn't go in our room, so we slept outside in the courtyard. It was cold, but we had to manage."

However, many participants were sensitized to the program. Some participants were given 1 day of notice, whereas others were given from 2 days to as much as 2 weeks of notice. One participant said that 2 weeks before the program began, AGAMal officials came to the Nabdam District Assembly and Nangodi Health Centre to tell the community about the IRS program. One man explained, "Everyone was asked to do it [the spraying] and to talk to their neighbor about the benefits." This man said that he also heard about the spraying program on the radio.

Despite this initial community orientation about the IRS program, many community members did not have a complete understanding of the program. People also described the lack of information given about the spray itself. Ten people reported that the spray had a potent odor that took months to disappear. Two people cited health problems (headache, suffocation, hard to breathe, rashes) because of the scent. Without information about how the spray worked, people were also more likely to misunderstand the timing of spraying program. For example, one man observed that the sprayers never came immediately before the rainy season, when most malaria cases occur. This apparent mistiming deterred one person from accepting IRS the second time. Although some experienced negative aspects of the spray and campaign, all but two households accepted IRS for the second round of spraying in December 2014, although others said that they might not participate in the future unless the strength of the chemical used was lessened or a different chemical was used because of its odor and wall stains (personal communication, O. Moro, Nangodi, May 5, 2016; Figure A3).

Community Members' Experiences With IRS

IRS was first implemented in the UER beginning in 2013 and the novelty of this method was reflected in a lack of organized information dissemination throughout the region with regard to program logistics. For example, some community members did not know that their home was to be sprayed until sprayers had arrived, although the standard protocol was to inform community members up to 2 weeks in advance. In addition, community members were told varying information about how long they were to remain outdoors after spraying (ranging from 1 hr to 2 days), and not all community members were told how to mitigate the potentially harmful side effects of spraying. Nonetheless, the IRS program was generally positively received in Nangodi. Overall, 33 of the 35 participants stated they would like to have IRS done in their household again despite the negative health effects that were noted (see Table 3). For example,

> Yes, receive it again because of their health, no more mosquitoes and for malaria. (Interview 9, Nangodi, May 25, 2015)

> Yes, my wish is to see them back because after spraying no mosquitoes in house and no malaria; for 4 months the power is still there. (Interview 25, May 30, 2015)

However, participants did experience significant negative effects from the spraying program as well.

> Not able to breathe the way supposed to. How to breathe was a problem because you think you are inhaling the scent of the drug. Although the smell is gone now, the insecticide will not go away completely. (Interview 4, Nangodi, May 24, 2015)

> I was breastfeeding at the time and did not like scent . . . I always felt like vomiting because of the scent . . . The second spraying was strongest of them all, the first time I did not have this problem. The second spraying, scent was stronger and rooms were very hot. [Because of the] scent, I couldn't breathe and had severe headaches. All children having runny nose and some were weak. The baby who was breastfeeding was not as active and I felt weak. Also they wanted to spray fowl and 20 died. (Interview 28, Nangodi, May 30, 2015)

The problem with the loss of poultry was another problem for residents, particularly after the first round of spraying before they knew the importance of burying insects killed by the spray. Eight people mentioned their loss of chickens and guinea fowl after spraying due to livestock ingesting dead insects:

> When my neighbors sprayed, I knew it was strong and it would make me ill. My fowl went to the neighbor's house and consumed insects and died . . . about 17 guinea fowl and about 5 smaller chickens died . . . (Interview 32, Nangodi, June 1, 2015)

> Three guinea fowl died—they might have eaten insects on the floor. (Interview 5, Nangodi, May 24, 2015)

> During first round of spraying, I didn't know fowl would die if they ate insects so five hens died, the second time they advised us to bury insects. (Interview 25, Nangodi, May 30, 2015)

> They wanted to spray the area where the coop is, I raise poultry so I was thinking [it would be good] to spray and we sprayed it. All the little ones died and the mother died too. About 24 died; one of my friends had 100 guinea fowl and all were finished. (Interview 28, May 30, 2015)

In total, eight participants reported the death of adult guinea fowl, chickens, or chicks because of the spray. One participant even reported that after the second round of spraying, 30 of his chicks died although they did not spray the coop. He said that when the chicks entered his bedroom, they suffocated and died. People did realize, however, that the dead fowl were not edible; thus, they buried them (Personal communication, I. Amoore, Nangodi, September 2015).

Despite these negative outcomes, the overwhelming majority of participants stated that they would invite sprayers to return to their home because of the reduction of insects and pests as well as decreased malaria cases:

> We would welcome it [the spraying] because don't have insects, cockroaches, scorpions in rooms anymore. (Interview 33, Nangodi, June 1, 2015)

Indeed, 29 of the 35 participants reported decreased malaria cases in their household since the IRS program took place. Although some continued to use bednets, 18 participants reported

Table 3. Consequences, Health Problems, and Benefits of IRS in Nangodi.

Consequences of IRS mentioned (number who mentioned)	
Persistent bad odor	10
Discoloration of house walls	1
Mosquitoes, insects, mice, wall geckos, and cockroaches died	24
Poultry died	8
Health problems mentioned	
Rash	1
Problems breathing	2
Sickness in the household, weakness of breastfeeding child	1

Benefits					
Malaria in household since IRS?	Yes	No	Reduced	Data missing	Total
	—	29	4	2	35

Note. IRS = indoor residual spraying.

not having a reliable net (not having one at all or having one with holes in it, spoiled, or torn). Participants who do not have reliable access to a bednet may depend upon the AGAMal Programme as their main method of malaria prevention.

IRS Benefits

Although 32 of the 35 participants mentioned the reduction of malaria cases in their household as a benefit of the program, several other benefits were also mentioned, including the collateral reduction of several household pests (including cockroaches, spiders, wall geckos, and mice) and malaria-transmitting mosquitoes as well as sound sleep at night due to fewer disturbances by mosquitoes. These results may be seen in Table 3.

IRS Worker Responses

Interviews with health care workers and the sprayers involved with the IRS campaign showed both similarities and differences with community-member responses. Health care workers' responses reflected a more informed view of the IRS program, although like Nangodi residents, they had personal concerns about the IRS campaign.

All three sprayers who were interviewed mentioned a prescribed protocol, whereby sprayers preinformed all households at least 2 days before they were coming to spray. Yet, this protocol was not always followed (see also Montgomery et al., 2010). One sprayer reported that if they could not get to a house the day before spraying, they would tell people in the

neighborhood to inform others that the sprayers were coming the next day. One sprayer explained that this short notice about the spraying program prompted some household heads initially to reject the IRS program. Another sprayer said that at first, most people did not know about the benefits of the spraying, so they did not accept it. But later, as they learned more about it and saw their neighbors accepting IRS, many more people accepted it. Even those who rejected the spraying at first tended to call the sprayers back.

One of the sprayers gave detailed instructions on the standard protocol involved for informing households:

> When you enter inform them you have come to spray. If they are not prepared, make sure all their personal belongings are brought out of the room and don't spray in rooms with sick people or people who cannot leave the room for 2–3 hours. You can spray in rooms with pregnant women if they can leave. Then help them pack things if they agree. The house owner must be there. Every room must be ready before you spray. Old people, sick people, newborns in rooms, these rooms you cannot spray. And some rooms are shrines or sacred rooms, which you also cannot spray. (Sprayer interview 1, Nangodi, May 22, 2015)

The sprayers also reported their own health concerns for doing their job. Regarding the effects of the chemicals, one sprayer stated, "If you don't protect yourself, headaches, body weakens, body feels warm." He also suggested improvements such as providing greater protective equipment for sprayers. After completing spraying, he stated that they only received soap and water to clean themselves, which he did not feel was adequate. Despite this drawback, he supported the program due to the monetary incentive to participate.

Community-Member Recommendations

Many participants mentioned both negative and positive effects of the IRS program. Participants commented on the physical effects of the spray (e.g., bad odor, color change on household walls, and the death of all insects, mosquitoes, cockroaches, wall geckos, and mice) as well as the negative health effects on people and animals (e.g., rash, problems breathing, sickness in the household, and weakness of breastfeeding child). Many participants discussed the strong scent from the chemical used for spraying. Although some related this strong smell to health problems, such as headaches, nausea, and difficulties breathing, one young woman said that she liked the smell because it meant that insects would die and malaria was reduced.

Although some health problems were associated with IRS, this public health intervention was generally received positively. Twenty-nine participants reported there had been no malaria cases in their household since the spraying, and four reported reduced malaria cases. Many people noted problems with bednets as a result of not being able to read the English instructions, which recommended airing a new net for 24 hr prior to use. This initial airing would not have affected some respondents' experiences of discomfort with using LLINs; however, LLINs were generally seen as beneficial although they are uncomfortable to sleep in during the dry season. All 14 participants who were asked whether they felt pressure to participate stated that they did not, and "participated happily" and "did it at will." Another man stated, "[I was] not forced to if I don't want to spray."

Although many participants stated positive aspects of the IRS campaign, participants recommended improvements. Five participants requested to change the color of the spray. They did not like that the chemical sprayed turned the walls of their rooms white. One man stated that when spraying, "It changes color of paint from blue to white." He stated, "It scares you—make [the spray has] a color."

Furthermore, 10 participants commented on the very strong smell of the chemical and recommended that the smell be improved and lowered in strength, making it weaker and more mild. One man stated, "Reduce the strength, cannot breathe in it. I want it to continue, but one should be able to sleep inside without suffocation. We don't have good ventilation." Another woman stated, "We wish that they could lower the power of the chemical. It is too strong. It smelled very bad for many months. We couldn't stay in the room."

Two participants recommended that community members receive face masks to protect themselves from the smell. One man stated, "I will want to appeal to decrease the odor of the chemical and provide nose or face masks so when they sleep they will not be bothered by the smell." Another participant stated that IRS would only be good for her if she was given something to cover her nose because the chemical is too strong.

Finally, one participant suggested that IRS be done when malaria cases and mosquitoes were most common, during the rainy season. "The sprayers never come right before the rainy season, but it is the most important time to come." However, 10 participants could not think of any more suggestions. One participant stated that the improvements should be left to people who brought the program. Another stated, "If it remains the same, it is good."

Discussion

Key themes emerged surrounding community members' experiences with the IRS program, local knowledge concerning the causes and treatments of malaria, and assessments of bednet use. The interviews also revealed different interpretations of benefits from the AGAMal Spraying Program, as well as a variety of experiences with adverse side effects. Malaria appeared to be a priority, and community members expressed a variety of methods to treat and prevent malaria. Generally, malaria prevention and treatment depended on knowledge and access to resources, especially regarding financial access. Overall, many community members received the AGAMal Spraying Program positively because of its accessibility and perceived effectiveness.

Community members demonstrated extensive knowledge on malaria, its symptoms, treatment, and prevention, particularly with LLINs. Twenty-five of the study participants associated environmental conditions with malaria, along with mosquitoes. Most community members linked the cause of malaria to environmental conditions such as stagnant water, dirty environment, uncovered food, and rainy weather. Participants also demonstrated extensive knowledge on symptoms, treatment, and prevention methods for malaria, including both local etiologic concepts and biomedical ways to treat malaria. Many community members seemed to prefer to treat malaria in the hospital and reported that they wanted to sleep under a bednet but did not have access to one. This reveals that a major barrier to malaria prevention was a lack of resources and money, rather than a lack of knowledge. This has critical implications on developing interventions for malaria prevention and their

effectiveness. Many reported that they only received bednets when they visited the hospital, so future interventions must consider that people may only visit the hospital when they have the money to do so. Thus, using hospital visits as a primary method of bednet distribution may not be effective, and the importance of having IRS programs to complement bednet use is critical.

Participants generally viewed the program's benefits as significantly greater. Although the IRS program had negative effects on the health of community members and livestock as well as inconveniences in daily living, most people reported that they wanted their households sprayed again. One participant was concerned because the sprayers never mentioned returning to Nangodi after the last spraying period in 2014. The results of this study suggest that compliance with the IRS program did not rely solely on people's desire to prevent malaria but also on their concerns with daily living such as eliminating disturbances from mosquitoes while sleeping and nuisance of other pests. One research study also found people mainly did not accept a spraying program in rural Northwest Tanzania because it involved killing of animals as well as the potent scent (Mazigo et al., 2010).

Despite these findings, limitations do exist. Researchers did not have a vested interest in the implementation of IRS programs, which was communicated to participants. However, some of the community members may have been unconvinced, thinking that the research team was associated with AGAMal. This assumption may have increased community members' responses to favor the program positively rather than emphasize negative aspects of the program. Furthermore, due to the qualitative nature of the study, the number of participants involved was small and was not representative of the population of Nangodi. These findings are specific to the AGAMal Program, and cannot be applied to other malaria intervention programs. They do, however, provide several issues that future programs should be cautious of.

Participants suggested that future IRS programs provide better communication of instructions, preparation, and background information on the spraying program so that residents can make more informed decisions based on their personal living circumstances. More specifically, information and rationale for the program could be related more to symptoms and treatment rather than the causes of malaria. Some participants had more critical suggestions for improving the IRS program, which included better measures to prevent losses in livestock and poultry. A few participants also experienced health-related problems and some noted the spray's strong scent as a negative consequence of the IRS program. Future research should examine these results, which may be used to improve the implementation of the IRS program to increase its effectiveness.

Conclusion

Overall, community members received the IRS program with reservations, but enjoyed the benefits of the program. IRS intervention officials should publicize reduction of the nuisance of insect pests as well as malaria prevention in future programming to increase acceptance of the program. Participants suggested that future IRS programs provide better communication of instructions, preparation, and background information on the spraying program, so that residents can make more informed decisions based on their personal living circumstances. Some participants had more critical suggestions for improving the IRS program, which included better measures to prevent losses in livestock and poultry. Given that the majority

of those living in Nangodi work in agriculture, sensitizing participants to proper care for livestock after IRS is important. A few participants also experienced health-related problems and some noted the spray's strong scent as a negative consequence of the IRS program. Given that the chemicals used in IRS are potent and potentially harmful to human health, it is imperative that community members receive adequate information on how to prepare their homes for IRS.

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Appendix

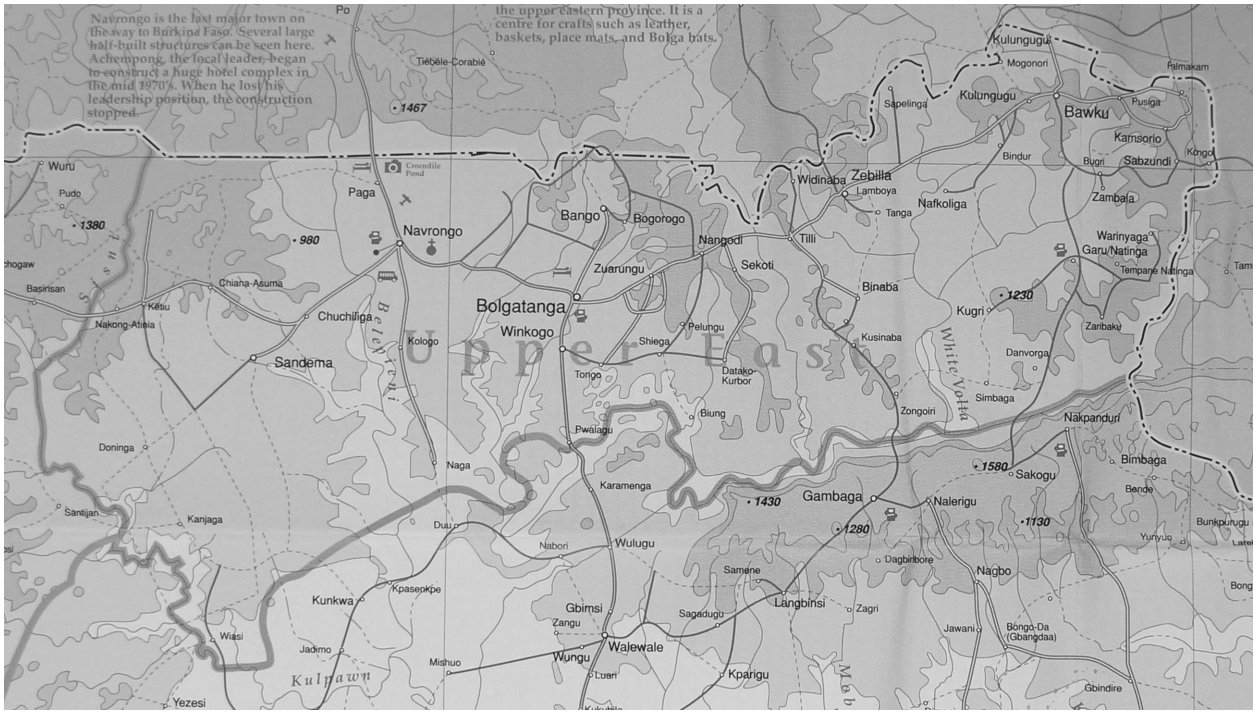

Figure A1. Map of the Upper East Region, showing Nangodi and other towns where indoor residual spraying was conducted in 2013 and 2014 (Courtesy of International Travel Map, 1998).

Figure A2. Poster with information concerning the AGAMal Programme, Tongo Hospital, Tongo, Talensi District, Upper East Region (photograph by E. P. Renne, Tongo, May 29, 2015).

Figure A3. Method for bednet hanging in Nangodi and a bedroom wall with stain from IRS spraying in Nangodi (photograph by Swati Sudarsan) Nangodi, May 25, 2015.

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LITERATURE REVIEW

The Development of Clinical Trials and Safety Determination of HPV Vaccinations for Men

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Abstract:

The humanpapillomavirus (HPV) vaccinations, Gardasil and Cervarix, were recently approved by the U.S. Food and Drug Administration (FDA) for protection against certain strains of HPV. Although there are claims that HPV vaccinations will decrease deaths caused by cancer, their effectiveness is uncertain and will be until the first generation of recipients matures. In addition, they are administered at much higher rates to women than men because they play a role in possibly reducing the rates of cervical cancer, though they can also help prevent common cancers among men. Scientific evidence-based primary literature was analyzed using the keywords "HPV vaccinations" and "clinical trials" through the University of Michigan PubMed database. The articles showed that Cervarix was licensed for women and Gardasil for women and men following clinical trials. The short-term effects of these vaccines are promising, but there is a need for more rigorous investigations on their long-term benefits. The clinical trials for women were larger and more complete than for men, creating a gap in our understanding of the vaccinations. Surveys following the clinical trials showed that despite the fact that Gardasil was proven to be safe for men, they still have lower rates of HPV vaccination than women. Mathematical models demonstrated that when men are included in vaccination programs, HPV-related morbidity and mortality could decrease dramatically. Long-term follow-up data on vaccine recipients who have benefitted from these vaccinations will most likely help convince more men and women to receive HPV vaccinations.

Keywords: HPV, Clinical Trial, Men

Introduction

Human papillomavirus (HPV) is the term for a group of DNA viruses that are commonly spread through intimate skin–skin contact (Division of STD Prevention, 1999). In most cases, HPV does not cause any health problems and clears within 1 to 2 years, but when the virus does not go away on its own, it can cause chronic conditions, such as HPV-related cancers (Centers for Disease Control and Prevention [CDC], 2012). Approximately, 30 strains induce infections and are characterized as high-risk types (e.g., HPV 16, 18, 31, 33, 35, 39, 45, 51, 52) or low-risk types (e.g., HPV 6, 11, 42, 43, 44). The high-risk types are associated with cervical cancer and other cancers; the low-risk types are associated with genital warts and recurrent

respiratory papillomatosis (RRP; Division of STD Prevention, 1999). The epidemiologic and laboratory data on HPV were found to be sufficient enough for the International Agency for Research on Cancer and the National Institutes of Health to conclude that high-risk genital HPV types act as carcinogens in the development of cancers (Division of STD Prevention, 1999). These viruses currently affect approximately 20 million people in the United States, making HPV the most common sexually transmitted disease (Stabb & Buckley, 2011). In fact, the CDC estimated that 80% to 90% of sexually active men and women will be infected with at least one strain of HPV throughout their lifetime (Chesson, Dunne, Hariri, & Markowitz, 2014).

Papillomaviruses complete their life cycle only in fully differentiated epithelial cells, making them difficult to study in cell culture, which has limited the study of their life cycle, immunology, transmission, diagnosis, and therapy (Division of STD Prevention, 1999). However, in the United States, prevention of these cancers includes secondary prevention through cervical cancer screening or primary prevention through HPV vaccination, which has the potential to protect against many cancers, including vulvar, vaginal, penile, anal, and oropharyngeal cancers (CDC, 2012). HPV vaccines can be given to both men and women, preferably between the ages of 11 and 12, to prevent these viruses from spreading (Stabb & Buckley, 2011). Two vaccines, Cervarix, manufactured by GlaxoSmithKline (GSK), and Gardasil, by Merck and Co, help individuals build up immunity against certain HPV strains (Gissmann, 2009). These two available HPV vaccinations went through extensive safety testing before they were licensed by the U.S. Food and Drug Administration (FDA). Gardasil was approved in June 2006 and Cervarix in October 2009 (Stabb & Buckley, 2011). They differ because Cervarix protects against HPV strains 16 and 18 and is intended for females to prevent cervical cancer. Gardasil protects against HPV strains 6, 11, 16, and 18. It is intended to prevent cervical cancer in females and genital warts and other cancers in both males and females. Gardasil is the only HPV vaccine available for use in both boys and girls (Stabb & Buckley, 2011).

Gardasil was studied in clinical trials with more than 29,000 females and males, and Cervarix was studied in trials with more than 30,000 females (Schiller, Castellsagué, & Garland, 2012). Although HPV infections cause more than 17,000 cancers in women and more than 9,000 cancers in men each year (Schiller et al., 2012), the HPV vaccine is more commonly provided to girls than boys. There were various study designs that were created for the HPV vaccine research development in men that can be used to show that the vaccinations are safe and can greatly reduce HPV-related morbidity and mortality. This article will be a review of the benefits and limitations of the studies on the two HPV vaccinations.

Method

The systematic literature review that was conducted through a search of the most current literature using the PubMed database at the University of Michigan dating back to 2009 yielded many relevant articles. The key search terms used were "HPV vaccine," "clinical trials," "vaccine efficacy," "Cervarix," "Gardasil," "impact," "safety," and "adolescent males and females." A variety of studies, such as clinical trials, surveys, and mathematical models, were used to analyze the studies that allowed for the approval of the two HPV vaccinations as well as evaluate the general population's views of men receiving them.

Study Designs

Initial Clinical Trials in Women

Vaccination programs are being widely implemented following the approval of Gardasil and Cervarix, but they primarily target girls (Bornstein, 2010). Based on the previous clinical trials for these vaccines, a majority of which included adolescent girls as participants, Gardasil and Cervarix continue to be immunogenic and are safe for at least 9 years after vaccination (De Vincenzo, Conte, Ricci, Scambia, & Capelli, 2014). For example, the FUTURE I/II trials (Gardasil), PATRICIA (Cervarix), and the Costa Rica HPV Vaccine Trial (Cervarix) were large clinical trials (5,500–18,500 vaccines) that were blinded, randomized, controlled, and made up of young women around 20 years of age (Schiller et al., 2012). The most common negative reports for both vaccines in the Phase III clinical trials on adolescent girls were that they experienced pain and swelling in the spot where the vaccine was given. The outcomes of the vaccinations during those trials displayed no statistically significant differences between the experimental and control groups (De Vincenzo et al., 2014). For example, symptoms present from the vaccine 30 days after any dose were similar between the HPV and control groups (30% and 29.7%, respectively). Throughout the study period, reports of medically significant conditions (25% and 28.3%, respectively) and serious conditions (7.9% and 9.3%, respectively) were also distributed evenly between the treatment and control groups (De Vincenzo et al., 2014). Despite the positive evaluations and safety determination of Gardasil and Cervarix from these trials on women, the information was limited because men were excluded from them.

Expanding Clinical Trials to Men

A study followed several trials solely on females to expand the use of HPV vaccinations to include males. In this study, a double-blinded, randomized, Phase III clinical trial took place with 500 men between the ages of 16 and 26 years (Van Damme et al., 2016). It was created to investigate the immunogenicity and safety of the three-dose regimen of Gardasil in men. The antibody responses were positive, proving Gardasil vaccination was both effective and safe for men.

A larger, more crucial clinical trial that preceded HPV vaccination approval for men was a randomized, placebo-controlled, double-blinded study, which included approximately 4,000 healthy boys and men between the ages of 16 and 26 (Giuliano et al., 2011). Unlike other smaller clinical trials on HPV vaccines in males, this study created groups that were balanced with respect to age, race or ethnic groups, region, smoking status, circumcision status, and sexual history, which helped to reduce confounding variables. Not only did this study have a larger population size, making it more representative of the population as a whole and increasing the chance of finding a significant difference, it also combined results from 18 countries.

The study involved placing the participants into a placebo group or vaccination group, regardless of whether or not they had HPV. Throughout the study, 14.1% of people who were given the placebo and 14.6% of recipients who received the vaccine reported adverse drug reactions, which did not make the differences statistically significant. This proves that there are no short-term symptoms related to receiving the vaccine. There were also no serious

adverse events reported in either category. At the conclusion of this study, the researchers were able to state that the group given the HPV vaccine had lower rates of EGLs compared with the placebo group. The vaccine was found to be 90% effective in preventing HPV-related EGL, which was a highly statistically significant event (Mechcatie, 2009). Although this was a beneficial study, the researchers were only able to study the incidence of EGLs related to HPV and not cancer incidence due to their study design. The strengths of it allowed the drug to be approved for use in males. Following this major study, the HPV vaccine was approved for use in boys and men aged 9 to 26 by the FDA (Currie, 2009). The aspects of the clinical trial that had to be improved with further studies were the short follow-up period that did not allow the researchers to test how long the effects of the vaccination lasted and the narrow age range of the participants.

Expanding the Age Range of the Vaccinations

To expand the possible age range of HPV vaccinations that the previous trial defined, clinical trials were performed in men older than the recommended age range of 11 to 26 years. A Phase II clinical trial of Gardasil was created to test the immunogenicity and safety of the vaccine in mid-adult men aged 27 to 45 years (Giuliano et al., 2015). One hundred fifty men from Tampa, Florida, United States, and Cuernavaca, Mexico, were enrolled in the study and given the vaccine, making it a single-arm study. Each participant developed antibodies against the four components of the vaccine and did not state any safety concerns. Furthermore, their immune responses were similar to what was observed in younger men, proving that the vaccines were effective and safe for men above the age of 26; however, it is still recommended for males to receive HPV vaccinations at a younger age because it gives them more years of protection against HPV. The researchers also pooled men from only two communities, and it would have been more beneficial if they had chosen their participants over a larger area. Supplementary trials are needed to assess the durability of the vaccine because similar to the other clinical trials, there was no long-term follow-up of the participants.

Surveys on the Use of HPV Vaccinations

After the approval of these HPV vaccinations from clinical trials, several observational surveys were created to assess whether the general population was aware that Gardasil was available for both men and women. A study on a national sample of 406 mothers who had adolescent daughters and sons was distributed to analyze whether mothers were knowledgeable about the availability of HPV vaccinations and whether they had discussed the vaccine with their sons (Reiter, McRee, Gottlieb, & Brewer, 2010). The study sorted the women by demographic characteristics and health behaviors, but overall the mothers were found to have on average limited knowledge of the vaccines. The results were that about 30% of mothers' adolescent daughters aged 11 to 14 years had received an HPV vaccine. However, 15% of mothers were aware prior to the survey that HPV vaccines can be given to boys, and only 10% had talked with their sons about the vaccine. However, they did find that mothers whose adolescent daughters had received the HPV vaccine were more willing to give their sons the HPV vaccine, likely due to these mothers having high overall opinions of the vaccine (Reiter, Gilkey, & Brewer, 2013).

A similar study from the National Immunization Survey–Teen used provider-verified vaccination records from 13- to 17-year-olds (Reiter et al., 2013). The use of health care provider records helped the survey have a large, nationally representative sample of adolescent males. The surveyors found that 4.9% of adolescent males had initiated the HPV vaccine regimen and 0.7% completed the three-dose regimen. The most common reasons for parents not intending to vaccinate their sons were that they believed that the vaccination was not necessary (24.5%), they did not have a provider recommendation (22.1%), there was a lack of knowledge (15.9%), their son was not sexually active (14.7%), or their child was male (12.0%). These studies are important for generating hypotheses on why fewer males are receiving the HPV vaccine than females, especially when the clinical trials suggested that they are safe for both, and providing a direction toward the steps that need to be taken to further educate the general population.

Hypothetical Population Model

A final study using hypothetical mathematical population models accounted for the direct and indirect effects of vaccination using public data, published literature, and clinical trials (Elbasha & Dasbach, 2010). It helped conclude along with the other evidence that the inclusion of men in the vaccination programs would further reduce HPV-related morbidity and mortality. Compared with vaccination programs involving girls and women only, including boys and men in these programs would decrease the number of cases of genital warts, cancer cases, and cancer deaths.

Discussion

Based on the results of the HPV vaccine clinical trials, Cervarix has been licensed for use in women and Gardasil has been licensed for use in both genders. The safety profiles of these vaccines have been confirmed by not only clinical trials but also clinical practice and their use in the immunization schedules of 28 countries. There have not been any major contraindications so far for the use of these vaccines (Bornstein, 2010). The short-term immunogenicity and safety of HPV vaccines were examined in adolescents, but to date, no long-term studies on these factors have been reported in this age group. It is clear that there is a need for more rigorous investigations on each vaccine's potential long-term benefits.

Although both vaccines successfully defend against various strains of HPV, Cervarix has been tested and proven to protect against cervical cancer, whereas Gardasil has been proven to protect against vulvar, vaginal, and anal cancers as well as cervical cancer (Elbasha & Dasbach, 2010). Men should receive Gardasil because this will reduce the rates of cancers caused by HPV for themselves and anyone they can transmit the virus to. Although the incidence of most HPV-related cancers is estimated to be 5- to 10-fold lower than that of cervical cancers, a large proportion of anal and a subset of vulvar, vaginal, and penile cancers are strongly associated with high-risk HPV (Division of STD Prevention, 1999).

These direct experiments may never be able to answer the question of whether HPV vaccinations will reduce cancer in real-world conditions. Thus, randomized clinical trials have acted as the best approximations for the primary target group for the HPV vaccines. A majority of the participants across these past studies were women, which is a disadvantage because the vaccines were created for the use of men and women. The sizes of the trials, including

approximately 4,000 males at most or 5,500 to 18,500 vaccines for females, show that the studies on males were more limited than females. This causes there to be several additional gaps in our understanding of the complete role that HPV vaccinations play in long-term health.

Results

Based on the results of these clinical trials and surveys, it would be useful to expand education of the HPV vaccination to all families. Both men and women should be proactive and protect themselves with these vaccinations because HPV can be passed on to both sexes. HPV vaccination use is low among adolescent males in the United States, but knowledge about the safety provided from the clinical trials and provider recommendations for vaccination will most likely improve uptake. Future research is needed to examine changes in the acceptability of the vaccine uptake among males over time as more data become available on vaccine efficacy in males.

The mathematical models show that providing these vaccines to men and women will drastically reduce HPV-related morbidity and mortality. If men and women both take responsibility for receiving all three doses of the HPV vaccination, then there may be a lower chance of transmission of HPV and related symptoms, including a decrease in HPV-related cancers. In turn, this will markedly reduce the need for medical care for other forms of prevention and treatment of HPV as well as alleviate the associated anxieties and health care costs (Steinbrook, 2006).

When girls are vaccinated more often than boys, it is not completely helping the population as a whole because men who are not vaccinated can still be carriers and transmit HPV to nonvaccinated men and women. Nonetheless, whenever a new medical intervention is implemented, health professionals have to decide whether we know enough about its potential benefits and risks to recommend its use or whether it is more important to be cautious or hopeful about brand new interventions. It can be even more difficult for health providers to make the decision whether or not to use vaccinations to prevent future diseases, especially when the drugs are given to otherwise healthy people. Because the impact of HPV on future cancer rates will not be observed for decades, the decisions made on the approved vaccinations were from clinical trials that reported immediate effects. Although the vaccines are too new to show in studies that they reduce cancer incidence, they are assumed to do this if the affects they have on immunity do not decrease over time, and if they do, then health care professionals will most likely use booster shots. Therefore, future studies on the potential long-term benefits for both men and women who received the HPV vaccine are necessary for health professionals and patients to be more confident about these vaccines. Long-term follow-up data, along with other extensive postapproval safety surveillance data, should help to reinforce national recommendations for HPV vaccination of all young adolescents. Gardasil and Cervarix are considered recently approved, so it is important to study the effects of the vaccination both on individuals and the population as a whole throughout the lifetimes of people who received these HPV vaccinations.

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PERSPECTIVES

"More of the Same" Not Enough to Reduce U.S. Suicide Rate

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Abstract:

Through both mental health and general health care policies, the federal and state governments of the United States have contributed to the decade-long upward climb of the national suicide rate. Despite the passage of some well-meaning initiatives over this span of time, the Centers for Disease Control and Prevention (CDC) reports that the problem of suicide in the United States has worsened. This failure is partially attributable to a pervasive reluctance to change, in any substantial sense, the character of legislation that pertains to suicide prevention. For one, federal and state governments have exhibited hesitance to discontinue policies that have proven ineffectual, thus wasting funds that could be better spent elsewhere. Second, the federal government, in its subservience to powerful moneyed interests, has been reluctant to seriously consider alternative solutions to this budding crisis. In effect, a chasm exists between current mental health policies and the scientific literature concerning which methods are most effective at preventing suicide. Particular attention will be given in this article to federal and state governmental support of so-called "public awareness" campaigns, as well as to the effects of federal health policy on the cost of antidepressant medications. In addition, this article identifies policies that have been demonstrated to be effective in reducing suicide, and recommends that they be implemented by state and federal legislatures.

Keywords: Public Awareness, Evidence-Based, Effectiveness, Antidepressants

Introduction

On September 8, 2003, Garrett Lee Smith, only 1 day away from his 22nd birthday, committed suicide in his Utah apartment. Many commonalities exist between his death and those of many of the other 31,483 Americans who are known to have taken their own lives during that year (Hoyert, 2016). Smith was a young male living in a sparsely populated region of the country; he suffered from depression and often consumed alcohol to excess. One facet of Smith's identity, however, was unique: At the time of his suicide, his father, Gordon Smith, represented Oregon in the U.S. Senate. The heartbroken Senator devoted the year following his son's death to crafting legislation that he hoped would lower suicide rates in the United States. His efforts yielded the Garrett Lee Smith Memorial Act, which authorized increased

federal funding for suicide awareness campaigns, depression screenings on college campuses, and other preexisting suicide prevention programs (Goldston et al, 2010). After being given unanimous approval in Congress, the bill was made a law on October 21, 2004, and heralded as an exemplar of productive bipartisanship.

The legislation, in short, failed. According to data collected by the Centers for Disease Control and Prevention (CDC; Curtin, Warner, & Hedegaard, 2016), 42,773 Americans voluntarily ended their lives in 2014. This number constitutes, in the decade since the passage of the Act, an increase in the national suicide rate from 11 deaths by suicide for every 100,000 people to 13 (Curtin et al., 2016; McIntosh, 2016). And this difference, crucially, is no aberration: The American Foundation for Suicide Prevention (2016) reported that the rate has risen, however marginally, during every year since 2005. What can account for this bleak reality? The answer to this question encompasses far more than just the Garrett Lee Smith Act. What follows is an examination of the ways in which federal and state governments have contributed to the growing specter of suicide, through both the programs that they support and the reforms that they refuse to undertake.

Continued Backing of Ineffectual "Public Awareness" Programs

As mentioned previously, the Garrett Lee Smith Act authorized funding for "public awareness campaigns" designed to improve public understanding of severe mental illnesses and destigmatize suicidal ideation (Goldston et al, 2010). In theory, these initiatives would lead to more suicidal individuals seeking help instead of internalizing their suffering. However, scant evidence indicates that public awareness campaigns are effective in lowering suicide rates. In fact, a meta-analysis of studies on suicide prevention programs, published by the *Journal of the American Medical Association*, concludes that awareness campaigns "have no detectable effect on primary outcomes of decreasing suicidal acts or on intermediate measures, such as more treatment seeking or increased antidepressant use" (Mann et al., 2005, p. 2067). The results of this study indicate that whether or not the general public is "aware" of the prevalence of suicide has little bearing on the incidence of behaviors known to curb suicide rates (Mann et al., 2005). Lanny Berman, the executive director of the American Association of Suicidology, explains this by theorizing that mass-marketed campaigns cast too wide a net, failing to identify and provide meaningful support for high-risk individuals (Sanburn, 2013). Speaking with the *TIME* magazine in 2013, Berman states, "I don't know that public awareness campaigns work for the people you most want to reach, the people who are already suicidal" (Sanburn, 2013, p. 2). Information campaigns, in short, appear to do little of import for the segment of the public most likely to suffer from suicidal ideation.

This conclusion, unfortunately, is not reflected in the suicide prevention policies of both the federal government and some state governments. Public awareness campaigns, to explain, often constitute significant portions, if not the cornerstones, of national- and state-level mental health initiatives (Sanburn, 2013). One example at the federal level includes the mass marketing of the National Suicide Prevention Lifeline. Funded by the Substance Abuse and Mental Health Services Administration (SAMHSA), the Lifeline not only provides counseling services to individuals contemplating suicide, but also spends millions marketing itself to the general population (Sanburn, 2013).This approach, the Center for Health Journalism reports, amounts to millions of dollars being spent on promoting the call center to

individuals who will never consider using the service (Jaffe, 2014). In further detail, the CDC estimates that in 2013, approximately, 3.9% of the American population experienced suicidal thoughts (Curtin et al., 2016). As such, with this in mind, the Center for Health Journalism argues that the Lifeline would likely be more successful in its goal of providing support to suicidal individuals if it were to divert its funding away from advertisements that mean little to more than 95% of Americans. This money could then be spent on increasing the capacity of the call centers themselves, whose efficacy, to contrast with awareness campaigns, has been supported by scientific study (Gould, Kalafat, Harrismunfakh, & Kleinman, 2007). The same suggestion, moreover, could be made to the SAMHSA itself, which, in 2014, requested US$2 million more for its National Strategy for Suicide prevention, the department within SAMHSA responsible for designing awareness campaigns (U.S. Department of Health and Human Services, 2012).

A similar preference for advertising campaigns over evidence-based policies pervades state-level suicide prevention efforts as well. Consider, for example, California and Wyoming, states with fundamentally distinct mental health landscape: Wyoming suffers from the highest suicide rate in the nation, whereas California has the eighth-lowest suicide rate (American Foundation for Suicide Prevention, 2016). The states are united, however, in their continued support for inefficient public awareness campaigns. Both launched suicide prevention programs in 2012 that consisted mainly of disseminating supportive messages and information about suicide to the general population. For example, in Wyoming's Park County, the state's Department of Health devoted US$50,000 to producing local TV billboard, and print ads encouraging men to make use of the state's newly created "depression hotline" (Sanburn, 2013). After the first 4 months of the program's existence, it was reported that the hotline received an underwhelming total of 10 calls over that span of time (Sanburn, 2013). No statistics were even collected, furthermore, on whether any of the callers expressed suicidal ideation, so the claim that the awareness campaign prevented anyone from committing suicide is unsubstantiated.

A similar dearth of relevant data characterizes California's recently launched information campaign. In further detail, the California Mental Health Services Authority (CalMHSA), as part of its Suicide Prevention initiative, has conducted what it calls a "mass media campaign" intent on training Californians to identify and support individuals at risk of suicide. To this end, CalMHSA spent US$32 million in public funds on "TV, radio, billboard, online, mobile and print advertising" within 2 years (Jaffe, 2014). Contrasted with the alacrity with which it has spent taxpayer money on the campaign, CalMHSA has made no substantive effort to determine whether their campaign has led to improved outcomes (Jaffe, 2013). A study commissioned by CalMHSA and conducted by the RAND corporation, for instance, does not even mention suicidal ideation once (Burnam, Berry, Cerully, & Eberhart, 2014). Instead, it reports that the public awareness campaign has improved "confidence in the ability to discuss suicide" and "ability to identify individuals at risk" (Ramchand et al., 2013, pp. 9, 15), neither of which specifically address the topic of suicidal ideation. It cannot be conclusively stated, therefore, that CalMHSA's public awareness campaign succeeded in its objective to lower the suicide rate. Indeed, it is not unlikely that the campaign's most salient accomplishments were increasing the prominence of the CalMHSA itself and bolstering the reputations of lawmakers who support its actions. Suicide researcher Diego De Leo, writing in the *British Journal of Psychiatry*, corroborates this prediction when he argues that "[t]he conflict between

political convenience and scientific adequacy in suicide prevention is usually resolved in favor of the former" (De Leo, 2002, p. 373). Continued support for public awareness campaigns may be best understood as being motivated by optics and not by evidence.

Lack of Support for Evidence-Based Policies

The 2005 meta-analysis referenced earlier is straightforward when describing the role that the prevalence of untreated mood disorders plays in the nation's suicide rate. It reports that "[p]sychiatric disorders are present in at least 90% of suicides and more than 80% are untreated at time of death" (Mann et al., 2005, p. 2069), suggesting that as much as 72% of all suicides in the United States involve untreated psychiatric disorders. Concerning the efficacy of antidepressant medications in preventing suicide, the study states that "[p]atient population studies report lower suicide attempt rates in adults treated with antidepressant medication" (Mann et al., 2005, p. 2069). It stands to reason, therefore, that national legislators would act in accordance with these findings, creating health policies that make treatments for psychiatric disorders more affordable. In reality, however, the federal government has enacted legislation that eschews scientific literature in favor of the interests of pharmaceutical corporations. To explain, the government accountability organization OpenSecrets (Silverstein, 2016) reveals that pharmaceutical companies spend more than any other industry on congressional lobbying. Their lobbying has translated to the passage of legislation that effectively grants these companies perpetual free reign to set the prices of their products without fear of consumer or regulatory retribution (Silverstein, 2016). Two examples of such legislation are outlined below. In both instances, federal legislators have implemented policies that fail to increase the accessibility of antidepressants, ignoring evidence suggesting that doing so would lower suicide rates.

An attitude of regulatory laxness toward major pharmaceutical companies has been codified into federal law, contributing to the rising price of prescription medications. In a recent article examining this behavior, a team of researchers from Harvard University concluded that "[t]he primary reason for increasing drug spending is the high price of branded products protected by market exclusivity provisions" (Kesselheim, Avorn, & Sarpatwari, 2016, p. 860). To explain, the U.S. Food and Drug Administration (FDA) grants periods of market exclusivity to drug manufacturers for the medications that they invent, preventing competitors from selling a similar product for at least 5 years (U.S. FDA, 2016c). This practice, mandated by the 1984 Waxman-Hatch Act, effectively creates a monopoly for the drug companies, allowing them to continually increase the price of their products without facing penalties. Furthermore, the researchers elaborate that many companies employ legal strategies that lengthen their exclusivity periods: They found that "widely used drugs" enjoy 12.5 years of exclusivity on average (Kesselheim et al., 2016). This length is even greater, unfortunately, for Prozac, one of the medications most often prescribed to individuals with mental illnesses. First brought to market in 1986, the drug's market exclusivity has been extended to the present day: Its expiration date is currently listed in FDA databases as November 1, 2017 (FDA, 2016b). This regulatory lenience has allowed the makers of Prozac to charge, according to a 2013 report published in 2013 by Consumer Reports, an average of US$2,388 per year for their least expensive formula of the drug, a potentially prohibitive sum. Given that correlations have been observed between antidepressant use and declining rates of suicide (Mann et al., 2005), the growing cost of those medications does not bode well for the prospects of high-risk individuals.

This problem could be mitigated through robust regulation of pharmaceutical and health insurance corporations, ensuring that mood disorder treatment, recognized as "a central component of suicide prevention" (Mann et al., 2005, p. 2069), is still affordable. National legislators, however, have often done the opposite, catering to the interests of these companies. Take, for example, the details of the Medicare Part D program, which was created in an effort to make the cost of prescription drugs more manageable for senior citizens. One major stipulation of this program is that Medicare is barred from negotiating the prices of the drugs covered under this program. This task is left to health insurance companies, which have a motive to keep prices high (Kesselheim et al., 2016). This feature of the law has resulted in the ballooning of prescription prices under Part D; it is estimated that Part D spending constitutes nearly 30% of what the nation spends on prescription medications (Kesselheim et al., 2016). In effect, a promising opportunity to make antidepressants (among other medications) more affordable for the age group that suffers from the highest rate of suicide (Curtin et al., 2016) has not been realized.

Potential Policies for Implementation at State and National Levels

The policies presented below constitute additional evidence-based approaches that, if executed, would help to lower the national suicide rate. In both cases, the policy that is described does not currently exist on a national scale, but has proven effective at curbing suicide in other countries. While determining the effect that these policies would have on the national suicide rate is beyond the scope of this article, the fact that empirical evidence exists that justifies their adoption is sufficient grounds for implementing them.

A substantial amount of literature exists in support of the theory that the decision to commit suicide can be influenced by the manner in which suicides are reported by the news media. In the seminal investigation of this topic, sociologist David Phillips (1974) found that the monthly suicide rates in the United States and Great Britain rose after the story of a suicide was reported on the front pages of major newspapers (Phillips, 1974). With this in mind, it would be wise for the CDC or another relevant agency to share this information with news agencies. In a similar vein, the American Foundation for Suicide Prevention regularly publishes reporting guidelines intent on educating the media on how to report on suicide in such a way that does not encourage others to take their lives (American Foundation for Suicide Prevention, 2016). These guidelines are based on the idea that high-risk individuals are more likely to commit suicide if the media has glamorized previous suicides (Mann et al., 2005). This phenomenon, and its converse, has been demonstrated in scientific study: Etzersdorfer and Sonneck (1998) found that issuing guidelines to media groups that reported on suicides in the Viennese subway system led to a fall in suicides by those means. It is likely that the same outcome would be observed in the United States if federal and state governments compiled and disseminated standardized recommendations for media outlets.

It is not uncommon to hear lawmakers repeat the talking point, popularized by the influential National Rifle Association, that "guns don't kill people; people do." However, a study of the relationship between access to firearms and rates of suicide, conducted by Lubin et al. (2010) and published in *Suicide and Life-Threatening Behavior*, indicates otherwise. They examined the decision made by the Israeli military, which had been plagued by high suicide rates within their ranks, to prohibit their soldiers from taking their weapons with them when on

home leave. It was found that this ban reduced suicides within their ranks by 40% (Lubin et al., 2010). The consequences of this policy demonstrate that those who seek to kill themselves with a gun do not always resort to other means when they do not have access to a firearm. It would be reasonable, therefore, to implement policies that make it more difficult for an individual experiencing suicidal urges to obtain a gun. Examples of these policies include mandating the purchase of gun safes, as well as the lengthening of prepurchase waiting periods.

Conclusion

The federal and state governments of the United States have adopted an approach to addressing suicides that can be generously described as "more of the same." Instead of summoning the will to enact novel solutions, the prioritizing of optics and deference to lobbying groups have worsened the prospects of the highest risk populations. For one, while a modest number of mental health initiatives are given adequate funding, little consideration is given to how effective the initiatives actually are. In conjunction with that behavior, many lawmakers are compliant in special-interest-driven efforts to extinguish the adoption of policies that would lower the suicide rate. In effect, lawmakers have balked at opportunities to expand upon current suicide prevention strategies and have continued to support inefficient programs. This pernicious trend has made the resources needed by at-risk populations largely inaccessible. In short, lawmakers at the federal and state levels have responded to an issue worthy of their greatest efforts with indifference and selfishness. The time has long come for them to begin taking the topic of suicide seriously

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PERSPECTIVES

The Effect of Climate Change on Vector-Borne Infectious Diseases

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Abstract:

Within the last century, there has been a clear increase in the presence of infectious diseases around the globe with both the emergence of new diseases and the reemergence of previously occurring illnesses. In addition, industrialization and the resulting increase in atmospheric greenhouse gases have caused global temperatures, humidity, and the incidence of extreme weather events to rise. Recent evidence shows that this climate change likely escalates both the spread and survival of several vector-borne infectious diseases, including dengue fever and Lyme disease. Dengue fever is a viral infectious disease spread through mosquitoes that thrive in high humidity and are present in tropical and subtropical areas worldwide. Meanwhile, Lyme disease results from a bacterial infection transmitted through *Ixodes* species of ticks that are prominent in temperate zones of the Northern Hemisphere. Both the geographical area that these vectors survive in, as well as the length of seasons during which they can transmit the disease have increased with contemporary climate change. Due to this, the incidence of disease has increased, resulting in the rise of the overall cost for disease treatment and maintenance. Areas with poor sanitation and living conditions will likely be affected the most by these factors, resulting in an increase in health inequities throughout the world. Thus, methods of controlling these diseases as well as ways to reduce the effects of climate change must be studied further and promptly addressed to prevent increases in disease spread, cost, and health inequities. To accomplish this, though, the changes in the presence and spread of vector-borne infectious diseases due to climate change and the resulting effects on human populations must be investigated further.

Keywords: Infectious Disease, Climate Change, Dengue Fever, Lyme Disease

Introduction

Since 1975, the World Health Organization (WHO) has reported the emergence of over 30 new diseases, such as Lyme disease, Ebola, and AIDS (Mcnicoll, 1997). In addition, the reemergence of several other illnesses, including malaria and cholera, has been recorded (Mcnicoll, 1997). Many of these are infectious, meaning that they are caused by pathogenic microorganisms such as bacteria, fungi, parasites, and viruses (WHO, 2016c). These diseases

may be passed directly from person to person or indirectly through an inanimate object (i.e., fomite) or through animal or insect vectors (WHO, 2016c). More recently, there has been an increase in the transmission and incidence of infectious diseases due to a variety of factors, including climate change. Hikes in anthropogenic greenhouse gas emissions, particularly during the 20th and 21st centuries, have resulted in a higher average surface temperature of the Earth (Mirski, Bartoszcze, & Bielawska-Drozd, 2012). For the second half of the 20th century, there was an average increase in worldwide mean temperature of 0.10°C to 0.16°C per decade, causing more extreme weather events and emerging as a threat to the biosphere (Léger, Vourc'H, Vial, Chevillon, & Mccoy, 2012). These factors are altering the incidence, duration, and intensity of disease outbreaks around the globe by facilitating the geographic expansion of disease-carrying vectors and disrupting efforts to avoid or decrease disease presence (Mirski et al., 2012).

Thus, it appears that human-induced climate change is having an observable and concerning effect on the spread and incidence of infectious diseases, especially those that are vector borne. Global temperature increases allow insects, such as mosquitoes and ticks, to survive at higher altitudes and to broaden their territories to more northern and/or southern latitudes; this causes any infectious diseases that these insects harbor to spread to more and new populations (Mirski et al., 2012). More than half of the earth's population is currently at risk of vector-borne diseases, which currently account for about one sixth of the disability and illnesses suffered worldwide; therefore, their increased incidence is a great concern (Zaat, 2004). There is a possibility, though, that climate change could cause the extinction of pathogens, parasites, and/or the vectors carrying these diseases, ultimately reducing infectious disease incidence locally (Altizer, Ostfeld, Johnson, Kutz, & Harvell, 2013). This may happen in some areas, but overall incidence will likely rise due to the emergence or reemergence of pathogenic organisms in other areas of the world.

Therefore, with one billion people becoming infected and over one million deaths per year due to vector-borne diseases, the effect of Earth's steadily increasing temperatures on the spread of these diseases must be evaluated (Campbell-Lendrum, Manga, Bagayoko, & Sommerfeld, 2015). These disease vectors are most commonly arthropods; thus, even though they are influenced by a variety of factors, temperature is particularly important. Arthropods are cold-blooded and depend on external temperature and their environment to regulate internal temperature; thus, warmer temperatures typically contribute to a higher rate of survival (Khasnis & Nettleman, 2005). Two of the most common insect vectors are mosquitoes and ticks, both of which can harbor a menagerie of infectious disease agents depending on the host species and pathogenic microorganisms present. Recently, the effect of climate change on the transmission of dengue fever and Lyme disease through mosquito and tick vectors has come to the forefront of infectious disease research. Strategies to track changes in distribution of both the vectors and the disease have revealed concerning results regarding the effect of changing climate on the spread of these diseases.

Dengue Fever

Dengue fever is a vector-borne, viral infectious disease transmitted primarily through the mosquito *Aedes aegypti*, but also via *Aedes albopictus* (Khasnis & Nettleman, 2005; WHO, 2016a). Today, nearly 40% of the world's population, or 2.5 billion people, live in areas where

local mosquitoes may harbor this disease (Knowlton, Rotkin-Ellman, & Soloman, 2009). More than 50 to 100 million infections, 500,000 hospitalizations, and 22,000 deaths occur due to dengue fever each year (Knowlton et al., 2009). Symptoms of this illness include high fever, rash, severe headache, and aching bones, joints, and muscles; these symptoms typically appear between 4 and 7 days after the initial mosquito bite (Knowlton et al., 2009). There is currently no vaccine or specific medication to cure dengue; most treatments rely on supportive therapy (WHO, 2016a). After being infected, one is immune to the specific variation, known as a serotype, that caused the disease but is still susceptible to the three other known serotypes of dengue viruses (WHO, 2016a). Furthermore, a secondary infection is more likely to result in a case of severe dengue fever (WHO, 2016a).

Overall, climate change may create warmer and wetter conditions that will favor the growth and reproduction of *Ae. aegypti*, thus increasing the probability of transmission to humans (Knowlton et al., 2009). The temperature fluctuations due to climate change are particularly important for dengue fever transmission because the virus is only able to replicate inside of the mosquito above 20°C (Kilpatrick, Meola, Moudy, & Kramer, 2008). This means that as global temperatures rise, the ability of this virus to replicate will increase. In addition, increasing temperatures may cause dengue fever to spread to higher altitudes and more northern and southern latitudes by creating conditions suitable for the mosquito vector (Hopp & Foley, 2003; Knowlton et al., 2009). Rising temperatures could also increase the length of the transmission season in temperate regions worldwide (Hopp & Foley, 2003; Knowlton et al., 2009). Furthermore, increases in humidity allow for better survival of both eggs and adult mosquitoes, thus intensifying mosquito populations and the likelihood of transmission (Hopp & Foley, 2003; Knowlton et al., 2009).

The increase in frequency and intensity of extreme weather events caused by climate change may also heighten the incidence of dengue fever in certain areas (Knowlton et al., 2009). *Ae. aegypti* is well suited for urban environments and can breed in any type of container with stagnant water, such as discarded cans, plastic containers, and tires (Khasnis & Nettleman, 2005). Thus, when events disrupt vital shelter, water, sewer, and sanitation services within a community, human to mosquito contact tends to increase, along with the likelihood of transmission (Knowlton et al., 2009). Events disrupting safe drinking water supplies, such as drought, can cause the incidence of dengue fever to rise as these events oftentimes cause the local population to store water in their homes, creating an ideal breeding site for *Ae. aegypti* (Knowlton et al., 2009). Thus, areas that lack adequate drinking water and proper sanitation tend to be affected more greatly than industrialized regions with continuous and reliable access to water services (Knowlton et al., 2009).

The future implications of climate change on dengue fever are huge; over the last 50 years, the incidence of this disease has increased 30-fold (Phillips, 2008). In the Americas alone, the total number of cases increased from 8,228 in 1995 to more than 26,000 in 2007 (Knowlton et al., 2009). By 2085, it is estimated that 5.2 billion people worldwide, 3 billion more than today, will reside in areas at risk of dengue fever, primarily due to increases in humidity caused by climate change that favor the survival and reproduction of *Ae. aegypti* (Hales, Wet, Maindonald, & Woodward, 2002). Furthermore, as the number of months per year that are suitable for transmission increase, the cost of dengue management is expected to rise three- to fivefold (Knowlton et al., 2009).

Globalization also facilitates the spread of dengue fever. This disease is likely transmitted from country to country due to the movement of infected people, not necessarily the spread of the vector (Knowlton et al., 2009). In other words, if a person infected with dengue fever travels to a country without the virus but with *Ae. aegypti* mosquitoes, they may get bitten and give the virus to the mosquito vector; this mosquito can then spread it to other humans. Once this occurs, though, the effects of climate change on the vector and disease spread become apparent and help facilitate the transmission of dengue fever to even larger geographical areas.

Overall, increases in temperature, humidity, and extreme weather events due to global climate change all affect the spread of *Ae. aegypti* and the incidence of dengue fever. This results in a greater disease burden for many areas of the world and is expected to continue to become more of a problem over larger geographical areas. With all of this, the cost of dengue treatment and management has risen, making it imperative that a more specific and cost-effective treatment as well as better preventative measures, such as a vaccine, be created before the burden of disease becomes significantly greater. Currently, there are vaccines for dengue fever in clinical trials by Sanofi Pasteur and several other organizations (WHO, 2016b). However, development and efficacy face many barriers including lack of an adequate animal model for the disease and problems with creating a vaccine that is effective against all of the serotypes of the dengue fever virus (WHO, 2016b). Thus, dengue fever is already a challenging and present infectious disease, yet its burden on humankind is likely to become even greater as the effects of climate change become more prevalent.

Lyme Disease

Lyme disease is a vector-borne bacterial infectious disease transmitted through several *Ixodes* tick species throughout the Northern Hemisphere (Centers for Disease Control and Prevention, 2016). In the temperate zone of the Northern Hemisphere, Lyme disease is the most commonly occurring vector-borne disease (Mirski et al., 2012). Annually, there are an estimated 85,000 cases in Europe and 15,000 to 20,000 cases in the United States, with 15 states being endemic for the disease (Steere, 2001). Symptoms include fever, rash, facial paralysis, and arthritis (Centers for Disease Control and Prevention, 2016). Typical treatment methods include antibiotics such as doxycycline, amoxicillin, and cefuroxime axetil that are effective against the disease-causing bacterium, *Borrelia burgdorferi*; in addition, intravenous treatments with drugs such as penicillin may be needed if the patient has certain neurological or cardiac forms of Lyme disease (Centers for Disease Control and Prevention, 2016).

Ixodes ticks are highly dependent on environmental conditions and the dispersal of their host species. These ticks are particularly vulnerable to environmental factors during the short free-living portion of their life cycle, during which they require very specific temperature and humidity conditions (Léger et al., 2012). This suggests that the ticks' survival abilities may be more affected by climatic conditions even though the *Ixodes* ticks are mostly dependent on the presence and abundance of their host species for dispersal and colonization (Léger et al., 2012). Furthermore, ticks are ectothermic, so their fitness is heavily temperature dependent while their activity and survival are more reliant on the level of humidity (Jore et al., 2014). Thus, the changing temperature and precipitation variations due to global climate change likely affect the geographic dispersion of this species of tick and the distribution of Lyme disease.

The changes in altitudinal and latitudinal spread of ticks resulting from climate change are less impactful on the increased incidence of Lyme disease than the expanded number of months during which the ticks are able to live and transmit the disease due to increasing temperatures (Medlock & Leach, 2015). Climate change has resulted in more mild, wet winters with shorter freeze periods and warmer springs; these factors allow the ticks to survive longer, increasing their activity and the incidence of Lyme disease (Léger et al., 2012; Medlock & Leach, 2015). During winters with no snow cover and sufficiently high daily temperatures, ticks are still able to pursue new hosts and cause more infections (Jore et al., 2014). These temperature increases may cause a decrease in tick activity during summer, but this slight reduction in activity during one season will likely not be enough to negate the increased activity during the winter and spring months (Medlock & Leach, 2015). Furthermore, warmer temperatures cause people to spend more time outdoors and wear fewer items of clothing, increasing their likelihood of exposure to disease-carrying ticks (Medlock & Leach, 2015). Similarly, urban green spaces are becoming more common in cities to try to offset the urban heat island effect of climate change and industrialization; however, these green spaces attract many host species for ticks and heighten the possibility of exposure to Lyme disease in the urban landscape (Medlock & Leach, 2015).

The spread of Lyme disease due to climate change is not only dependent on the distribution of the *Ixodes* ticks, but it is also susceptible to the dispersion of the host species. For example, if the population size of a reservoir host species, which maintains *B. burgdorferi* for transmission to ticks, increases within a geographical area, the tick density and prevalence of Lyme disease may increase significantly within that same range (Léger et al., 2012). Furthermore, *B. burgdorferi* can live within many different wild mammals and birds; how the changing climate affects these host species must also be considered when trying to determine the effects of global temperature and humidity changes on tick distribution and Lyme disease (Medlock & Leach, 2015). This is extremely difficult to study and quantify, though, due to the wide range of potential reservoir host species present in temperate climates.

Tick abundance and distribution have been expanding steadily, especially northward and to higher altitudes, for the last 30 years (Léger et al., 2012). Furthermore, ticks are known to be able to adapt very well to environmental changes, so we will likely continue to experience tick-borne infectious diseases (Léger et al., 2012). As the distribution of *Ixodes* ticks expand, so do the vector-borne infectious diseases that they carry, given that there are hosts available. With increased disease, there is always increased cost; even though Lyme disease is more easily treated than many other vector-borne infectious diseases, there is still expense associated with any sort of medical condition such as testing, treatment, and any long-term conditions that may result. Thus, individuals must be aware of the possible spread of disease-carrying ticks to their area due to the changing climate and practice techniques that reduce their likelihood of contact with ticks, such as wearing long pants and avoiding tick-infested areas, to avoid becoming infected with Lyme disease.

Conclusion and Future Implications

In addition to all the impacts that global climate change is having or is expected to have on the future of our planet, there is also likely to be an increase in the spread of vector-borne infectious diseases. These diseases will become increasingly prominent both over more

widespread geographical regions and at higher altitudes than previously seen. Furthermore, the season for transmission of vector-borne infectious diseases is likely to expand with the steady increase in temperature and changes in humidity that accompany climate change. The incidence of dengue fever and Lyme disease has already been increasing and is expected to continue to rise. Currently, research priorities must include finding the regions in which humans, wildlife, and other natural systems are most susceptible to the increased incidence of infectious diseases and how this is going to affect global health and security (Altizer et al., 2013). However, educating citizens and the individual's role in preventing climate change must also be considered.

Extensive industrialization and the resulting pollution have been the primary drivers of anthropogenic hikes in the greenhouse gases that are largely responsible for modern-day climate change, but individuals must realize that large-scale efforts are not the only way to counterbalance the resulting problems. Being an informed citizen and working to educate others of the threats that these changes present are the first steps toward finding solutions to the increasing global temperatures, extreme weather events, and resulting impacts on vector-borne infectious diseases. Small endeavors such as driving more fuel-efficient vehicles, recycling, and eating less meat can have a large impact on atmospheric carbon dioxide levels when done by many (Carbon Offsets to Alleviate Poverty, n.d.). In addition, government-supported research is needed to optimize strategies that mitigate the effects of climate change in the fight against the warming planet.

Furthermore, vector-borne diseases are spreading toward geographical areas that have never experienced their effects before, which is especially concerning in the case of diseases such as dengue fever. For this disease, there is no specific treatment or vaccine; thus, dengue spread could devastate persons in parts of the world that are unaware of ways to provide supportive care against dengue fever. Additionally, health inequities increase with the spread of infectious diseases; populations that do not have access to high-quality health care or that are unaware of the consequences of certain illnesses will be more affected by increased disease spread than individuals who live in well-developed, industrialized areas. People of lower socioeconomic class may not be able to afford treatment while the uneducated may simply be unaware of the disease threat that many vectors pose and put themselves at a higher risk of disease by not taking preventative measures. Thus, informed citizens and governments that help support research toward the prevention of spread, treatment and vaccination options, and potential ways to eradicate these diseases are vital. Without this, the prevalence of vector-borne infectious diseases will continue to increase and their burden on the world's health and global economy will only get larger. Therefore, the increasing incidence of vector-borne infectious diseases due to climate change must be properly addressed through research, education, and strategies to mitigate the changing climate before it becomes a public health problem that is too burdensome to overcome.

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PERSPECTIVES

The Progression, Persistence, and Future of the Opioid Epidemic

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Abstract:

As prescription drug medication slowly found its way into the lives of millions of chronic pain sufferers in recent decades, the foundation for a national opioid epidemic was cemented that has since erupted into a massive public health crisis. The emphasis on pain management beginning in the 1990s has provided the medical community with a wide array of prescription pain medications that have contributed to the relief of countless chronic pain sufferers. However, the benefits of prescription pain medication have been emasculated by the harms that have ensued from their intensified usage, and increased opioid prescription has closely mirrored a dramatic increase in the number of opioid-related deaths over the past 20 years. A combination of factors, including the establishment of pain as a fifth vital sign in the late 1990s and the creation of various prescription pain opioids, has subsequently led to a heightened reliance on such medications among chronic pain sufferers. As a result, opioid abuse and addiction have risen, and a nationwide epidemic has emerged. It has thus become imperative that adequate steps be taken to reduce the heavy impact left behind from increased opioid prescription. The future of the opioid epidemic ultimately depends on increasing funding for chronic pain research, working to expand physician education and medical school programs centered on pain practices and pain medication, mandating statewide usage of prescription drug monitoring programs, and placing additional emphasis on alternatives to medication for chronic pain sufferers.

Keywords: Opioid, Opiate, Chronic Pain, Prescription Drug Monitoring Program

How Opioids Reached Their Current Level of Prominence

Many of the rampant increases in opioid overdose can be traced back to an emphasis on pain management that was sparked during the 1990s. Starting in 1995, the drug manufacturer Purdue Pharma began marketing a new prescription medication that they claimed to be less addictive and less prone to abuse than other opioid-based medications that had been used in the past. After being federally approved in 1995 by the U.S. Food and Drug Administration (FDA), Purdue Pharma's new product entitled "OxyContin" was introduced into the market in 1996. Purdue Pharma spent US$200 million in a single year alone to market their new drug

(Mars, Bourgois, Karandinos, Montero, & Ciccarone, 2013). In the years following its release, sales for OxyContin grew from US$48 million in 1996 to nearly US$1.1 billion by the year 2000 (Zee, 2009). With the groundwork set for the takeover of a new prescription medication that had an increasingly growing market, the concept of pain treatment itself was also changing. In 1999, an initiative known as "Pain as the 5th Vital Sign" emerged, which called for physicians to treat pain as the fifth vital sign in addition to body temperature, pulse, respiratory rate, and blood pressure when a patient came in for a visit (Mularski et al., 2006). A 2001 report from the Joint Commission on Accreditation of Healthcare Organizations only strengthened the increasing sentiment that more attention needed to be granted to pain. The report made it a national standard for hospitals to better assess and manage patients' pain (Berry & Dahl, 2000). With the medical community aware that the new standard was to address pain with essentially the same attention that blood pressure and heart rate should receive, prescriptions for pain medication began to rise. In 2000, the total number of prescriptions written for opioid pain medications was 43.8 million. By 2010, this number had increased by 104% to 89.2 million prescriptions (Sites, Beach, & Davis, 2015). Although these initiatives that helped to change the landscape of prescription medication were well-intentioned, they were somewhat ruthlessly capitalized on. The U.S. Drug Enforcement Agency took particular notice of Purdue Pharma's heavy emphasis on OxyContin's reduced addictive qualities in a 2007 court case against the manufacturer. Purdue Pharma eventually pleaded guilty to inaccurately portraying OxyContin as less addictive than other opioid analgesics during the 1990s, but by the time this admission was made, it was much too late to turn the tide of the growing national issue at hand (Mars et al., 2013). Ultimately, the late 1990s and early 21st century helped to cement an obsession with opioid pain medication that would eventually spark a widespread and excessively prevalent misuse and abuse of prescription pain medication. The large scope of opioid abuse within the United States has amounted to what many have described as a full-fledged epidemic. In examining the methods that brought opioids to their current level of prominence, it becomes clear that the foundations for opioid use were carefully laid out in a way that made it easy for the medical community to begin relying on them to alleviate patients' pain.

How a Surge in Opioid Prescription Medications led to Epidemic Levels of Overdose

It is no coincidence that an increase in opioid prescriptions in the United States during the early part of the 21st century led to an increase in opioid overdoses. As physicians began writing more and more prescriptions, pills accumulated in excess and obtaining them illegally became increasingly easy for those determined to find them. Nonmedical use of prescription medication increased, and, as a result, so did overdose-related deaths. Since 2000, there has been a 200% increase in pain medication–related overdose deaths according to the Centers for Disease Control and Prevention (CDC; Rudd, Aleshire, Zibbell, & Gladden, 2016). Today, drug abuse is the primary cause of accidental death within the United States, and opioid-based overdose as well as heroin overdose stand as the leading sources of this statistic (Hedegaard, Chen, & Warner, 2015). Although both opiates and opioids have a connection to the opium poppy plant, opioids stand in a class of their own separate from opiates. This is because opioids, or pain medications, are synthetically derived and simply produce opiate-like effects, whereas opiates are naturally occurring substances that hail directly from the opium poppy plant. As a result, opiates like heroin produce pleasure-inducing effects that

mirror those of opioid medications, yet come at a much lower cost and are often easier to obtain when compared with opioid pain medications. As a result, abusers of opioid pain medications often turn to heroin as a substitute (Cicero, Ellis, Surratt & Kurtz, 2014). In recent years, a likely relationship has been found between pain medication use and heroin abuse. According to the American Society of Addiction Medicine, four in five new heroin users initially began abusing prescription medication (Jones, 2013). Today, heroin use in the United States is at a 20-year high, and heroin-related deaths have increased by a factor of 5 since the year 2000 (United Nations Office on Drugs and Crime, 2016). Usage of a newer synthetic opioid drug called fentanyl has also led to an increase in fatal overdoses in recent years. Fentanyl is much stronger and cheaper than heroin, and data compiled from the *Wall Street Journal* in 2015 found that reports of fentanyl-related seizures increased from about 1,000 in 2013 to nearly 6,000 by mid 2015. The number of fentanyl-related deaths also increased by more than 200 between 2013 and 2015 (Kamp & Campo-Flores, 2016). Ultimately, there have been increases in the number of overdose-related deaths in recent years with regard to both heroin and fentanyl, two narcotics that produce effects very similar to those of opioid pain medications. Combining this with the rise in the number of opioid pain medications that have been prescribed, the damaging reality of prescription pain medication abuse becomes clear. The increase in prescription pain medication has likely contributed to a damaging amount of subsequent heroin and fentanyl overdoses. Thus, what began as an effort to place increased attention on chronic pain management and to emphasize the comfort of patients has slowly led to a full-fledged epidemic within the United States. This epidemic has manifested not only in terms of pain medication abuse itself but also in terms of narcotic abuse. To say that the increase in overdose rates for both heroin and the synthetic opioid analog fentanyl are not related to the increase in the number of prescriptions for opioid pain relievers written in the past 20 years is to undermine a potentially groundbreaking mitigation of narcotic abuse issues. Heroin and fentanyl use is inextricably linked in many cases to opioid pain medication abuse, and in recognizing this link and increasing vigilance in prescribing practices, it may be possible to reduce the unfortunate rise in narcotic usage.

The Chronic Pain Problem

To fully understand the opioid epidemic, it is also important to understand the vicious cycle that chronic pain sufferers often find themselves in when they begin using pain medications. Whereas acute pain is pain that ceases after a certain period of time, chronic pain is a persistent and unrelenting form of pain that has the potential to drastically interfere with daily life. More specifically, chronic pain is pain that is characterized as that which lasts for more than 3 months beyond the time of normal tissue healing (Dowell, Haegerich, & Chou, 2016). Chronic pain can often come as a result of past injuries such as car-accident injuries, previous surgeries, cancer, or even long-term conditions such as fibromyalgia. According to a study conducted by the Institute of Medicine, 100 million U.S. adults suffer from chronic (daily) pain (Institute of Medicine, Board on Health Sciences Policy, & Committee on Advancing Pain Research, Care, and Education, 2011). With a drastically high number of Americans suffering from chronic pain, pain medication is a frequently sought remedy. In addition, physicians often prescribe such medications to patients. Opioid analgesics, or in other words opioid pain medications, are high in strength and ultimately work by reducing the number of signals the nervous system sends to the brain alerting the presence of pain. Many chronic pain

sufferers turn to opioid analgesics simply because their pain is too strong and too bothersome to bear otherwise, and opioid analgesics are among the strongest of medicinal therapies available for pain. Despite the relief that patients often feel as a result of pain medication, the danger in their usage lies in the highly addictive quality inherent to opioid analgesics. Over time, patients' bodies can become reliant on the effects of pain medication and can become tolerant to the same dosage. Patients who build up a tolerance to opioid-based medications begin to require a higher dosage to feel the same pain-relieving effects as they once did. In certain cases, continued use of opioid pain medications for chronic pain can also lead to opioid-induced hyperalgesia. When this occurs, pain paradoxically increases when medication is taken, and increasing the dosage only worsens the pain that patients experience. In addition, opioids stimulate the reward center of the brain and provide a sense of pleasure. The strong pain-relieving qualities of such medications mixed with the pleasure-inducing state they help to produce collectively work to make opioids an extremely addictive class of drugs (Stoicea et al., 2015). For those who are prescribed opioid pain medications for chronic pain, it can thus be both a blessing and a curse. Medication can not only provide temporary relief, but it can also lay the foundations for later abuse.

Moving Forward

So what happens next? Where is the medical community to turn when millions of chronic pain sufferers are often forced to turn to medication to feel any sense of comfort, despite the immense risks opioid prescription medications pose for addiction? The answer to this question lies in the form of a few key changes. The opioid epidemic can be considered as stemming from a lack of funding for research into pain, unsatisfactory medical training in pain practices and medication, underutilization of prescription drug monitoring programs (PDMPs), and lack of patient awareness to alternatives to medication. Thus, to tackle the growing issue, it is imperative that the amount of funding chronic pain research receives is increased, physicians receive more adequate training in dealing with patients who have chronic pain as well as their medications, PDMP usage becomes mandated statewide, and that patients themselves obtain a more comprehensive understanding of the additional steps they can take beyond medication to assuage their discomfort.

In considering the sheer number of people who suffer from chronic pain in the United States, it is surprising how little funding actually goes into researching such a widespread condition. A reported 100 million Americans suffer from chronic pain, and in 2015, the National Institutes of Health (NIH) spent US$463 million on pain research (National Institutes of Health, 2016). By contrast, 14.5 million Americans suffer from cancer (American Cancer Society, 2015) and 29.1 million Americans suffer from diabetes (Centers for Disease Control and Prevention, 2014). Each of these conditions received respective funding amounts of US$5.389 billion and US$1.01 billion from the NIH in 2015, dollar amounts much higher than the funding allocated toward pain research (National Institutes of Health, 2016). It is clear based on these figures that chronic pain research is severely lacking in financial support. The proportion of Americans who suffer from chronic pain is nowhere near proportional to the amount of funding that research for the condition receives. The lack of funding for pain research means that any potential advancements toward finding therapy methods for pain aside from opioid analgesics are either lost or left unpursued. A report from the Institute of Medicine states, "Pain is a topic of interest to virtually every NIH institute and

center, but not a central concern of any one of them" (Institute of Medicine et al., 2011, p. 11). Without a strong financial impetus to continue pursuing potential therapies and more advanced management strategies, the medical community will be forced to continue handing out unprecedented numbers of prescriptions. The opioid epidemic poses a massive challenge to the public health community, but as with any large public health issue that has ever been fairly dealt with, change requires funding.

Furthermore, pain poses an immense daily cost to patients, but it also poses a large cost to the economy. The cost of pain to the economy is estimated at US$560 to US$635 billion annually, including the cost of pain to personal caregivers, incarcerated individuals, children, nursing home patients, members of the military, as well as losses in productivity (Institute of Medicine et al., 2011). With such a high financial burden, a sharp rise in overdose and addiction levels, and the inherent destruction to quality of life that chronic pain causes, it is a nationwide imperative that chronic pain be given more attention and more funding. It is the duty of the scientific community to stand up for individuals who are only able to find relief through risky medications, and it is the duty of the scientific community to help put a stop to the egregious numbers of overdoses that pain medication often leads to.

The next change that must occur in dealing with the opioid public health epidemic is transforming the way in which medical personnel are educated on pain management and care. Aside from a lack of financial backing for research, another large issue that has exacerbated the growth of opioid abuse is unsatisfactory physician education on pain practices and medication. With opioids being involved in around 90 deaths a day in 2015, many have argued that the failure of the medical community to adequately treat pain management is to blame (Rudd, Seth, David, & Scholl, 2016). This can in part be attributed to flaws in education (Rudd, Aleshire, et al., 2016). For people who deal with chronic pain, physicians are often their first line of defense. If physicians have not been educated properly in how to effectively prescribe opioid pain medication, patients may begin using their prescription medication without properly understanding the risks. Even worse, if a physician has not been suitably trained in pain assessment, patients with a propensity for addiction may be wrongly prescribed opioid pain medication. A report from the Institute of Medicine outlines that medical education does not provide the most comprehensive look into both understanding how pain functions or how to best assist patients in dealing with pain (Institute of Medicine et al., 2011). Despite the increased emphasis that the medical community placed on recognizing and dealing with pain in 1999 through the "Pain as the 5th Vital Sign" initiative and the 2001 Joint Commission on Accreditation of Healthcare Organizations report, increasing physician education in dealing with patient pain was not a part of this emphasis. Prescription numbers rose, but physician understanding of the risks inherent to using opioid medications remained generally stagnant. These gaps in education have produced physicians who sometimes do not know how to successfully and fairly counsel patients in dealing with their pain. In certain cases, prescriptions are written for patients in situations where medication was not necessarily needed and other management methods would have proved more effective (Cheatle, Comer, Wunsch, Skoufalos, & Reddy, 2014). Such unfair prescribing practices have undoubtedly contributed to the expansion of the opioid epidemic, and to best attack the current abuse rates, physicians must be more rigorously educated on how to fairly and ethically prescribe opioid pain medication.

To best tackle this issue, medical school curriculum and residency programs should place a greater emphasis on how to prescribe medication safely to patients. Training programs should also provide a more in-depth understanding to physicians on how to look for potential opioid abuse candidates to prevent prescribing medication to at-risk patients. Although the medical education community has recently expressed deep interest in enhancing opioid-related education, there has not been as much in the way of actual implementation. According to a report from the Johns Hopkins Bloomberg School of Public Health in November 2015, the American Association of Medical Colleges (AAMC) has pledged support for revamping education on pain practices and medicine; however, no official standards have been implemented for such changes. Since the Bloomberg School of Public Health report, the AAMC issued a statement in March of 2016 promoting the continued commitment of medical schools and teaching hospitals to opioid-based education. Seventy-four medical schools have since agreed and signed the AAMC statement. In addition, the CDC released a new set of guidelines for prescribing opioids in cases of chronic pain in March of 2016, and the AAMC states that a wide range of institutions have stated their hope to incorporate these guidelines into their education platforms (Krisberg, 2016). Despite all these stated commitments to enhancing medical education for pain and pain medications, there is more to be done in terms of actually enacting and following through with implementing more in-depth pain curricula in medical institutions. Currently, a full-length residency program that provides training in pain education and medicine does not exist in the United States, and postgraduate fellowship programs are reserved for only certain subspecialties of medicine. Such programs are not available for primary care physicians (Alexander, Frattaroli, & Gielen, 2015). The issue with this lies in the fact that patients who suffer from chronic pain often turn to their primary care physician when pain first arises (Institute of Medicine et al., 2011). Primary care physicians, therefore, play a unique role in setting the tone for how patients initially deal with chronic pain, and it is important that such providers are given adequate tools to safely and effectively treat chronic pain sufferers with opioid pain medication. Thus, enhanced education for pain practices and medication for primary care physicians is a necessity, and such programs should not be solely reserved for particular specialties such as anesthesiology and neurology. In one study, 47% of primary care physicians reported that they did not feel their medical schooling provided them with adequate tools to effectively handle opioid pain medication reliance, and 40% stated that they did not feel that their training prepared them to sufficiently deal with chronic pain (Keller et al., 2012). With such high levels of abuse and overdose, it is important that medical training shifts its focus from simply pledging its devotion to enhancing education for pain practices and medication to actually implementing much more rigorous training programs. Deepening pain education curricula in today's institutions needs to become a nationwide endeavor that is adopted and enacted by all medical institutions within the United States, and rigid standards need to be put in place requiring such changes in every state.

In addition, prescription monitoring program usage needs to become more widespread. When patients begin abusing prescription medication, oftentimes they will visit multiple doctors to obtain the medications they have become reliant on, in what is often referred to as "doctor shopping" (Sansone & Sansone, 2012). To circumvent this issue, PDMPs have been enacted in all states except for Missouri. Such monitoring programs were created with

the intention of providing physicians with a way to access previous prescription info of patients including the drug name, dosage, and strength of past prescriptions. They allow physicians to better identify patients who are at a high risk of abusing pain medication, screen those who may be engaged in "doctor shopping" practices, and ultimately monitor the pharmaceutical patterns of patients with the hopes of assisting physicians in ethically and fairly prescribing pain medication (Prescription Drug Monitoring Program Training and Technical Assistance Center, n.d.). With all of these benefits, PDMPs are an underutilized resource in the medical community. In a study hailing from the Johns Hopkins Bloomberg School of Public Health, 28% of physicians were unaware of the PDMP within their respective states (Rutkow, Turner, Lucas, Hwang, & Alexander, 2015). In addition, in instances where physicians did prescribe opioid pain medication, the data provided in PDMPs were accessed only a quarter of the time. In explaining their aversion to these systems, physicians state that using their state's PDMP is often too confusing and laborious (Alexander et al., 2015). There is also widespread variation in PDMP utilization across the country. As of December 2014, only seven states had full mandates requiring physician PDMP usage, and only 16 states had mandates in place for PDMP usage in certain cases (National Alliance for Model State Drug Laws, 2015). To ensure that physicians are taking advantage of the valuable data that PDMPs provide and are informing their clinical decisions with patients' previous prescription histories, physicians in every state should be legally required to use PDMPs in providing care to patients. Studies have shown that in certain states where PDMP usage is mandated, providers have substantially increased their request for patient prescription data. Thus, such statewide mandates actually do have an impact on PDMP utilization (PDMP Center of Excellence at Brandeis University, 2016). To best employ the numerous benefits of a PDMP system, physicians need to be required to enroll in them and use such systems. With the large and costly impacts that opioid abuse have presented in recent decades, it is important that the loophole of provider PDMP underutilization is tackled and addressed in every state. It should not be left to the individual discretion of physicians whether or not patient prescription information is accessed in informing clinical decisions, and all clinical interactions surrounding opioid pain medication prescription should involve these PDMPs.

Finally, it is important that patients with chronic pain understand that there are several alternatives to medication that they can utilize to help reduce their discomfort. Such strategies include self-management techniques as well as pain rehabilitation programs. A study conducted by the Mayo Clinic indicated that patients who typically used opioids for chronic pain experienced significant improvements in their pain levels after both entering comprehensive pain rehabilitation programs and ceasing their opioid use (Townsend et al., 2008). Additional strategies for pain reduction include acupuncture, exercise, relaxation therapy, as well as the vitamins and supplements. Although these may not provide as immediate of a relief as pain medication does, it is important that patients understand the additional, safer measures they can take to manage their pain. In dealing with chronic pain, each patient is different, and every individual's pain should be treated as such. Medication is so commonly used to calm chronic pain that it is easy to overlook the benefits inherent to self-management techniques, and increasing the emphasis physicians place on these additional strategies may help to reduce the incidence of opioid abuse.

Conclusion

Ultimately, there is no denying that opioid abuse rates have reached unprecedented levels in the United States today. The American people have been met with a culture that is obsessed with silencing and medicating pain, and the effects of this have been deadly. The story began with the heavily marketed introduction of OxyContin as well as the "Pain as a 5th Vital Sign" initiative during the 1990s. Over time, these efforts eventually led to a sharp increase in the number of prescriptions written for opioid analgesics during the late 1990s and early 21st century. The number of prescriptions written has only continued to increase since, and so have the rates of opioid analgesic–related deaths and both heroin- and fentanyl-related deaths. It would be a grave and critical mistake of the medical community to continue to so fervently add fuel to the growing fire that is the opioid epidemic. Steps must be taken today to prevent the death rates as a result of both prescription pain medication abuse and narcotic abuse from continuing to climb in the future. What initially began as an effort to reduce the discomfort of patients with chronic pain has now developed into a cry for help to stop individuals from medicating themselves to death. Funding must be increased to aid in the investigation of potential therapy techniques for chronic pain. In addition, today's institutions need to all work to fully implement and enact more stringent curricula surrounding pain education for rising physicians rather than just stating a commitment to do so. Finally, it is imperative that the medical community utilize state PDMPs in all instances where pain medication is involved in a current or past care plan. If these steps are taken, it may be possible to halt the surging rates of both overdose and death. It is the responsibility of the medical community and the scientific community to now work to ensure a better and safer future for the next generation of individuals who will suffer from chronic pain, and in doing so, it is likely that chronic pain will become less of a dangerous burden and more of a manageable condition.

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PERSPECTIVES

The Potential of Big Data and Data Science in Public Health Research

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Abstract:

Although big data already informs and influences the workings of many fields today, it has substantial potential to be applied in the field of public health. Big data refers to large amounts of data that cannot be analyzed with regular data analytics methods. To conduct such analysis, more involved data science methods have come in such as statistical methods, mathematical modeling, and other advanced algorithms, so the large amount of data can be properly mined and analyzed. These new methods of research and investigation in health care can provide new insights in disease management and drug discovery while informing health behaviors and health management. This article advocates for the use of big data when it comes to large data sets in health care such as pharmaceutical data, claims data, and clinical data such as doctors' notes. This also applies to any mobile apps built for public health–related initiatives using which data can be collected from users in real time for analysis. There is immense applicability of big data and analytical methods for handling public health crises on a global scale and for the improvement of health outcomes in low- and middle-income countries, as well as to better inform future public health research.

Keywords: Data Science, Public Health, Research Methods

Introduction

From newspaper articles, scholarly journal articles, blogs, videos, and other sources of information on the Internet and print, there are two buzzwords that have been increasingly featured in many different fields: big data and data science. Even more so, these two words have taken on a larger role in shaping public health research for the future by opening up more possibilities for data collection, data analytics, discovery of treatments for human diseases, and a better understanding of health behavior and management. Furthermore, as with any new innovative method, there are both advantages and disadvantages that characterize the application of big data and data science to research, particularly for public health crises. Despite the few disadvantages that may arise from utilizing big data, its advantages go beyond, making its usage powerful and effective.

Table 1. Sources of Big Data in Health Care.

Type of data	Features of data
Claims and cost data	Reveals cost, type, and amount of care with the potential to help track and identify cost-effective treatments
Clinical data	Consists of doctors' notes and patient medical records, which upon analysis can help identify at-risk individuals and a more comprehensive understanding of diseases
Pharmaceutical data	Consists of data from clinical trials of drugs that can be analyzed to understand participant demographics. It is also possible to use this data to compare drug performance across different trials and studies
Patient behavior and sentiment data	Consists of data from sources such as over-the-counter drug sales and patient behavior as monitored by devices; by understanding patient behavior, this data help gain a better understanding of how devices can be used to understand the population

Big Data, Data Science, and Data Analytics

In simplest of terms, "Big data" refers to large, complex data sets. The data may be "in such unprecedented quantities that terabytes (10^{12} bytes), petabytes (10^{15} bytes), or even zettabytes (10^{21} bytes) of storage may be required" for its storage, beyond the capacity of a single computer by itself (Wyber et al., 2015, p. 203). Not only does this data come in all different sizes but also from a variety of sources, thus supporting the idea that big data analytics can be performed in a variety of different fields. Considering the technology that exists today, such data can also be streamed in real time for analysis. For instance, consider a mobile app developed by a company that tracks a user's weight, diet, and medication. A data analyst at the company can collect in real time (stream) a user's information and analyze it to improve the app's design or better support the user with advice on their diet, and so forth. Thus, big data can be likened to "digital crumbs," which enable humans to have an "unprecedented, ubiquitous and continuous view of our individual lives and behavior: where we live and work, our activity level, travel patterns, shopping habits, what we eat and drink, and which people we interact with" (Pentland, Reid, & Heibeck, 2013, p. 4).

The term "data science" refers to the cleaning, processing, and analysis of data in order to extract insight, patterns, and relationships for variables. This involves a combination of "statistics, mathematics, programming, problem-solving" and more to extract insights from data (Monnappa, 2016). One such method applies machine-learning algorithms, which are predictive in nature and allow for a model that looks at a particular feature in the data to learn from itself. As more data is collected, the model is updated to more accurately reflect the data. Thus, it is natural for big data and data science to be paired together because the complexity of big data sets requires advanced data analytical tools.

According to Bernard Marr, a data scientist who writes for Data Science Central, a community website for individuals involved in big data and data science, there are four types of data from health care that can be analyzed using big data methods. Table 1 details these four types (Marr, 2015).

The data sources described in Table 1 represent the large data sets in public health that have the potential to be analyzed using data science methods for new insights. All of this data regarding patients in hospitals exists across the United States in the form of clinical data, and by tapping into big data and data science, public health research initiatives can be developed to address patient management or bring about new information about health behaviors or diseases. Even the everyday actions of users on a mobile app can be analyzed to track the public's health and give insight into the realm of public health.

Furthermore, not only is examining one data source possible with big data and data science but cross-comparison analysis of multiple, large data sets can also be performed. This is especially valuable for public health. By examining data such as electronic health records, genetic information, and other data sets together, there is greater potential to discover treatments in medicine, uncover patterns in human behavior, search for improvements to reconfigure health systems, or even analyze epidemics to create better prevention measures. Such large amounts of data can be mined using data science methods to uncover relationships and significance that previously would have been undetectable due to statistical constraints and missing information if analyzed by itself. Thus, there are many sources of data in public health that can be powerfully analyzed using big data and data science methods.

Global Efforts in Expanding Use of Big Data in Research Initiative

Using big data has potential in the field of public health, no matter where it is implemented: There is significant potential for their application in low- and middle-income countries. For example, such an approach has changed the epidemic pattern of dengue fever in Lahore, Pakistan, over the past few years. In 2011, the worst outbreak of dengue fever affected the city (Pentland et al., 2013). In 2012 and 2013, however, the combination of smartphones and big data analytics changed this. The development of software created from an open-source repository by the Centers for Disease Control and Prevention (CDC) in the United States enabled early detection of dengue fever once it was modified from its original use to detect outbreaks of flu epidemics (Pentland et al., 2013). The modifications allowed investigators to "identify high-risk areas for infection, and then to aggressively eliminate breeding grounds for the mosquito larvae" (Pentland et al., 2013, p. 25). In this manner, data science has applications that reach beyond the grasp of countries like the United States to help with public health measures instituted in other countries.

On the global scale, there is also a push for implementing data science and using big data for research initiatives, particularly public health–focused ones. The United Nations Global Pulse is a network of innovation labs that work to implement big data practices efficiently across the globe. Set up by the United Nations Secretary General, Global Pulse's mission aims to "accelerate discovery, development and scaled adoption of big data innovation for sustainable development and humanitarian action" (United Nations Global Pulse, n.d.). There are many projects piloted by the United Nations Global Pulse that operate in many different countries around the globe. One such project involves implementing an HIV Mother-to-Child prevention program. This lab is operating in Kampala, Uganda, and aims to use an application to monitor in real time the administration of an antiretroviral treatment that helps protect against HIV in women (United Nations Global Pulse, n.d.). Other projects analyze social media for an increased understanding of public knowledge and their attitudes related to

public health crises such as sanitation. For instance, a lab in Jakarta, Indonesia, is using social media to understand the public's views on immunization, tapping into a search for understanding health behavior in relation to a public health topic of concern (United Nations Global Pulse, n.d.). With such a focus on expanding big data and data science applications in public health on a global scale, there is widespread agreement on the power contained in these methods of data analytics and a push for more application of them in the future.

Disadvantages of Big Data

There are many advantages to using big data and data science methods as outlined above, but there are also a few disadvantages because with more data, there is more potential for errors in analysis, false outcomes, and confounding. False outcomes may surface due to "large-scale examination of putative associations with disease outcomes," where relationships may be discovered between variables that are seemingly significant but in reality insignificant (Khoury & Ioannidis, 2014, p. 1054). Another way to imagine this large-scale data problem is to refer to it as "finding a needle in a haystack" or as "signal and noise" where "separating the true signal from the gigantic amount of noise is neither easy nor straightforward, but it is a challenge that must be tackled if information is ever to be translated into societal well-being" (Khoury & Ioannidis, 2014, p. 1054). However, to combat this, principles of scientific research, statistical design, and refined data analytical methods can be used. Reproducibility of findings is a key factor in determining whether signals are actually signals in fields like genomics (Khoury & Ioannidis, 2014). Moreover, having research teams comprised of specialists in certain areas of statistical analysis, programming methods, and other data science areas can be effective as well. In this manner, the power of big data can be harnessed and false findings avoided. From this, it is clear that the benefits of using big data and data science analytics in public health research outweigh the potential negative consequences if certain procedures are followed and data is analyzed effectively.

Conclusion

Overall, it is clear that using big data and data science methods for data analytics is an emerging, interdisciplinary approach that is increasingly becoming relevant to the field of public health. By applying such an approach toward the handling of public health crises, public health researchers can redefine the way research is conducted. This approach may also result in new discoveries of treatments or provide new insight into health behavior and management. At the global level, the United Nations is pursuing this through innovative labs around the world in all kinds of countries from low income to high. It is clear that the potential of big data and its positive effects on the general public outweigh any negative consequences that may arise from data analysis. Through repeated testing and combination of data sets to confirm new discoveries, big data and data science can lead to more technological innovation and ultimately save lives.

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