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Endemic infectious diseases: Focusing the world's attention on neglected killers

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On October 23, 2014, at the height of the Ebola epidemic in Africa, the Washington Post published a massive graphic showing 310 million tiny human figures, each representing a resident of the United States. Readers who took the time to scroll to the bottom of the graphic found that three of the figures were coloured red to indicate the three Americans who had contracted Ebola to that point. (One died; two survived.) The accompanying headline sought to put the epidemic into context for U.S. residents; it read, “Want to feel better about Ebola? This (massive) chart should do the trick.”¹

Unfortunately, other contemporaneous headlines didn’t help Americans feel better about Ebola. As USA Today media columnist Rem Rieder wrote just days after the Washington Post published its graphic, “The breathless, alarmist reports, many from CNN and Fox, are the antithesis of what responsible journalists should be doing. As was the ludicrous effort by CNN’s Ashleigh Banfield to hammer the notion that Ebola is the ISIS of biological agents and raise the spectre of suicide attackers brandishing Ebola.” (Since Ebola is only spread through transfer of bodily fluids, it’s difficult to imagine how such suicide attacks would occur or could cause many casualties.)²

The saturation coverage of Ebola by outlets like CNN both overemphasised the disease’s impact on the West and minimised the real crisis in Africa, where nearly all of the outbreak’s 11,325 fatalities occurred. The coverage also distracted readers and health professionals alike from less exotic but far more prevalent health concerns like influenza, which affected 40,435,474 Americans during the 2014-2015 ‘flu season, according to the U.S. Centers for Disease Control. Had the Washington Post’s graphic focused on ‘flu instead of Ebola, one in every eight figures would have been coloured red. (For more on Ebola and other emergent threats, see the Aetna International opinion paper “Pandemic: Controlling infectious diseases before they spread”.)³

The unintended consequences of high-profile pandemics

This is not to say that news media don’t play an important role in informing the public and disseminating critical health messages. Moreover, stories in traditional media and social media alike often alert health officials to emerging threats; in fact, research has shown the potential for “infodemiology” efforts that use near real-time analysis of social media sites to detect and monitor outbreaks.⁴

At Aetna International, our concern is not with how western news media cover various diseases. Instead, our concern is with how that coverage — as well as the public fears that fuel it and are fuelled by it — can skew health practices and research spending. When the medical and research communities focus intently on emergent threats like Ebola or Zika, attention invariably shifts away from less “trendy” endemic threats like malaria and tuberculosis that are far more prevalent. And that can have deadly results.

According to researchers at Yale University’s Center for Infectious Disease Modeling and Analysis, the Ebola crisis actually made it easier for malaria, HIV/AIDS and tuberculosis to spread. As the crisis deepened in Guinea, Sierra Leone and Liberia, many clinics closed, interrupting the delivery of routine health services like HIV testing and childhood immunisations. Moreover, individuals concerned with nosocomial (hospital-acquired) Ebola infections shunned those facilities that did remain open. The results, according to the researchers, were tragic. “As unprecedentedly catastrophic as the Ebola outbreak has been, we estimated that these indirect repercussions of the Ebola outbreak may have been even greater than the deaths directly attributable to Ebola in Guinea, Sierra Leone and Liberia,” they wrote. In other words, Ebola may have claimed more indirect victims than direct victims. Since the Yale research only considered the

1 <https://www.washingtonpost.com/news/the-fix/wp/2014/10/16/want-to-feel-better-about-ebola-this-massive-chart-should-do-the-trick>

2 <https://www.usatoday.com/story/money/columnist/rieder/2014/10/27/the-news-media-and-ebola/18003831/>

3 <https://www.cdc.gov/flu/about/disease/2014-15.htm>

4 <http://journals.plos.org/plosone/article?id=10.1371/journal.pone.0014118>

impact of the Ebola response on malaria, HIV/AIDS and tuberculosis, the impact was probably even worse.⁵

While emergent diseases chase patients away from clinics, they also suck research dollars away from other health issues. For example, in February 2014 the U.S. government shifted nearly \$600 million that had been budgeted for responding to the Ebola crisis to the new Zika crisis. A few months later, when mosquitos in the state of Florida were found to be transmitting Zika, President Barack Obama directed the National Institutes of Health to redirect \$34 million in research spending and \$47 million in other medical spending to the new threat. “This crosses a line,” an editorial in the journal *Nature* argued. “Even when one sets aside global scourges such as malaria — which affects millions of people each year and rarely draws strident calls for emergency funds — Zika is just one more virus that affects the United States. Others include West Nile virus (which has no approved human vaccine), dengue and chikungunya, as well as the seasonal and circulating influenza viruses that can kill thousands.”⁶

Moreover, increased funding related to emergent threats like Ebola and Zika can mask a decline in overall research spending. The annual G-FINDER survey, which tracks global investment in research and development (R&D) to fight 39 neglected diseases, found that global R&D funding reached historic lows in 2015; in fact, it said year-over-year funding had fallen \$180 million from its 2012 peak. The survey also found

that the total spent on Ebola and other African viral haemorrhagic fevers (VHFs) was second only to the total invested in HIV/AIDS, which claimed nearly 100 times more lives per year than Ebola did at its peak. According to the survey, HIV/AIDS received 33 percent of global R&D funding, while Ebola and other VHFs received 21 percent.^{7,8}

One solution advocated by politicians and health experts alike is the creation of a “rainy day” fund to deal with emergent threats without diverting resources from other research. In the United States, President Donald Trump has proposed such a fund, and a bipartisan group of Senators led by Sen. Bill Cassidy, M.D., has introduced the Public Health Emergency Response and Accountability Act. In announcing this legislation, Cassidy said, “Future public health emergencies like Zika are inevitable. The pattern is well known, an outbreak of disease occurs, public panic grows, Congress scrambles and appropriates money. This is an inefficient and dangerous way to deal with public health emergencies. As a doctor, with a background in public health, I know there is a better way. If a hurricane hits our nation, [the Federal Emergency Management Agency] already has a budget which is automatically triggered, it is not held up by partisanship, it allows the resources needed to immediately flow to where they are needed the most.” Unfortunately, the legislation has not been enacted.^{9,10,11}

5 <https://wwwnc.cdc.gov/eid/article/22/3/pdfs/15-0977.pdf>

6 <https://www.nature.com/news/zika-response-must-not-drain-research-funds-1.20511>

7 <http://www.policycuresresearch.org/downloads/Y9%20GFINDER%20full%20report%20web.pdf>

8 <http://www.unaids.org/en/resources/fact-sheet>

9 <https://www.scientificamerican.com/article/robust-emergency-fund-needed-to-respond-to-future-disease-outbreaks/>

10 <https://www.cassidy.senate.gov/newsroom/press-releases/cassidy-schatz-rubio-durbin-nelson-introduce-the-public-health-emergency-response-and-accountability-act>

11 <https://www.congress.gov/bill/115th-congress/senate-bill/196>

Clarifying terms

In studying and discussing disease outbreaks, it's important to understand those outbreaks' scope. The following terms are sometimes used interchangeably but have specific, discrete meanings:

Outbreak: an occurrence of a disease than is larger than would ordinarily be expected

Epidemic: a widespread increase of a disease within a given population

Endemic: a consistently heightened rate of a disease within a given population

Pandemic: a widespread increase of a disease over multiple populations around the world

Travel patterns and modes of transmission impact whether any given outbreak remains localised or becomes an epidemic or a pandemic. Despite pervasive fears, Ebola didn't gain a significant foothold outside West Africa, in part because patients were too sick to travel and in part because the virus can only be transmitted through bodily fluids, not through airborne particles. Neither condition is true for influenza.¹²

An infectious disease hall of shame

Although many infectious diseases plague the world, especially in low-income countries, a mere handful are responsible for more than one in eight deaths globally. They are:

Lower respiratory tract infections. This category, which includes pneumonia, accounts for more than 4 million deaths annually, mostly in the developing world. Pneumonia is the leading cause of death among the very young.

Diarrhoeal disease. Caused by dirty water, poor hygiene and inadequate or non-existent sanitary facilities, diarrhoeal disease is a symptom of infections caused by bacterial, viral and parasitic organisms spread largely through faeces-contaminated water. It kills 1.5 million people annually, half of them under the age of 5.¹³

Tuberculosis. This bacterium-caused disease causes 1.5 million deaths a year. More than half of deaths occur in Asia, and most of the rest occur in other parts of the developing world. A staggering one-third of the world's population carry TB, although most are latent carriers.

HIV/AIDS. HIV, the virus that causes AIDS, is transmitted through sexual contact, sharing needles or transfusion of tainted blood; infected mothers can also pass the virus to their unborn children or through breastfeeding after birth. AIDS kills 1.1 million people annually.

Malaria. This parasitic disease claims 438,000 lives annually, most of them children who live in sub-Saharan Africa. It has rebounded in areas where mosquito eradication has been halted due to environmental concerns.¹⁴

¹² <http://www.who.int/mediacentre/news/statements/2014/ebola-travel-trasport/en/>

¹³ <http://www.who.int/mediacentre/factsheets/fs330/en/>

¹⁴ <http://needtoknow.nas.edu/id/threats/global-killers/>

Viruses on the move

It's common knowledge that viruses are constantly mutating, which is why each year's influenza vaccine must be reformulated. In fact, influenza viruses change in two different ways. There are small changes over time — called antigenic drift — that gradually accumulate until people's immune systems no longer recognise the virus and they get ill again. And there are abrupt, major changes — called antigenic shift — that result in new viruses for which few people have protection. The appearance of the H1N1 "swine flu" virus in 2009 was the result of such an antigenic shift. It led to a pandemic that caused more than 18,000 laboratory-confirmed deaths in more than 214 countries and territories. (Some researchers think the death toll was 10 times higher.)^{15, 16, 17}

But viruses and other disease-causing microorganisms don't just mutate. They also move. That has been the case with the parasites that cause Old World cutaneous leishmaniasis (CL), a generally nonfatal condition that causes disfiguring scars, which in turn can lead to social stigmatisation, anxiety, depression and other problems.

Endemic in Syria for more than two centuries, CL has hitched a ride with people displaced by a long-running civil war that has caused 6.5 million internal displacements and 4.4 million external

displacements. In 2013, the number of cases of CL in the country was perhaps four times the number from a decade before, and the disease has cropped up in Lebanon, Tunisia and Turkey among refugee populations. As an editorial in PLOS Neglected Tropical Diseases explained, "As populations migrate to endemic and non-endemic regions, they are exposed to infections for the first time or introduce diseases into new areas, respectively. Additionally, the chaos and instability often lends to poor living conditions, which further exacerbate the risk for rapid transmission of infectious diseases."¹⁸

The solution to the CL outbreak is both simple to prescribe and hard to implement, according to one scholar: "The most effective policies in addressing the potentially devastating CL situation that is emerging from some conflict zones in MENA [the World Health Organization's Middle East and North Africa region] are initiatives that will promote disease control while simultaneously promoting the survival of refugees. Provisions of clean water, food, hygiene services and adequate shelter will improve the living conditions of refugees while simultaneously addressing many of the socioeconomic and environmental risk factors that make refugees highly susceptible to infectious diseases."

15 <https://www.cdc.gov/flu/about/viruses/change.htm>

16 http://www.who.int/csr/don/2010_05_14/en/

17 <http://www.npr.org/sections/health-shots/2013/11/26/247379604/2009-flu-pandemic-was-10-times-more-deadly-than-previously-thought>

18 <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004545>

Such measures would also help in the fight against other diseases. The organisation Health Outreach to the Middle East (HOME) has drawn connections between civil unrest and marked increases in cholera, poliomyelitis, measles and other infectious diseases. For example, polio returned to Syria in 2014, 15 years after being eradicated, due to sewage-contaminated water, overcrowding in refugee camps and a huge drop in the immunisation rate (from 91 percent in 2010 to perhaps 45 percent in 2013). Moreover, the polio strain in Syria has been tentatively linked to a jihadist fighter who travelled from Pakistan, another indication of how infectious disease can move into new territories.¹⁹

Tracking the flow of research dollars

It would be logical to assume that research dollars flow toward those diseases that have the most devastating impact, but that's not always the case. Political pressure, advocacy, donor fatigue and the perceived risk to the donor's home country can all play a role. (A similar situation occurs with cancer funding, where breast and prostate cancer receive far more funding relative to their incidence than do bladder and lung cancer.²⁰)

Those factors don't just impact emergent diseases like Ebola. According to the Q-FINDER survey, the top five neglected and most deadly diseases described above receive vastly different levels of R&D funding:

1. lower respiratory tract infections, 3 percent of global funding;
2. diarrhoeal disease, 5 percent;
3. tuberculosis, 19 percent;
4. HIV/AIDS, 33 percent; and malaria, 19 percent.

Put another way, HIV/AIDS is the fourth most deadly disease on the list, yet it receives more funding than the previous three diseases combined.²¹

Diarrhoeal disease: a case study

Work by the charity PATH (formerly the Program for Appropriate Technology in Health) illustrates the impact of shifting priorities. In the 1980s and 1990s, the group reports, the health community made diarrhoeal disease a global priority. The WHO created the Diarrhoeal Disease Control Programme. UNICEF promoted the use of oral rehydration solution as an effective treatment for severe diarrhoea. An array of NGOs worked to train health care workers and communities. Development brought water to more than 2 billion people and sanitation to more than 1.5 billion people. But then priorities shifted and momentum slowed. Now, nearly 4,000 children succumb each day, 90 percent of whom could avoid contracting diarrhoeal disease with known interventions.²²

Part of the problem could be that people mistakenly think the problem has already been solved; after all, it hardly exists in the developed world where clean water and sanitation are ubiquitous. But another problem could be related to the mind-set of donor organisations and nations. As members of the UN Millennium Project's Task Force on Water and Sanitation wrote in *The Lancet*, "Far more people endure the largely preventable effects of poor sanitation and water supply than are affected by war, terrorism and weapons of mass destruction combined. Yet those other issues capture the public and political imagination — and public resources — in a way that water and sanitation issues do not. Why? Perhaps in part because most people who read articles such as this find it hard to imagine defecating daily in plastic bags, buckets, open pits, agricultural fields and public areas for want of a private hygienic alternative (as do some 2.6 billion people). Or perhaps they cannot relate to the everyday life of the 1.1 billion people without access to even a protected well or spring within reasonable walking distance of their homes."²³

19 <http://docs.house.gov/meetings/FA/FA16/20160302/104377/HHRG-114-FA16-Wstate-Raadl-20160302.pdf>

20 <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3411479/>

21 <http://www.policycuresresearch.org/downloads/Y9%20GFINDER%20full%20report%20web.pdf>

22 https://www.path.org/publications/files/IMM_solutions_global_killer_pp1-14.pdf

23 [http://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(05\)17991-4/fulltext](http://www.thelancet.com/journals/lancet/article/PIIS0140-6736(05)17991-4/fulltext)

Framing a global response

While crises like Ebola and Zika can cause knee-jerk overreactions, they can also lead to more thoughtful responses. In the wake of the Ebola outbreak, the Commission on a Global Health Risk Framework was formed to “set out a framework of institutions, policy and finance that would be resilient to a wide range of such potential threats, whether known — such as influenzas, coronaviruses and haemorrhagic fevers — or as yet unknown.” The 17 commissioners, who represented a dozen countries, held 11 days of public meetings on four continents and heard from more than 250 invited presenters.²⁴

The commission’s 2016 report, “The Neglected Dimension of Global Security: A Framework to Counter Infectious Disease Crises,” offers concrete recommendations in three broad areas: “first, reinforcing national public health capabilities and infrastructure as the foundation of a country’s health system and the first line of defence against potential pandemics; second, reinforcing international leadership and coordination for preparedness and response; and third, accelerating research and development in the infectious disease arena.”²⁵

We believe that following the commission’s recommendations would go far toward preparing the world for the next pandemic. It would also help the world deal with endemic threats like malaria and tuberculosis that may never emerge as global threats but that continue to claim thousands of lives every day.

Local solutions to local problems

The Commission on a Global Health Risk Framework focused largely on national and international efforts. While there’s much to be done in those arenas, local efforts are also important. After all, local health

workers often have the ability to prevent or at least contain outbreaks of infectious disease at the source.

Take the apparently straightforward example of introducing toilets to schools in India, which can greatly reduce incidence of diarrhoeal disease among children. According to M.A. Balasubramaniam from the Swami Vivekananda Youth Movement, “we actually had to negotiate the space for toilets in the school in the first place. The credibility of the initiator is the major factor. You cannot enter the school as a stranger and expect to succeed if you don’t have credibility; what the people trust is the quality of the relationship; it is not the dollars! To build trust you need to respect people, be transparent — how open are you to address the issues that people are raising once you have explained your project — and accountable. When you start working on these core issues, trust gets nurtured, interventions become possible and impact is possible.”

Balasubramaniam’s comments could relate equally well to promoting child immunisation or HIV testing or self-quarantine during an epidemic. Local people enjoy a level of trust outsiders never can. If that trust is coupled with knowledge, positive health outcomes are possible.²⁶

For example, residents of India’s vast rural regions rely on Anganwadi workers (AWWs), community health workers who provide everything from antenatal care to supplementary nutrition to informal preschool education. (The name literally means “courtyard shelter,” reflecting the worker’s place at the centre of village life.) A network of some two million AWWs serve perhaps 70 million Indians, referring those who need follow-up care to a primary health centre. As one researcher has written, “The AWW is a force to be reckoned with. She is an agent of change in the community.”^{27, 28}

24 <https://www.nap.edu/catalog/21891/the-neglected-dimension-of-global-security-a-framework-to-counter>

25 <https://www.nap.edu/catalog/21891/the-neglected-dimension-of-global-security-a-framework-to-counter>

26 <http://www.wateraid.org/~media/Publications/School-WASH-reports/WaterAid-school-WASH-research-report-India.pdf?la=en>

27 <http://healthopine.com/the-anganwadi-workers-of-india-connecting-for-health-at-the-grassroots/>

28 <http://www.joaor.org/knowledge-attitude-and-practices-of-anganwadi-workers-regarding-oral-health-of-children-in-virajpet-taluk-article.html>

One important role AWWs play is supporting India's annual Pulse Polio immunisation drives. On the 2017 campaign date, Chennai state alone opened 43,051 immunisation booths at schools, government hospitals, schools and Anganwadi centres. Thanks to efforts like that, the World Health Organization declared India to be polio free in 2014.^{29,30}

Also important at the local level are efforts to minimise health risks at animal-human-environment interfaces. Today, three-quarters of infectious pathogens are zoonotic, meaning they are transmitted from animals to humans. The poor are the most likely to live in close proximity with livestock and wild animals, which heightens their risk of contracting diseases like avian 'flu, brucellosis and rubella. In fact, zoonotic pathogens kill 2.2 million in the developing world each year. Strengthening both human and veterinary health systems would help to address this problem.³¹

Zoonotic infectious diseases are of special concern in Southeast Asia. According to researchers at the National University of Singapore, "Rapid population growth, urbanisation, climate change, an intensification of livestock production, increased human mobility and trade in livestock and wildlife across national borders, changes in land-use and deforestation all underpin and exacerbate the region's susceptibility to infectious diseases, capable of achieving pandemic proportions." Unfortunately, they say, the International Health Regulations — which require reporting of disease outbreaks — intentionally omit zoonotic threats.³²

Conclusion

Beyond strengthening basic health services, we believe the world community needs to be more proactive toward infectious disease. All too often, we take a "Whack-a-Mole" approach, focusing on a specific disease while it is dominating headlines, meanwhile ignoring other diseases and, more importantly, the underlying issues that allow these diseases to become crises.

We also think it's critical to invest in global development. According to the Gates Foundation, nearly 2.5 billion people live on less than \$1.90 a day and more than 1 billion suffer from chronic hunger. Their lack of adequate food, shelter and sanitation puts them at heightened risk of an array of diseases — not to mention creating misery. (One factor in Syria's CL outbreak has been that inadequate housing exposes refugees to parasite-carrying sand-flies.)^{33,34}

Finally, we think disease-specific research is also important — although research money should be better allocated than it is today. We recommend that top pharmaceutical companies earmark 0.25 percent of their sales revenue for research around diseases that don't affect the Western world. Imagine the impact that \$1 billion or more a year could have in Africa. We have already seen the impact of focused research on Ebola with recent reports of a successful vaccine trial.³⁵

At a time when people in many countries are retreating behind their borders, it can be tempting to turn a blind eye on conditions in the Middle East, sub-Saharan Africa or other corners of the developing world. However, doing so would be immoral and ultimately counterproductive. The world is always just one failed state away from a humanitarian crisis that can overwhelm border controls and one mutated virus away from an historic pandemic.

29 <http://timesofindia.indiatimes.com/city/chennai/polio-vaccination-in-43000-booths-today/articleshow/58441039.cms>

30 <http://www.thebetterindia.com/22182/success-story-of-eradication-of-polio-in-india/>

31 <http://www.worldbank.org/en/news/feature/2013/03/05/flu-outbreaks-reminder-of-pandemic-threat>

32 <http://global-is-asian.nus.edu.sg/index.php/controlling-emerging-infectious-diseases/>

33 <http://www.gatesfoundation.org/What-We-Do>

34 <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004545>

35 [http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736\(16\)32621-6.pdf](http://www.thelancet.com/pdfs/journals/lancet/PIIS0140-6736(16)32621-6.pdf)



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Whitepaper Volume IV — which explores cardiovascular disease — is due out later in the summer

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