

TODAY'S CHALLENGES IN OUTBREAK PREPAREDNESS

The Role of Surveillance

“Rapid trans-boundary spread of infectious diseases, emerging infectious diseases, rising antimicrobial-drug resistance and the threat of bioterrorism are some of today’s most pressing global health security issues. Getting the basics right for infectious disease surveillance is now more pertinent than ever before. Yet in order for a surveillance system to continue to be effective... it needs to evolve to meet the current and foreseeable challenges.”



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ABSTRACT

The costs of infectious disease (ID) outbreaks can be staggering in terms of human suffering, burden on society and economic loss. While past public health reforms in sanitation, public works, vaccination and the development of antimicrobial drugs have led to great leaps in the battle against ID outbreaks, new challenges have surfaced for public health communities. Emerging infectious diseases (EIDs) are being discovered at an average rate of one per year, antimicrobial resistance is on the rise and bioterrorism is a looming threat. The world's intensifying interconnectedness have opened the way for IDs to spread rapidly and cross national boundaries. Outbreaks are no longer merely domestic concerns; it is now in the interest of the global community to ensure that national outbreaks are prevented, contained and effectively managed.

Surveillance forms the backbone of all outbreak alert and response systems and is key to minimizing the impact of outbreaks. In spite of existing surveillance efforts, outbreaks that were unexpected – in emergence, spread or scale – have happened in recent years. This paper discusses the reasons for surveillance failures – human negligence, system inadequacies and inefficiencies, low quality data, underestimation of incidence, delayed reporting, inadequate surveillance reach and the unexpected unknowns (“black swans”).

Improvements to the existing surveillance systems are pertinent. Yet outbreak

surveillance continues to evolve with methods and approaches that have arisen from recent advances in science, technology and understanding of EIDs. Some of these developments are explored in the paper.

We examine the promises and implications of new methods in data and intelligence gathering, participatory surveillance, mapping and modeling of epidemiology and population movements, genomic analyses of pathogen strains, and the use of big data science. We then consider how recent technological developments can increase the potential for syndromic surveillance to augment the shortfalls of traditional surveillance. We also discuss the call to a ‘One Health’ approach in response to intensified connections in human, animal and ecological health.

Finally, we look at the main challenges in integrating the new methods and approaches with existing surveillance systems, and the issues that are relevant for deciding if a new surveillance initiative is worth adopting.

In order to remain effective, surveillance systems must continually “learn” and evolve. The threat of IDs to global public health may have increased. However, the global community can rise to these challenges through closer surveillance partnerships, and creatively applying scientific and technological advances to surveillance methods, while continuously strengthening capabilities to do the basics well.

GLOBAL BURDEN OF INFECTIOUS DISEASE OUTBREAKS

It is a sobering exercise to ponder the devastating impact epidemics have had on individuals, families, communities and nations – human suffering, disability, death, stigma, economic costs and significant set-back in national development efforts. Consider tuberculosis (TB). In 2014 alone, 9.6 million people, including 1 million children, fell ill with TB and 1.5 million (of whom 140,000 are children) died from it. ^[1] As the leading infectious cause of adult death in the world, the impact of TB falls heaviest on developing nations (95% of new cases and 99% of deaths) ^[2], many of whom face poverty, socio-economic and political instability, and vulnerability to other infectious diseases (IDs). The consequences of TB are worse for those with conditions that weaken their immune systems (e.g. HIV, diabetes and cancer). TB costs the global economy about US\$12 billion a year and in high-burden countries, it can decrease GDP by 4% to 7%. ^[3] In cases of drug-resistant TB, the impact of the disease increases manifold - about 20% of cases are diagnosed and treated, and only 10% of those are successfully treated; while it costs US\$17,000 to treat someone with drug-susceptible TB, the cost is nine-fold for multidrug-resistant TB (MDR-TB) at US\$150,000, and twenty eight-fold for extensive drug-resistant TB (XDR-TB) at US\$482,000. ^[3] It was estimated that MDR-TB may cost the world economy US\$16.7 trillion between 2015-2050.^[3] At the individual level, TB means 3-4 months loss in work time on average annually, 20%-30% decrease in household income and 15 years of lost income for families of those who die from the disease.^[2] While the health and economic costs can be measured, it is much

harder to fully understand the disease's impact on the lives of children orphaned by it and those who become more deeply entrenched in poverty because of it.

In recent memory, IDs that had caused global alarm included variant Creutzfeldt-Jakob disease (vCJD) in 1996, Severe Acute Respiratory Syndrome (SARS) in 2002/3, Influenza A H1N1 (“swine flu”) in 2009, Middle-east Respiratory Syndrome (MERS) in 2012, Ebola in 2014 and most recently, the 2015 Zika outbreak in Brazil. Box 1 describes the impact of some of these diseases. Dengue, for which there is currently no known effective anti-viral and vaccine, was identified as the world's “most rapidly spreading mosquito-borne viral disease” by the World Health Organization (WHO) in 2012. There is also a growing sense of urgency to address the dramatic rise in anti-microbial resistance (AMR) around the world. In September 2016, the 71st session of the United Nations General Assembly (UN GA) called for member states to affirm their commitment to take concrete steps and curb this growing public health threat (it was only the fourth time a health issue had been taken up by the UN GA).

Recognizing the potential for local outbreaks to become pandemics that threaten global security and stability, the International Health Regulations (IHR) include the provision for WHO's Director-General to declare a disease a ‘Public Health Emergency of International Concern’ (PHEIC) and obligates member countries to report, in addition to the list of specified diseases, “any disease of urgent international public health importance”. ^[4]

BOX 1: IMPACT OF RECENT PANDEMICS

Variant Creutzfeldt-Jakob Disease (vCJD)

This fatal human neurodegenerative disease became epidemic in the UK in 1996. Since its initial identification, 225 cases from 12 countries were found. [5, p131] Its cause was traced to exposure to cattle or cattle products infected with Bovine Spongiform Encephalopathy (BSE). The link to BSE led to plummeting demand for UK beef and the UK government spent £1.5 billion in 1996/97 on culling measures and compensation. [6] The estimated total economic cost consisting of the impact on the beef industry and operating costs of regulatory measures in the following year was between £740 million and £980 million. [6]

Severe Acute Respiratory Syndrome (SARS)

The pandemic lasted from November 2002 to August 2003 with a total of 8,422 cases and 916 deaths globally. [7] It cost the world about US\$40 billion to US\$54 billion. [8] During the pandemic, thousands were quarantined, schools were suspended, hospitals were closed, borders shut down, international travel fell by 50%-70%, hotel occupancy fell by more than 60% and affected businesses had to be curtailed. [9]

Influenza A H1N1

This virus was first confirmed in a human in California USA on 15 April 2009 and subsequently additional cases were identified. [10] It was later verified that the first cases occurred in Mexico in February that year. WHO declared the A (H1N1) virus outbreak in humans as a Public Health Emergency of International Concern (PHEIC) on 25 April 2009 and declared a global pandemic on 11 June 2009. [10] The pandemic lasted till 10 July 2010. The total number of

laboratory-confirmed A (H1N1) deaths reported to WHO was 18,449 from 214 countries; a number acknowledged to be a gross underestimate. [11] A later attempt toward a more accurate estimate places the global mortality in the range of 151,700 to 575,500. [12] Worldwide tally for the number of cases of infection was estimated to be "several tens of millions of cases to 200 million" [13], with children aged 5 or younger at higher risk. In the USA alone, there were about 60.8 million cases and 274,304 hospitalizations. [14] The main causes for economic loss due to the pandemic are direct costs of medical care and to the health system, fall in pork trade, culling and compensation costs, decreased travel and drop in productivity due to illness. Mexico lost US\$4 million in trade and travel (0.4% of their GDP). [5, p129] Depending on the outbreak's severity in each country and their response, GDP loss to affected countries was estimated to be between 0.5% to 1.5%. [15]

WHO pays particular attention to influenza viruses. Due to the ability of the influenza virus to evolve quickly, cross the animal-human species barrier and spread easily through water droplets in the air, influenza outbreaks are difficult to predict. Influenza pandemics can potentially lead to devastating global health, social and economic impact. Every year, 500,000 people die from influenza and a severe influenza pandemic could cost the world an estimated US\$3 trillion (about 4.8% of global GDP). [16]

Ebola virus disease (EVD)

In the most recent and severe EVD outbreak, initial cases occurred in March 2014 across multiple West African countries. [17] WHO declared it a PHEIC on 8 August 2014. [18] As at 10 June 2016, a total of 28,616 EVD cases had been reported in Guinea, Liberia and Sierra Leone with 11,310 deaths [19] and cost affected countries about US\$2.2 billion [20], a major setback to the development efforts of these nations who had some of the lowest GDP in the world [21]. Affected countries struggle to respond as the required human and financial resources were unplanned for and resources meant for other development projects had to be reallocated for outbreak management. [22] The economies of Sierra Leone, Guinea and Liberia, the three most affected countries, shrank due to decline in labor force, trade, travel, productivity, and government measures to restrict movements. [22] The global alarm over the outbreak was primarily due to fears of further international spread of EVD for which there was no known cure or vaccine. [22]

Zika virus

WHO declared the unusually high number of microcephaly cases seen in Brazil as a PHEIC on 1 February 2016. [23] These cases were linked to human infections by the mosquito-borne Zika virus. Since 2007, 70 countries have reported Zika transmissions, of which 53 reported their first outbreaks from 2015 onwards. [24] Symptoms of the virus are usually mild and require no specific treatment. However, the potential congenital complications in children born to women with Zika, including microcephaly, Guillain-Barré syndrome (an autoimmune neurological disorder), and other congenital abnormalities (termed 'congenital Zika syndrome'), are far more serious. Manifestations of congenital Zika syndrome include craniofacial disproportion, spasticity, seizures, irritability and brainstem dysfunction including feeding difficulties, ocular abnormalities, calcifications, cortical disorders and ventriculomegaly. [25] Preliminary data also suggests that genitourinary, cardiac and digestive systems can be affected. [25] WHO has prioritized Zika-related research and development for diagnostics, vaccines and vector-control tools. [26]

CURRENT CHALLENGES

Routine cross-border travel and trade are the engines driving global progress, and a dense web of trade and travel routes traverse the globe. IDs spread via these same routes. Globalization has also meant an increasing number of large mass international gatherings (e.g. religious pilgrimages, sporting events) and the consequent growing risk of importation and exportation of IDs. The threat of bioterrorism, where there is an intentional release of infectious agents into a targeted community, is also a growing concern for global and national health security. Intensified connectedness between countries have made the potential total burden and devastation of outbreaks greater than ever before.

Emerging infectious diseases (EID) are being discovered at an average rate of one per year. ^[5, p128] Most of the pandemics in recent decades that caused global alarm were caused by EIDs (e.g. AIDS/HIV, vCJD, A (H1N1), SARS, Ebola, MERS, Zika). By definition, when an EID appears, its occurrence is unexpected, its epidemiology is uncertain, and knowledge about treatment is usually absent or scant. The prospect of being “caught by surprise” by an EID and its potentially devastating impact on peoples and economies have made understanding and preparing for EID outbreaks a central concern for global health security.

SURVEILLANCE

In light of the challenges to pandemic preparedness posed by EIDs in a globalized world, the public health community has recognized that outbreaks are no longer merely a domestic concern; a global perspective is vital to an effective ID national surveillance system, and prevention is better than cure.

Surveillance forms the backbone of all outbreak alert and response systems. A nation's ability to prevent and manage epidemics is severely crippled without robust ID surveillance. On the other hand, good surveillance can significantly reduce the impact of outbreaks of both known and EIDs. Early detection of outbreaks enables public health authorities to take action as early as at an outbreak's onset and stem its spread, thereby mitigating its impact. Surveillance data ensure that outbreaks are contained as swiftly as possible by providing key information for resource allocation to target interventions for optimal outcomes, as well as tracking the effectiveness of interventions and treatments.

Most surveillance conducted in Southeast Asia rely on the traditional notification-based approach where national healthcare authorities make it mandatory for healthcare institutions, healthcare workers and

laboratories to send notifications when they detect any of the specified IDs. Countries in the region have also adopted WHO's recommended surveillance standards to varying degrees and participate in global efforts to meet international control/elimination targets for specific IDs (e.g. Global Polio Eradication Initiative, WHO's End TB Strategy, WHO's Global Strategy For Dengue Prevention & Control 2012-2020). There have also been multiple initiatives to develop regional partnerships for surveillance and pandemic preparedness that involve the sharing of surveillance data with one another (e.g. Mekong Basin Disease Surveillance Project, Greater Mekong Subregion Communicable Disease Control Project, Surveillance and Investigation of Epidemic Situations in Southeast Asia, ASEAN Plus Three Emerging Infectious Diseases Programme). On a global level, countries join international surveillance networks where they can share data and gather intelligence (e.g. Global Public Health Intelligence Network, Global Influenza Surveillance and Response System, Global Polio Laboratory Network). Most of these surveillance methods deal largely with clinical data requiring laboratory confirmation – a process that can take days or weeks, which may result in a loss of precious decision and response time in the event of an outbreak.

OUTBREAKS IN SPITE OF EXISTING SURVEILLANCE EFFORTS

In spite of existing surveillance efforts, outbreaks that were unexpected – in emergence, spread or scale – have happened in recent years. Globally there were SARS, A (H1N1), MERS, Ebola and Zika. Regional epidemics like Influenza A H5N1 and Nipah Virus raised concerns, and among the national outbreaks there were anthrax attacks in the USA in 2001, cholera in Haiti in 2010, a novel strain of *Escherichia coli* O104:H4 bacteria in Germany in 2011, viral hepatitis in US in 2013, bubonic plague in China in 2014, Singapore's Hepatitis C and Group B Streptococcus outbreaks in 2015, Salmonella Poona infections in the USA in 2016 and yellow fever in Angola in 2016. This is indicative of more that needs to be done to bring national surveillance efforts up to par. A review conducted in 2014 found that “only 64 of WHO's 194 Member States had the essential surveillance, laboratory, data management, and other capacities in place to fulfil their obligations” under the International Health Regulations (IHR), this was 7 years after the IHR came into force in 2007. [27] The following are some reasons for why surveillance efforts had failed. Examples are given in Box 2.

HUMAN FAILURE

Neglecting to study the surveillance data that are collected can be a costly mistake when crucial signs of an impending outbreak are missed. It was estimated by a research funder that 90% of collected data are never used. [28] Even if the data were studied, there can also be failure to detect or recognize the signs of an outbreak; these can be caused by

misinterpretation of the data or clinical signs, weak case definition, and inaccurate calibration or poor validation strategy of signal thresholds.

SYSTEM INADEQUACIES AND INEFFICIENCIES

Surveillance is greatly hindered when governance, infrastructure and processes are absent or dysfunctional. The reasons for this are myriad and complex – political, economic and socio-cultural. In addition, the historical tendency to develop surveillance programmes around diseases led to national surveillance systems that are a composite of various vertical disease-centred programmes, resulting in fragmented and disjointed systems.

In 1998, WHO introduced the Integrated Disease Surveillance and Response (IDSR) framework to help member states move toward a coordinated surveillance system supported by a single infrastructure, and achieve a more effective and efficient surveillance system. By 2013, 49 member states had adopted IDSR. Though progress has been seen, there continues to be challenges related to support infrastructure, processes, and personnel training. [29]

Fragmentation is exacerbated when there are multiple donor agencies with overlapping agendas – surveillance for a single ID can have several funding streams, each with its own governance, processes and budget. The overall result is a frontline workforce that is overburdened by the need to simultaneously manage different reporting systems, schedules and surveillance methods –

overwhelmed and demotivated. [30, p8] Furthermore, even the most motivated personnel cannot do much without the basic support infrastructure (e.g. telecommunication, equipment, software).

Finally, surveillance data collection is futile when surveillance is divorced from the “response” aspect of outbreak preparedness. Without consideration of the objectives and outcomes for a surveillance activity, and prior understanding of how each piece of data should inform response, the collected data benefits no one.

Systemic inadequacy is not only a challenge faced at the national level. In their report on the global response to Ebola, the independent panel jointly formed by Harvard Global Health Institute and the London School of Hygiene & Tropical Medicine was unequivocal in pointing out that gaping holes in the global surveillance and response system had given the Ebola virus opportunity to create the havoc it did. [31] The gaps identified by the panel were rooted in a fundamental lack of clarity in the roles, responsibilities and accountability among all parties (local, national, regional, international, public, private, non-profit). [31, p2205] Of the gaps identified, those pertaining directly to surveillance included i) shortage of national and donor support for building up national health systems; ii) insufficient monitoring of efforts to do so; iii) inadequate incentives for countries to report outbreaks; iv) “WHO was slow to mobilize global attention or assistance”; v) weak channels for lessons from previous Ebola outbreaks; and vi) lack of emphasis on community engagement. [31, p2208]

LOW QUALITY DATA OR INACCESSIBILITY TO (OR LACK OF) RELIABLE DATA SOURCES

In order for data to be useful, it must be of adequate quality (complete, valid, timely). Barriers to obtaining quality surveillance data include the two preceding points and personnel not having the necessary knowledge and skills. These barriers are more pronounced in low- and middle-income countries where a host of pressing issues needing resolution compete for a limited pool of resource. Furthermore, the absence of support legal and policy frameworks can impede data-sharing, especially in the absence of mutual trust and understanding.

UNDERESTIMATION OF INCIDENCE

Outbreaks are not detected early enough when there is underestimation of the number of cases and rate of spread. One cause of underestimation is under-ascertainment – when not all cases are captured by the system. This can happen when patients do not seek medical treatment for diseases that are asymptomatic or present only mild symptoms (e.g. Zika), when they cannot afford treatment, have no time, are fearful of stigma or do not trust the healthcare institutions. Also, cases among underserved marginalized populations (e.g. sex workers, refugees), and those that are seen by traditional healers are often not captured by the system. Underestimation also results when there is underreporting of symptoms by healthcare institutions due to misdiagnosis (resulting in miscoding), forgetting to report the case, or misclassification under an inappropriate case definition category. [30, p17]

PROLONGED VERIFICATION OF OUTBREAK OR DELAYED REPORTING

Delays in reporting outbreaks waste precious time that could be spent on early intervention to minimize an outbreak's impact. This can be due to a protracted period of verification of an outbreak or when its spread is deliberately withheld or played down. This can happen at the governmental level to avoid bad press, public anxiety, political backlash, economic loss; or at the private level to avoid stigma, and financial or job loss.

SURVEILLANCE REACH

To date, WHO had declared a Public Health Emergency of International Concern four times – A (H1N1), Polio, Ebola and Zika. Two of the four diseases are zoonoses (A(H1N1) and Ebola). Currently 60.3% of EIDs are zoonotic, of which 71.8% originate in wildlife. [5, p128]

Other recent global public health scares consisted mainly of zoonotic and vector-borne diseases (e.g. “bird flu”, SARS, MERS, Zika). The link between the health of animals, the environment and humans has become more pronounced. When surveillance activities do not reach far enough upstream to address animal and environmental health, IDs that originate there remain undetected until they become epidemic in humans.

THE UNEXPECTED UNKNOWN (“BLACK SWANS”)

Despite best efforts in surveillance, unexpected outbreaks of unknown diseases can still occur. However, the existence of a robust outbreak alert and response system can mitigate the impact of such events and position a country to quickly recover from the effects.

BOX 2: EXAMPLES OF SURVEILLANCE GAPS

Human failure

In 2015, Singapore General Hospital saw an outbreak of acute Hepatitis C Virus (HCV) between April and September in 2 of its wards. The Independent Review Committee tasked to investigate the outbreak found that the hospital's surveillance system was inadequate for detecting and managing outbreaks of unknown IDs. Of the several reasons cited, one was a failure of the hospital's Renal Unit to recognize the signs of the outbreak at its onset. This led to a delay in reporting and containment measures. A second reason was the failure to give timely notification to the Ministry of Health (MOH). As the abnormal results from patients' liver function tests did not meet the hospital's case definition for an acute infection, the MOH was not notified of the cases. In other words, the case definition and alert thresholds that were set could not identify the outbreak signals. [32]

System inadequacies and inefficiencies

Other reasons found for Singapore General Hospital's HCV 2015 outbreak were systemic and led to unclear ownership of the issues related to the outbreak. The hospital had no established protocol, and roles and responsibilities for handling unusual and unfamiliar events like the HCV outbreak. Similarly, the responsibility and capability to manage such issues did not reside within any specific division in the MOH. [32]

In 2015, WHO published a report on the 2014 Ebola virus disease (EVD) pandemic in which is a chapter on "Factors that contributed to undetected spread of the Ebola virus and impeded rapid containment". Listed among the factors was that the inadequate public health infrastructure in the three West African nations that were the most severely hit. Damaged

infrastructure hindered alerts, reporting, calls for help and public message communication. [33]

Prior to the West African outbreak, EVD infections were typically seen in equatorial Africa and confined to remote rural areas. Armed with experience and laboratory capacity, clinicians in equatorial Africa would know to send samples for confirmation whenever they saw a "mysterious disease", facilitating early detection and response if there was an outbreak. However, West African medical workers had neither the experience, skill set nor laboratory capacity to detect or manage the virulent EVD infections they encountered. This delayed the recognition of the outbreak and medical facilities initially had no proper protection measures, leading to infections and deaths among the medical workers. [33]

Recognizing the challenges posed by vertical disease-centred surveillance systems, WHO introduced the Integrated Disease Surveillance and Response (IDSR) framework in 1998 to help member states move toward a coordinated surveillance system supported by a single infrastructure, and achieve a more effective and efficient surveillance system. Fourteen years after its introduction, Phalkey RK, Yamamoto S, Awate P, et.al conducted a literature review to study the challenges faced in implementing IDSR. [29] The challenges found were largely related to systemic and infrastructural gaps.

Case notification was limited by issues such as insufficient reporting forms, poor understanding of deadlines and frequent changes in reporting formats. Complicated and tedious reporting taxed frontline staff in Eritrea and Lesotho. [29, p6] Tanzania faced issues with incomplete reports and a shortage of computers for staff to file

reports.^[29, p6] Reasons reported by Lesotho as to why data was often left unanalyzed included poor understanding of the link between surveillance and planning, lack of personnel with the required expertise, and shortage of basic equipment like calculators, computers and software.^[29, p6] Mozambique and Eritrea faced challenges in timely detection of outbreaks because of weak grasp of alert thresholds.^[29, p7] Inadequate laboratory support was another major hurdle. Gaps ranged from weak laboratory structures close to the field; low capacity for specimen handling, storage and transportation; incomplete or absent laboratory data that could be linked for surveillance; and shortage of trained staff.^[29, p8] Weak transportation and communications infrastructures often compromised timeliness in detection, alert and response.^[29, p8]

Underestimation of incidence

In WHO's report on the 2014 EVD pandemic, it noted that widespread suspicion of hospitals during the pandemic was a main reason for patients' reluctance to seek treatment at hospitals – hospitals were seen as places of death and contagion, a perception made worse by hospitals' prison-like barb-wire fences and the fact that those admitted usually never returned.^[33] Furthermore, the lack of access to healthcare facilities prior to the outbreaks meant that most people defaulted to seeking treatment from traditional healers.^[33] Response measures that were foreign (e.g. disinfecting houses, fever checks, undignified burial methods), seemingly ineffective (e.g. those admitted to the hospitals seldom returned, slow response to calls for help), and the stigma surrounding the disease, made people reluctant to seek help from the medical facilities and even caused some families to hide patients at home.^[33]

Timely detection of West Africa's EVD pandemic was also delayed due to misdiagnosis. EVD's early symptoms are similar to those of malaria and cholera, both endemic to the region.^[33] Lassa fever, like EVD, is a viral haemorrhagic fever and had a high incidence in West Africa.^[33] Initial cases of EVD were likely mistaken for some of these other diseases and no alert was raised.

Delayed reporting of outbreaks

Reports place the initial cases of the 2002/3 Severe Acute Respiratory Syndrome (SARS) pandemic in China in November 2002 or earlier. However, China's official report of the outbreak was only released in February 2003, by which time there were already 305 cases. The international spread of SARS was traced to a Hong Kong hotel where guests who stayed on the same floor as an infected medical doctor from Guangdong, China, in February 2003, caught the virus and brought it to their home countries. Timely reporting by the Chinese authorities would have ensured earlier intervention and could have possibly contained the virus before it spread overseas.^[34]

In combating A (H1N1) virus ("bird flu"), Cambodia faces the unique challenge of farmers' reluctance to report when they see signs of illness in their poultry. Signs of disease in poultry often go unreported because of Cambodia's "culling without compensation" policy. Farmers bear the full financial cost of the livestock that is lost to culling. Delays in detecting signs of an A (H1N1) outbreak prevents timely intervention; the sick birds are not removed and the outbreak is perpetuated among the other poultry, and the human community. The problem is exacerbated by the unwillingness of farmers to waste food, choosing to consume the dead infected birds instead of disposing of them, and getting infected.

^[35]

Surveillance reach

The Rift Valley Fever (RVF) outbreaks in Saudi Arabia (2000) and Sudan (2007) were unexpected, it had not been seen in Saudi Arabia before and had not been identified in Sudan for the previous 30 years. Both outbreaks were preceded by periods of unusually heavy rainfall and the areas close to swamps, wetlands and irrigation farming, conducive breeding grounds for mosquitoes (vectors for RVF), were most severely affected. It was also postulated that the Sudan outbreak was triggered by the construction of a dam in Merowe, in the Nile basin, in north Sudan. Previous RVF outbreaks in Egypt (1977), and Mauritania (1987) were caused by mosquitos that bred in the new dams close by (Aswan dam on Nile River in Egypt and Diama dam in Senegal River for Mauritania). A 'One Health' surveillance that extends to the ecology and environment would have flagged the changes that increased risks for mosquito-borne IDs and alerted officials to the need for preventive intervention (e.g. fogging, removing stagnant water) and step up surveillance. [36]

The unexpected unknowns (“black swans”)

The HCV outbreak in Singapore General Hospital, the RVF outbreaks in Saudi Arabia and Sudan, and the EVD pandemic mentioned above are also illustrations of “black swan” outbreaks that caught public health communities off-guard and for which

there were no preparations. The current and ongoing Zika pandemic that started in Brazil in July 2015 had also caught the world by surprise in its scale (as at 8 September 2016, Zika was reported in 60 countries [37]) and the severity of its complications (it is linked to microcephaly and Guillain-Barré Syndrome in the children born to women infected during pregnancy). The last known Zika outbreak was in the Island of Yap (Federated States of Micronesia) in 2007. Prior to that, the disease was known to be endemic in equatorial Africa and Asia but was rarely found in humans and caused only mild symptoms (before 2007, only 14 cases were ever reported worldwide). The 2007 outbreak was the first known large outbreak (more than 100 people infected), and it was only in 2013 that the Zika virus appeared to be linked with congenital neurological disorders. Possible reasons for the new way in which Zika is presented are i) a mutation of the virus (i.e. introduction of a strain different to the one that was seen before 2007); ii) the lack of herd immunity in Latin America and Micronesia (explaining the high incidence relative to equatorial Africa and Asia where Zika is endemic); and iii) underreporting due to misdiagnosis as Zika's symptoms are similar to that of dengue and chikungunya, two IDs found in the same regions as Zika. [38]

Rapid trans boundary spread of IDs, increasing numbers of EIDs, rising antimicrobial-drug resistance and the looming threat of bioterrorism are some of today's most pressing global health security issues. Getting the basics right and strengthening existing surveillance capacities and capabilities are now more pertinent than ever

before. Yet in order for a surveillance system to continue to be effective in supporting national outbreak alert and response, it needs to evolve to meet the current and foreseeable challenges. Thankfully, advances in science, technology and understanding of EIDs are making it possible to tackle some of the issues at hand.

INNOVATIONS IN SURVEILLANCE

New surveillance methods and approaches have surfaced in recent decades; though some are still in their nascent stages, all hold much promise for the future of surveillance.

NEW METHODS

NEAR REAL-TIME DATA AND INTELLIGENCE SHARING

Key to the global efforts at ID containment and pandemic prevention is the collaboration between nations to share information on local outbreaks for decision-making on interventions. The effectiveness of such partnerships hinges on, among other things, the timeliness of the available data. Platforms on the World Wide Web (WWW) have been leveraged for near real-time data sharing among multiple parties. Public health institutional stakeholders and other interested parties are tapping on such resources to exchange up-to-date outbreak data and intelligence.

The Global Public Health Intelligence Network (GPHIN) gathers and disseminates information on events that are important to global public health. [5, p141] Its sources comprise of official reports from countries, WHO offices around the world, media reports, news wires, forums and websites. It is a closed group and only open to formal public health institutions. [5, p141]

The Program for Monitoring Emerging Diseases (ProMED) “is an Internet-based reporting system dedicated to rapid global dissemination of information on outbreaks of

infectious diseases and acute exposures to toxins that affect human health, including those in animals and in plants grown for food or animal feed”. [39] The service is open to all and receives input from a variety of sources including official reports, media reports and local observers. Its reports are reviewed and checked by a team of experts in human, animal and plant diseases before being sent electronically to its group of subscribers, including the international community of public health practitioners, scientists, physicians, epidemiologists, ID experts and other interested stakeholders. [39] A main aim of ProMED is to crowdsource expertise from around the world to stem current epidemics by facilitating collaborations in outbreak investigation and prevention. [39] ProMED-Mail (ProMED’s email update subscription service) and GPHIN were credited with the detection and resulting global response, of SARS months before the Chinese government’s official report. [28, p3]

HealthMap is an automated system that continuously (“24/7/365”) trawls the WWW for publicly available information relevant to EIDs. [40] It collects information from sources like news aggregators, official reports, eye-witness accounts and discussion forums and shares them with a “diverse audience including libraries, local health departments, governments, and international travelers”. [40]

There also exist similar surveillance data sharing platforms at the regional level (e.g. Pacific Public Health Surveillance Network) and national level (e.g. France’s Sentiweb).

PARTICIPATORY SURVEILLANCE

The race to provide ever faster connectivity, larger bandwidth, more storage space and personal-sized mobile devices, while driving costs down, has placed the power of Information and Communication Technology (ICT) in the hands of the everyman. Ubiquitous use of ICT and unprecedented individual connectivity to the WWW paved the way for participatory forms of surveillance where data are crowdsourced and updated in near real-time. One such initiative is 'Flu Near You', where volunteers submit weekly anonymous reports on the state of their health.^[41] The system consolidates all reports on a weekly basis, maps the occurrence of flu-like symptoms across the USA, and makes it available to the public.^[41] Flu Near You is meant to augment existing traditional influenza surveillance by breaching the gap of under-ascertainment (by capturing data from those with flu-like symptoms but chose not to see a doctor) and eliminating the time-lag between reports from the frontline to health departments.^[41]

Ownership of mobile devices and internet usage is seeing a rise in emerging and developing nations ^[42]. Goutard et.al. envisaged how participatory surveillance can circumvent the structural and infrastructural limitations that confront surveillance efforts in these countries – the need for manpower is reduced; it removes the formality and suspicion that can accompany interactions between surveillance personnel and the community; it taps on community information networks; and it draws from local understanding of the disease and its epidemiology that can be used to inform interventions. ^[43]

In participatory forms of surveillance, information can flow both ways. Direct links between individuals and a central clearinghouse of information on IDs makes it possible to rapidly push public health information directly to individuals – something that will prove useful for correcting misinformation, addressing rumors, giving assurance to the public, and dampening public anxiety and alarm. While traditional and social media platforms are already being used to communicate public health messages, participatory surveillance platforms take it a step further by reaching a self-selected interested audience, individually.

MAPPING AND MODELING EPIDEMIOLOGY AND POPULATION MOVEMENTS

Whereas traditional ways for understanding the spread of a disease relied on methods that were tedious and approximate, existing technology enables epidemiologists to have accurate and near real-time visualizations of the geospatial spread of a disease and its pathogen. <http://spatialepidemiology.net/> is a platform where users can plot epidemiological and genetic data related to an ID onto maps, in order to understand the geospatial factors related to its spread. ^[44] Currently available on the site is a map that shows the geographical distribution of particular strains of bacteria using data from publicly available multilocus sequence typing (MLST, a technique to unambiguously identify bacterial strains and track their evolution) databases. ^[44] Researchers can compare their bacterial strain against the database to understand its evolution, origin and path of spread, and also contribute their own data. Another map on the website was created by

the European Antimicrobial Resistance Surveillance System to maintain a network to collect and share validated surveillance data that are relevant to antimicrobial spread in Europe. [44]

Mobile technology and its pervasiveness has made it possible to map population movements and interactions in near real-time, with more accuracy [45], and with more data points. The higher quality data enable health authorities and epidemiologists to plan interventions and track outcomes. In addition, when coupled with statistical modeling tools, these developments allow for the prediction of disease spread and help public health agencies target interventions to maximize effectiveness.

In 2001, the Dynamic Continuous-Area Space-Time (DYCAST) system successfully predicted five out of the seven cases of West Nile Virus (WNV) infection in New York City. [46] Information on the occurrence, location, date and time of dead crows (a marker for WNV) with other relevant information, were mapped. By studying the current map, and referencing the modelling of WNV human infection that was created using data from the preceding year, epidemiologists could pinpoint the areas where the next infections would likely occur. [46]

The ability to map population movements post-disaster or outbreak helps identify high-risk areas for the spread of diseases, places where surveillance and preventive interventions should be focused, and the healthcare facilities that should be given notice to prepare for a possible outbreak. After the January 2010 earthquake in Haiti,

population movement out of its capital, Port-au-Prince, was tracked using anonymized data on the locations of each SIM (subscriber identifier module) card. [47] The locations of the phone towers that connected the calls made from each SIM card indicated the whereabouts of the callers. The geographical distribution of the population movement found using this method matched closely to the UN Population Fund Household Survey conducted retrospectively, proving its accuracy. [47] Nine months later, researchers tracked the population movement in a similar way after a cholera outbreak in the country, and were able to provide movement data within 12 hours of receiving the data from the phone company. [47]

More recently, the Institute for Health Metrics and Evaluation (IHME) created an Ebola Mapping Tool to aid surveillance by identifying areas where future outbreaks will most likely happen. [48] The tool analyzes environmental factors and pinpoints places where conditions are most favorable for the presence of animal hosts of the zoonotic Ebola Virus Disease, and where zoonosis surveillance should first target. It also indicates the locations of index cases so that outbreak investigators know where to collect the information they need. With the tool, it is possible to create geographical visualizations for other factors that are relevant to disease spread; factors like population density, travel time, accessibility of nearest healthcare facility, and beliefs and cultural norms that may propagate disease spread.

One of the ways in which surveillance work can benefit from the combination of statistical modeling techniques with GIS tools is in the

ability to locate the original site of infection. Alex Cook from the Saw Swee Hock School of Public Health (SSHSPH) adapted the geographic profiling approach from criminology work (the analysis of locations linked to a series of crimes to estimate the perpetrator's locus of criminal activity), to identify the source site of an infection. [49] The algorithm that was developed was used to analyze the distances between the work and home addresses of early cases (extracted from the travel history from their commuter train tap-and-go cards). It proved to be more accurate and rapid in locating the source of infection, compared to the use of travel time or average of locations. This method can potentially apply to infections with long incubation periods (e.g. anthrax) and outbreaks with strong geographic element (e.g. dengue). [49]

The growing trend of Internet of Things (IoT) - the technology of connecting everyday objects to the internet to receive data/instructions and send data/responses - heralds the next frontier for surveillance data collection. IoT devices can not only interface with humans, they can also "talk" to each other. IoT opens the way for the collection and analysis of myriad types of data that may be useful for outbreak surveillance, including data on behavior, lifestyle, health status and decision-making patterns. For example, the proximity and interactions between people that can be measured using the devices that they wear (e.g. watches) and body temperatures that are detected by clothing.

GENOMIC SCIENCE FOR ANIMAL AND HUMAN HEALTH SURVEYS

Genomic science is used to provide information about the origins and evolution of pathogens. Existing techniques have made it possible to identify strains and trace the pattern of their spread with greater precision and accuracy than before. Such information is crucial for diagnostics, targeting interventions appropriately (e.g. location, timing, choice of anti-microbial drug, etc.), and for determining when an outbreak of a particular strain has ended and when an outbreak of a new strain has begun. Genomic technology has also been harnessed for surveillance of possible risks to human health that are associated with food security and the intensifying human-animal interface. An example of this was the identification of the country and distributor who were the likely sources of infection for the USA's 2016 Salmonella Poona infections linked to consumption of cucumbers.

In earlier ages of genomic science, samples had to be sent to laboratories from the field for genome sequencing. It would be months after the occurrence of an infection before a "snapshot" of the pathogen strain would be available. [50, p155] With current genomic technology, rapid sequencing can be conducted onsite with results available within days, providing researchers with near real-time view of a pathogen's evolution. [50, p155] The technology is currently limited in terms of accuracy and applicability, but is expected to improve rapidly over time. With current information sharing platforms (e.g. Dropbox, Google Drive, FTP), sequencing results can be shared worldwide and compared with other existing databases to determine the origin, evolution and spread of particular pathogen

strains.^[50,p156] Similar collaborations were put in place for Ebola surveillance in West Africa. However, such arrangements worldwide are still mostly ad-hoc and efforts should be made to establish and weave them into national, regional and global surveillance plans. ^[50, p156]

The ASEAN TB Database was established by SSHSPH's Public Health Genomics Programme as a collaboration across six Southeast Asian countries with high rates of drug-resistant TB (DR-TB). The database contains whole-genome sequences and deep drug-susceptibility phenotyping to second-line TB drugs. When the data was analyzed using algorithms that were jointly developed with the London School of Hygiene and Tropical Medicine, inference for drug-resistance proved highly accurate. Currently, DR-TB treatments tend to be processes of trial-and-error; this reduces patients' quality of life, delays successful treatment and adds to costs. ASEAN TB Database reduces the need for trial-and-error by guiding treatment protocols. It can also be used in mapping the likely sources of DR-TB infections found in Singapore by matching against strains found in Southeast Asia.

Genomic sequencing was used in Singapore to study the origins of locally reported Zika cases. The first imported case and two locally transmitted cases were studied. The imported case, reported in May 2016, was of the same strain found in the Americas; consistent with the fact that the patient had travelled to Brazil just before falling ill. However, a different strain was identified in the two locally transmitted cases; this was the strain that had been endemic to Asia since the

1960s. This meant that the locally transmitted outbreak is different from the outbreak in the Americas and could be the result of evolution in the endemic strain. ^[51] The sudden rise in Singapore's reported Zika cases after the outbreak in the Americas could also very well be due to more people seeking treatment for their Zika-like symptoms because of the increased awareness, rather than an actual rise in incidence. Nevertheless, there is a need for more research on the similarities or differences between both strains, in terms of severity and type of disease, to better inform interventions. ^[51]

BIG DATA

Big data deals with the collection and analysis of data sets that are massive in volume, variety and complexity. In the current age of digitization, large amounts of data that are generated by the routine exchanges, interactions and activities of life are being captured - commerce (e.g. credit card payments, internet banking, online shopping), communication (e.g. WhatsApp, Skype, voice calls, emails), commute (e.g. 'tap and go' subway and bus cards, street cameras), travel (e.g. flight information), and even lifestyle (e.g. Fitbit, smartphone apps that monitor heart rate, sleeping hours or diet). Richer data will become available with the rising trend of Internet of Things (IoT), where everyday objects have the capability to receive data/instructions and respond accordingly. IoT also connects objects via the internet to "talk" to each other (e.g. motion sensors, refrigerators and medicine cabinets that monitor stocks, and medical alert watches that monitor vital signs, connected to a communication system that can order fresh supplies and alert emergency services). Big

data can potentially predict, and give real-time information, on behavioral and decision-making patterns before, during and after an outbreak, providing useful insights for prevention and control measures.

NEW APPROACHES

SYNDROMIC SURVEILLANCE

Even though syndromic surveillance is not a new approach and has been in mainstream application for close to two decades [52], it warrants discussion because technological developments (including those listed earlier, specifically, in the areas of ICT, big data and IoT) have increased the potential for syndromic surveillance to augment the shortfalls of traditional surveillance in meeting the challenges posed by rising global interconnectedness and EIDs.

Syndromic surveillance complements traditional surveillance and is used to provide early warning (before laboratory confirmation) of potential public health threats for timely action, describe the impact and spread of known incidents to inform intervention and give assurance on the lack of impact of incidents. [53] Characteristics of syndromic surveillance are as follows.

- ❖ It is the “real-time (or near real-time) collection, analysis, interpretation and dissemination of health-related data”, that are usually not primarily collected for surveillance purpose. [53]
- ❖ It is based on “health indicators including clinical signs, symptoms as well as proxy measures” (e.g. absenteeism, sales of over the counter drugs, web searches, key words in social media or discussion forums), that

constitute a provisional diagnosis (or “syndrome”). [53]

- ❖ It tends to be non-specific, sensitive and rapid. [53]

In recent years, syndromic surveillance has been used in Europe during the A (H1N1) pandemic for early warning and monitoring (emergency care and primary care records, school absenteeism, helpline calls and web queries), early detection of diseases during the 2012 London Olympics, situational awareness when Europe was unexpectedly shrouded in volcanic ash cloud in 2010, and detection of the Schmallenberg virus in cattle in the Netherlands. [54]

Syndromic surveillance draws from clinical data sources (e.g. outpatient volume, emergency department logs, poison control center calls, unexplained deaths) and alternative data sources (e.g. absenteeism, over-the-counter medication sales, internet search queries, animal illnesses and deaths). Rising mobile and internet usage, developments in IoT technology, and the commonplace use of electronic systems for user-provider interface and back-end processes, have made it possible to collect data that are richer and more immediate. This can potentially boost surveillance in several ways:

- ❖ **Timeliness:**

A key role of surveillance is to “buy time” for the necessary action to be taken to prevent or contain an outbreak, especially vital for responding to EIDs. Syndromic surveillance aims to “buy more time” by detecting signs of an outbreak even before there is diagnostic confirmation (i.e. the time period between onset of symptoms and diagnosis). [55] Data

received closer to real-time enables earlier signal detection.

❖ **Accuracy:**

Data used in syndromic surveillance are non-specific and the analyses, highly susceptible to confounding factors. The availability of richer data, from multiple sources, allow for more cross comparison and validation of signals from any single source, thereby increasing the certainty of the signal's relevance. ^[55]

❖ **Assurance:**

Syndromic surveillance is used to provide assurance of the absence of negative health impacts of events. The assurance provided by syndromic surveillance can prevent rumors from creating unfounded public “panic responses” like hoarding medication, unnecessary doctor visits that overload the health system, travel and trade bans, and unnecessary prescription of antimicrobials by physicians. This is increasingly useful as mass gatherings with international delegates (potential for importation of IDs) become commonplace. In cases of influx of forced migrants, an increasing phenomenon in recent times and a major concern for many nations, such assurance can serve to quell prejudices that stem from misconceptions about forced migrants bringing diseases with them.

❖ **“Black swan” events:**

“Black swan” events, which include EIDs, are of particular concern to public health authorities – they are unexpected, and little is known about their epidemiology, impact and treatment. While specific prevention and preparation measures cannot be put in place for events that are unknown and unexpected, syndromic surveillance can be used to detect the anomalies caused by “black swans” and flag the need for further investigation, thereby increasing the chances for early detection and timely intervention. Furthermore, the syndromic data that is collected on an ongoing basis provides

historical data that can be used as baselines against which current syndromic data can be compared.

The key considerations for syndromic surveillance remain. A syndromic surveillance system should clearly define the syndromes for reporting, distinguish the effects of confounding factors, define baselines, stipulate signal thresholds and communicate findings effectively to decision makers in a timely fashion.

Syndromic surveillance algorithms should be sufficiently sensitive to flag signs of an outbreak at the earliest possible instance. Yet in order to avoid false positives, baselines must be set accurately and thresholds calibrated accordingly. ^[56] Besides distinguishing confounding factors, algorithms should account for variations in baselines that may occur due to foreseeable cyclical changes ^[56] (e.g. number of students in a boarding school during school terms versus school breaks, different age distribution (hence immunity levels) among nursing homes, seasonal changes in weather). Therefore, even for a given ID, there is still a need to tailor alert thresholds according to the variations in baselines. ^[56]

Syndromic surveillance should be deployed within an overarching outbreak preparedness framework containing an established decision-making matrix for the appropriate action to be taken once an alert is raised, as well as processes in place that will kick in to support the action. Syndromic surveillance draws from a diverse range of inputs and hence requires a degree of standardization of data and transmission standards so that

they can be combined and integrated for analysis and interpretation.

As mentioned, advances in ICT and big data science can be leveraged to take syndromic surveillance to new levels as richer data are made available with ever increasing immediacy. However, effective syndromic surveillance does not necessitate expensive infrastructure or complicated processes. The syndromic surveillance team for 2012's London Olympics received data via email from three of their four sources, and secure file transfer protocol (FTP) from the remaining source. [57] The data were stored in the Health Protection Agency's server and analysis was conducted using SQL queries, statistics and charts. [57] A simple system was used by the Uganda Ministry of Health to detect malaria outbreaks. It involved collecting and collating clinical data from health centers, keying them into a district level computer to obtain district level data and comparing it to historical data for anomalies. This system alerted Ugandan authorities more than two weeks before case numbers began to peak. [58]

ONE HEALTH

The One Health approach stems from a recognition that the health of humans, animals and the environment are intertwined. Though it is not a new concept, several shifts have intensified the connection:

- ❖ The expanded geographical reach of humans and increased international trade of livestock for food intensified contact with domestic animals and wildlife, providing more opportunities for diseases to pass from animals to humans. [59]
- ❖ Rise in certain human activities such as deforestation, intensive farming practices,

burning of fossil fuels that emit excessive amount of greenhouse gases, led to environmental disruptions that critically affect human and animal health. [59] Climate changes (e.g. floods, heat waves, droughts) can lead directly to deaths or sickness, create conditions for IDs to spread rapidly (e.g. malaria, diarrheal diseases, cholera) and force animals to migrate and spread the diseases they carry. Droughts affect the supply of arable land, as well as water for agriculture and consumption, and can adversely impact the nutrition supply to both humans and animals. Similarly, floods can also destroy crops and the food chains in ecosystems. [60]

- ❖ Intensified international travel and trade have meant that diseases in humans, plants and animals can quickly be spread across the world. [59]

According to WHO, "Approximately 60% of all human infectious diseases recognized so far, and about 75% of emerging infectious diseases that have affected people over the past three decades, have originated from animals." [61] The global economic cost from six major outbreaks of zoonotic diseases between 1997 and 2009 (Nipah Virus in Malaysia; West Nile Fever in the USA; SARS around the world; HPAI in Asia and Europe; Bovine Spongiform Encephalopathy in the US and UK; and Rift Valley Fever in Tanzania, Kenya and Somalia) was at least US\$80 billion and the world would have saved an average of US\$6.7 billion a year if these had been prevented. [62]

One Health approaches to outbreak surveillance seek to extend surveillance efforts "upstream" to animal and environmental health in a bid to discover zoonotic outbreaks before they infect humans,

contain them before they reach epidemic or pandemic levels, and preempt potential outbreaks caused by environmental changes. This requires cross-disciplinary (e.g. veterinary, ecology, epidemiology, meteorology, chemistry) and cross-sectorial (e.g. farmers, regulators, public health practitioners, conservationists, food manufacturers) collaborations with ongoing exchange of data and intelligence, that can be integrated and analyzed to provide early warnings and inform interventions.

Already there are multiple national and international One Health surveillance initiatives in existence. The UK's Human Animal Infections and Risk Surveillance (HAIRS) group comprises representatives from 11 agencies overseeing public health, food safety, environmental health, animal and plant health and healthcare services. ^[63] The Global Polio Laboratory Network (GPLN) conducts environmental surveillance to confirm cases of wild poliovirus infections, to supplement existing surveillance data and understand the spread of the virus. ^[64] In 2006, Food and Agriculture Organization of the United Nations (FAO), the World Organization for Animal Health (OIE), and the World Health Organization (WHO) jointly formed the Global Early Warning System for Major Animal Diseases Including Zoonoses (GLEWS) with the aim of detecting potential threats to human health caused by events at the human-animal interface, for early intervention to mitigate potential impacts. ^[65] GLEWS serves as a platform to integrate the surveillance data, expertise and networks of the three agencies for monitoring and assessment of potential threats. ^[65] The OIE/FAO Network of expertise on animal influenza (OFFLU) is an

organization with expertise in animal influenza and it works with WHO on pandemic preparedness for zoonotic influenza; including surveillance, diagnosis and vaccine development. ^[66] Surveillance for vector-borne diseases can also benefit from a One Health approach by combining meteorological data and entomological understanding to predict risks of disease transmission.

Recent years have seen the launch of several professional training programs focusing on One Health (e.g. University of Edinburgh's Master of Science One Health program, University of Florida's PhD in Public Health with specialization on One Health) and joint-training initiatives between medicine and veterinary students (e.g. joint training between Field Epidemiology Training Program for Veterinary and the Chinese Field Epidemiology Training Program). However, the majority are still focused on academia and there is a need to include other One Health stakeholders such as regulators and private sector players. ^[67, p127] It has also been suggested that professionals from different disciplines and sectors should be given opportunities and incentives to network in an issue-free environment, in order to facilitate information sharing and build the relationships that will be vital for collaboration in times of crises. ^[67, p129] Private-public partnerships are another essential element in One Health surveillance, especially in regards to the supply of produce and meat for food. Private stakeholders (e.g. farms, abattoirs, processing plants) throughout the supply chain must be actively engaged in surveillance, prevention and response measures. ^[67, p129]

SOME CONSIDERATIONS PRIOR TO INTRODUCING A NEW SURVEILLANCE INITIATIVE

Adopting new surveillance methods, especially active forms of surveillance, can be costly and often require significant changes to existing structures and processes. Therefore, important considerations should be made before embarking on new surveillance initiatives – issues related to integration with existing surveillance systems, cost-effectiveness and whether the proposed new measures are excessive for meeting surveillance needs.

ISSUES RELATED TO INTEGRATION WITH EXISTING SURVEILLANCE SYSTEMS

PARTICIPATORY SURVEILLANCE

Participatory surveillance is especially useful for IDs that are frequently underreported, usually due to the mildness of symptoms or the similarity of symptoms with other common IDs. In participatory surveillance, people report their symptoms and usually do not know the exact ID causing those symptoms. Hence, with IDs that have shared symptoms, there is the likelihood of overestimating the incidence of the ID being tracked. In order to minimize overestimation, it is important to also monitor all the other IDs that share similar symptoms. [68]

The representativeness of the data collected depends on individuals' willingness to participate, as well as their access to mobile technology or the internet. It is likely that those

who participate are individuals who are more health-conscious and motivated (like healthcare professionals), and come from socioeconomic groups that can afford access to mobile or internet technology. [68] This can result in the ironic situation where groups who are most susceptible to outbreaks are not represented in the data – including those who are not as vigilant about their health status, and individuals of low socioeconomic status (who tend to have limited means for health-promoting activities and usually live in densely populated low-cost housing with low hygiene standards). Furthermore, children and the elderly tend to be less represented in participatory surveillance [55], hence such forms of surveillance are not suitable for IDs that these groups are more at risk of.

Admittedly, participatory surveillance is meant to be only one tool that can be deployed as part of a comprehensive surveillance system, but its limitations should be kept in mind when deciding when to adopt such initiatives.

MAPPING EPIDEMIOLOGY AND POPULATION MOVEMENTS

In their systematic literature review Carroll, Au, Detwiler et.al. surveyed the landscape of visualization and analytics tools and identified the barriers to adoption of the tools. In particular, they looked at tools dealing with geographic information systems (GIS), molecular epidemiology and social network analyses. [69] The usefulness of such tools lie in their ability to integrate and synthesize diverse data sources and present these

interactions geographically and temporally. The challenges to the adoption of such tools are found at the system-, organization-, and individual- levels.

Needless to say, it is vital that users are able to access data that can be put together in a manner suitable for meaningful analysis. However, this can be a challenge with the lack of shared data standards, interoperability issues among jurisdictions, and varying data quality among sources. [69, p294] Agencies also tend to be reluctant to share data for fear of violating confidentiality. This highlights the need for the development of legal support and definition of clear parameters that will facilitate data-sharing while protecting confidentiality. [69, p294]

Another impediment to a widespread use of such tools lie in the fact that they are often proprietary systems that are developed for the specific needs of an agency, and are not made available for public use. Moreover, the incompatibility among tools that are developed separately prohibits users from combining data sets from the different tools for further analyses. [69, p294]

The lack of financial resources, organizational support and training are some of the organization-level barriers that are faced. [69, p289] Free web-based tools, open source codes and publicly available data on the WWW are possible solutions to the lack of resources. [69, p291]

User-level barriers include the lack of understanding for how to use the tools, stemming from the belief that such tools are complex to master and a reluctance to invest

time in learning them. [69, p294] A limited understanding of how these tools work lead to mistrust in the tools' reliability, further discouraging users from using the tools. [69, p294] Besides concerns with data quality and accuracy [69, p296], users are also wary of misinterpretation of data and the susceptibility of data to being misrepresented in maps (for example the ways variables are presented, and the geographic scale and resolution chosen). [70]

GENOMIC SCIENCE

Genomic science has been used in surveillance for some time now. Recent developments in the science and technology have enhanced the rapidity and resolution of sequencing results, enabling epidemiologists to identify pathogens more unambiguously than before. In particular, researchers are looking to whole-genome sequencing (WGS) as the tool for routine typing in national surveillance; comparative analysis of WGS is already commonly being used in reference typing. [71, p4] In August 2016, the European Centre for Disease Prevention and Control (ECDC) published its recommended strategy for enabling an EU-wide adoption of WGS as the preferred method for sequence typing in public health surveillance, replacing other methods. [71, p1] In its report, ECDC identified current challenges to the implementation of WGS in surveillance: i) the lack of assurance of data accuracy and inter-laboratory comparability of data due to the disparity in quality control among the platforms being used; ii) absence of a standard framework for translating raw data to usable formats to be put through the series of different computer programmes used in the process of sequence typing (i.e. no standard bioinformatics

pipeline); iii) difficulty in comparing and discussing results due to the lack of a standard pathogen-specific nomenclature, and the need to ensure that the eventual nomenclature used caters for the varying types of genomic information and degree of resolution required for the varying disease-specific surveillance objectives; and iv) the lack of compatibility with older typing systems. [71, p4]

WGS may not be suitable for surveillance for all IDs; there is a need to assess applicability, as well as its cost-effectiveness and feasibility in comparison to the systems currently at use. Evaluations on the use of using WGS in the surveillance of specific diseases were carried out for some ECDC pilot projects and the adoption of WGS was recommended for foodborne bacterial diseases, its adoption was deemed unsuitable for TB, and the business case is yet to be made for its adoption for antibiotic-resistant gonococcal infection and carbapenemase-producing enterobacteriaceae infection. [71, Appendix 1]

Another challenge for expanding the adoption of WGS in surveillance is its current dependence on the availability of clinical isolates. The availability of clinical isolates is shrinking because laboratories are moving toward culture-independent diagnostic testing (CIDT) and doing away with the need for the primary isolation of pathogens. [72] In a bid to maintain access to cultures needed for WGS, clinical laboratories in the USA have been asked to conduct cultures alongside CIDT, an additional cost to the laboratory with no apparent benefit to the individual patient. This highlights the need for assessments of the value and costs of using WGS for public health surveillance, a public good meant to

prevent potentially massive costs of outbreaks. [72]

BIG DATA

Some of the challenges to broaden the use of big data in outbreak surveillance were highlighted by Google's much publicized failed attempt to predict the seasonal flu outbreak in 2013 – difficulty in distinguishing true signals from irrelevant “noise” and the need to adjust the algorithms to account for changes in behavior. [73] Similar to mapping and visualization tools, challenges to integrating big data with existing surveillance systems include varying data quality and standards, and interoperability.

Discussions on privacy and how big data can be used ethically for the public good are still ongoing. Questions on what sorts of data should be made available, in what format and to whom, must be resolved before there can be widespread use of big data in surveillance. Sweden's Flowminder Foundation [74] and the UN's Global Pulse projects are notable attempts at ethical use of big data for the advancement of public health.

ONE HEALTH

Adopting the One Health approach toward outbreak preparedness can have vast implications for governance structures, infrastructure, processes, resource allocation and cost. On the other hand, its potential for significantly mitigating the health and economic impacts of outbreaks cannot be ignored. There remains a need to show a business case for the One Health approach and discussions have been ongoing on possible ways of assessing the value that it brings. [75] One example is the proposed

conceptual framework to assess the economic value of zoonoses surveillance by Martins, Rushton and Stärk. [67] The framework takes into account that there are distinct surveillance objectives for each stage of an outbreak. Consequently, the required form of zoonoses surveillance, and their associated costs, differs for each stage. Similarly, the contribution of zoonoses surveillance toward surveillance objectives, and the associated benefits, for each stage varies. Hence an economic assessment must take into account such shifts in costs and benefits, including those that are intangible and intermediate. The authors focused on zoonoses surveillance but clearly, their proposed framework can also apply to environmental surveillance.

Unfortunately, One Health is still largely seen as veterinary-led and often not a priority for the health and environment sectors. In order for the approach to work, the involvement of the health and environmental sectors must be stepped up. Moreover, much needs to be done to develop governance and administrative structures, as well as funding models that are coherent and conducive to the One Health approach. [67, p4&5] Data-sharing is integral to successful One Health surveillance and, the legal and policy environments must be reviewed to make the necessary provisions to support this. [67, p5]

One Health funding is targeted mainly at research, and funding to build up One Health national and regional surveillance systems, especially in resource-poor nations, has been meagre. [67, p5] This highlights the need for a business case for One Health surveillance and persuade governments and funders to invest in it.

The information generated by the surveillance work of the animal livestock industry can contribute significantly to outbreak surveillance. However, such information is seldom shared, perhaps due to a fear of negative repercussions (like prosecution, fines or forced suspension) if outbreaks are detected among livestock. [67, p5&6] Furthermore, there is little incentive for industry to do the extra work required for sharing. Implementations of One Health surveillance should include the building of public-private partnerships and look into incentivizing industry to collaborate. [67, p6]

JUSTIFYING THE INTRODUCTION OF NEW SURVEILLANCE INITIATIVES

As seen in the preceding section, a large part of the challenges to integrating new surveillance methods or approaches relates to lack of funding, as well as inadequate support structures (governance, administration, legal, policy). Introducing these new surveillance initiatives may not just utilize substantial funds, but may also require deep and pervasive changes at multiple levels. Thus any nation desiring to embark on a new surveillance initiative should first consider whether it is indeed worthwhile to do so by weighing the costs and the value it will bring to the national surveillance system.

Even though there are ample resources to guide the evaluation of the effectiveness of surveillance systems and sub-systems (CDC, WHO, ECDC), less has been said about evaluating whether it will be worthwhile to implement a surveillance system/sub-system

in the first place. In WHO's discussion paper *Evaluating the costs and benefits of national surveillance and response systems* [77], it listed eleven fundamental issues that need to be wrestled with in order to formulate a framework that can be used for evaluating if it is justifiable to take adopt a particular surveillance initiative. The eleven issues are as follows:

- i. whether separate studies of costs and benefits would be useful;
- ii. whether it is advisable at the present time to undertake cost–utility, cost– effectiveness or cost–benefit analyses;
- iii. whether surveillance systems and response systems should be studied separately or together;
- iv. which activities should be included in surveillance systems;
- v. which activities should be included in response systems;
- vi. the extent to which services provided by the routine health facilities during an outbreak should be considered to be part of response;
- vii. which perspective should be considered: that of the government, the health sector, the economic sector, individuals, families or society as a whole;
- viii. whether local, national or international perspectives should be used;
- ix. which baseline surveillance and response system should be used as a comparator to evaluate costs and benefits;
- x. the use of retrospective, prospective and future scenarios for evaluation of costs and benefits;

- xi. the reference time period to be used to evaluate costs and benefits. [77, p7]

Some of the recommended solutions were based on current availability of data and evidence, feasibility, the goals of surveillance and response, and the relationship between surveillance and response (i-v,x-xi) [77, p7-19], while others were contingent on the aims of the evaluation and the intended audience [77, p7-19]. The resulting framework can be used to evaluate the relative costs and merits of a proposed surveillance initiative against what already exists in the current system.

Related to justifying the introduction of a new surveillance initiative is the issue of sufficing (what constitutes 'good enough'). Outbreak surveillance is the systematic and ongoing, collection and analysis of data for the purpose of sparking or informing action related to the prevention, containment and management of the spread of IDs. In deliberating a new surveillance initiative, nations should survey the relevant objectives and targets to distinguish among what is 'necessary', 'good enough' and 'good to have', in order for a surveillance system to fulfil its functions and attain the intended outcomes. These will vary depending on whether the objectives are for early detection and response, trend monitoring, eradication or elimination, and each country's unique circumstances. Identifying what is 'good enough' for achieving intended surveillance targets can illuminate decisions on whether to invest in a proposed new surveillance initiative, given the performance of the existing system, merits of other options, available resources and other national priorities.

SURVEILLANCE SYSTEMS THAT EVOLVE AND LEARN

In order to remain effective, surveillance systems must continually “learn” and evolve with each outbreak. Outbreaks should be studied with a view to establishing the necessary measures to prevent similar outbreaks in the future. In 2015, Singapore experienced an unusual outbreak of Group B Streptococcus (GBS). Up till then, the known GBS cases were caused by GBS bacteria that is commonly found in the human gastrointestinal system (Serotype III ST17) and seen only in those with compromised immune systems (e.g. elderly, infants, chronic disease patients), usually affecting soft tissue, bones and joints.^[78] The 2015 outbreak was uncharacteristic in that it hit young adults with no pre-existing medical issues and affected

the central nervous system. Using WGS, it was found that the GBS strain in question was not the type typically seen in humans, but another strain usually seen in freshwater fish (Serotype III ST283) and not known to have been passed from fish to humans before.^[78] Interviews with patients revealed that 60%-70% had eaten raw Asian bighead carp prior to falling ill.^[78] Further tests confirmed that the bacterium was likely to have passed from fish to human through consumption of raw infected fish.^[78] Once it was known that the more virulent ST283 strain can infect humans by consumption, GBS surveillance now includes testing for its presence in patients, freshwater fish supply and food products.^[78]

SURVEILLANCE SYSTEMS THAT FIT “ALL-HAZARDS”

Humanitarian crises, such as natural or man-made disasters and conflicts, often lead to displacements of large groups of people. The conditions that displaced populations live in are likely to pose the risk of spread of infectious diseases. The types of communicable diseases that have been associated with population displacement include water-related communicable diseases, diseases associated with crowding, and vector-borne diseases. Therefore, surveillance systems should also cater for emergency crises and be sufficiently “hardy”

to hold up under those conditions. This “all-hazards” criterion is aligned with the WHO’s Health Emergency Risk Management recommendations to guide member states in pandemic preparedness. In order to successfully meet the criterion, it is important to have the multi-disciplinary and multi-sectorial contributions of experts and stakeholders, and have frequent communication and testing of these surveillance systems by means of table-top exercises and simulations.

CONCLUSION

Even though each new method/approach was discussed separately above, they come together in practice in many ways (e.g. big data analyses of genomic sequences or syndromic surveillance data, syndromic surveillance that includes surveillance of animal health). They also help address some of the current challenges in surveillance.

- ❖ In response to the transboundary nature of ID spread, countries partner in near real-time sharing of surveillance intelligence and global collaborations to investigate outbreaks. The combination of sophisticated spatial-temporal mapping techniques with epidemiologically relevant data is making the prediction of outbreaks and disease spread more accurate and efficient.
- ❖ The collection and sharing of surveillance data with informal sources make it harder for authorities to deliberately withhold outbreak information, it also disincentivizes such moves by increasing the likelihood of being exposed.
- ❖ Underestimation that result from under-ascertainment is minimized as people report their symptoms directly to crowdsourcing platforms like Flu Near You. In places where there are lack of trust between the populations and health authorities, outbreak control measures are slower and less effective [79]; crowdsourcing platforms can become a way of circumventing the chasm.
- ❖ Low-resource countries often struggle to collect good quality data due to the gaps in their health systems. These challenges will take time to be addressed. Meanwhile, innovative ways of collecting data like participatory surveillance methods and creative use of syndromic surveillance data can help circumvent existing shortfalls.
- ❖ By extending surveillance to animal health, the One Health approach enables the global community to tackle the rising number of zoonoses.
- ❖ One Health and syndromic surveillance, along with better international intelligence exchange and collaboration, help prepare the global community for detecting and responding to “black swan” incidences and new EIDs.

The threat of IDs to global public health may have increased due to intensified trade and travel, rise in zoonoses and EIDs, and higher risk of bioterrorism. However, the global community can rise to these challenges through closer surveillance partnerships, and creatively applying scientific and technological advances to surveillance methods, while continuously strengthening capabilities to do the basics well.

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LEADERSHIP INSTITUTE FOR GLOBAL HEALTH TRANSFORMATION (LIGHT)

To be the catalyst for transformational change in health and healthcare innovation and development for Singapore and beyond.

The Leadership Institute for Global Health Transformation (LIGHT) will serve as a receptacle to work with relevant partners from around the world. It aims to be a progressive and meaningful think-tank to encourage cross-fertilisation of ideas and foster active collaboration to build a cadre of creative leaders. By studying issues and finding solutions to the health problems that confront Singapore and Asia, it hopes to transform old paradigms of health to achieve enduring outcomes for our communities. LIGHT will adopt a cross-disciplinary approach in pursuing an active agenda in building up thought-leadership and core competencies in health development. There are many other international programmes that embody the cultivation and training of exceptional

leaders who will transform health and healthcare for a changing world. LIGHT hopes to emulate these renowned programmes in strengthening our connections among research, teaching, and practice to elevate our impact on the standards of public health and healthcare delivery.

Additionally, LIGHT has been conceptualised to further and strengthen the development of the School's regional and international engagement, and will strive to be a regional centre of leadership excellence. This includes undertaking the important role in training future generations of leaders in healthcare both nationally and regionally in Southeast Asia. For greater impact, The Institute will also build upon the existing Global Health modules from our Masters of Public Health (MPH) programme. We hope to excite, energise and empower new and young leaders who will spearhead this transformational movement to greater heights of achievements for better health.

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