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One Health Timeliness Metrics: A Cross-Cutting Tool to Advance Epidemic and Pandemic Preparedness and Prevention

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One Health Timeliness Metrics: A Cross-Cutting Tool to Advance Epidemic and Pandemic Preparedness and Prevention

by

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Contributions

Chapter Two of this dissertation was published in *eClinicalMedicine* in 2022 and was co-authored by Nistara Randhawa, Elizabeth Fair, Brian Bird, Woutrina Smith, and Jonna Mazet.

Chapter Three of this dissertation has been submitted for publication in *BMJ Global Health* and was co-authored by Lydia Nakiire, Joshua Kayiwa, Claire Brindis, Ashley Mitchell, Issa Makumbi, Alex Riolexus Ario, Elizabeth Fair, Jonna A.K. Mazet, and Mohammed Lamorde.

These papers have been approved for inclusion in this dissertation by the Dissertation Committee as they were written primarily by the first author, Jane Fieldhouse.

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Abstract

One Health Timeliness Metrics:

A Cross-Cutting Tool to Advance Epidemic and Pandemic Preparedness and Prevention

Jane Kees Fieldhouse

Due to a confluence of environmental, ecological, societal, and epidemiological considerations, the risk of disease outbreak occurrence is increasing both in frequency and intensity. When spillover events cannot be stopped at their source, it is a race against the clock for health systems to prevent outbreaks from spreading into protracted epidemics or pandemics. To avoid unnecessary morbidity and mortality among humans and animals alike, as well as the associated socioeconomic consequences resulting from interventions required to control disease transmission, experts worldwide are developing and employing innovative strategies to strengthen the performance of health systems during outbreaks.

Timeliness metrics have been proposed as a tool to track, measure, and assess the speed with which health systems detect and respond to outbreaks. Given that a majority of outbreaks affect or involve the health of humans, animals, plants, or the environment, a set of One Health timeliness metrics have been proposed to ensure the tool is applicable to multisectoral outbreaks. In addition to measuring timeliness for milestones such as the outbreak start, date of detection, notification to relevant authorities, verification, diagnostic confirmation, response enacted, public communication, and outbreak end, the One Health timeliness metrics seek to track dates for predictive alerts signaling potential outbreaks, preventive responses to those alerts, and after-action review meetings between multidisciplinary stakeholders. This dissertation explores several aspects of the One Health timeliness metrics, including questions related to how milestones are being reported during multisectoral outbreaks, how feasible and useful implementation of this tool is, and what we can learn from the One Health timeliness metrics.

Evidence from both a global scoping review of thousands of outbreaks and a country-level analysis of multisectoral outbreaks in Uganda between 2018 and 2022 illustrate that while most One Health outbreak milestones are being reported with relative frequency, dates for predictive alerts of outbreaks, preventive responses, and after-action reviews are not. However, given findings from the scoping review that outbreaks reporting both a predictive alert and preventive response had shorter timeliness (defined as the median time in days) between most intervals compared to outbreaks not reporting preventive responses, this dissertation concludes that tracking these key One Health outbreak milestones may help optimize outbreak preparedness and prevention efforts. Furthermore, the perceived feasibility and utility of timeliness metrics, assessed through a mixed- methods study in Uganda, a country prone to outbreaks of diseases of high risk for epidemic or pandemic potential, suggests that stakeholders support the adoption of these metrics, despite remaining implementation challenges.

From an analysis of timeliness metrics during multisectoral outbreaks in Uganda between 2018 and 2022, we found that the two greatest predictors of speed in outbreak response were past experience with similar disease outbreaks and whether the outbreak was of a viral hemorrhagic fever. These findings highlight important lessons to be learned from timeliness metrics: Uganda remains unprepared for outbreaks of diseases the country is less familiar with, which includes a novel *Disease X*. However, we believe adoption of these metrics may facilitate the operationalization of the One Health approach, which stakeholders described as important but challenging in practice, which ultimately may contribute to faster overall timeliness for detection and response during multisectoral outbreaks.

This dissertation provides empirical evidence that the One Health timeliness metrics should be considered as a useful and informative tool to facilitate epidemic and pandemic preparedness and prevention efforts at a time when cross-cutting innovations to address this multifactorial challenge are essential.

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List of Abbreviations

AAR	After-Action Review
AFRO	World Health Organization's African region
AMR	Antimicrobial resistance
CCHF	Crimean-Congo Hemorrhagic Fever
CDC	U.S. Centers for Disease Control and Prevention
CI	Confidence Intervals
COVID-19	Coronavirus disease-2019
DONs	Disease Outbreak News
DVO	District Veterinary Officer
eIDSR	Electronic Integrated Disease Surveillance and Response
EMRO	World Health Organization's Eastern Mediterranean region
EOC	Emergency Operations Center
EURO	World Health Organization's European region
EVD	Ebola Virus Disease
FAO	Food and Agriculture Organization
GHSI	Global Health Security Index
GoU	Government of Uganda
HR	Hazard ratio
IDI	Infectious Diseases Institute at Makerere University
IDSR	Integrated Disease Surveillance and Response
IPPPR	Independent Panel for Pandemic Preparedness and Response
IQR	Interquartile range
IRB	Institutional Review Board

JEE	Joint External Evaluation
MAAIF	Ministry of Agriculture, Animal Industries and Fisheries, Republic of Uganda
MMWR	Morbidity and Mortality Weekly Report
MoH	Ministry of Health
NOHP	National One Health Platform, Uganda
NTF	National Task Force
OHHLEP	One Health High-Level Expert Panel
PAHO	World Health Organization's Pan-American region
PCR	Polymerase chain reaction
PHE	Public Health Emergency
PHEOC	Public Health Emergency Operations Centre
ProMED	International Society for Infectious Diseases' Program for Monitoring Emerging Diseases
R&D	Research and Development
RVF	Rift Valley fever
SARS-CoV-2	Severe acute respiratory syndrome coronavirus 2
SEARO	World Health Organization's South-east Asian region
SMS	Short message service
SOP	Standard operating procedure
USAID	U.S. Agency for International Development
VHF	Viral hemorrhagic fever
VIF	Variance inflation factor
WHO	World Health Organization
WOAH	World Organisation for Animal Health (formerly OIE)
WPRO	World Health Organization's Western Pacific region
YF	Yellow fever

Chapter 1. Introduction

Overview

Among the growing number of wicked problems[1] that society faces today, in 2020, communities worldwide became acutely aware of threat of pandemics and the far-reaching and potentially devastating consequences of uncontrolled disease outbreaks. Though experts had warned world leaders, policy makers, and the public of the dangers and increasing risk of epidemics, COVID-19 served as a brutal wake-up call to all countries worldwide that the threat of pandemics is indeed a very real and complex challenge.

As COVID-19 surged, so too did a plethora of research and policy analyses, dissecting what went wrong during the pandemic response, and what innovative strategies might lead to improved outcomes during future epidemics, or even prevent outbreaks from becoming protracted pandemics. This dissertation explores one of several tools that have been proposed to assess performance during outbreak detection and response: timeliness metrics. Timeliness metrics offer a framework to measure speed during outbreaks by measuring the time between any two key events, or milestones, during an outbreak. The subsequent chapters of this dissertation center on the One Health timeliness metrics, a framework specifically designed to be applicable to any health event for which there are activities that integrate the human, animal, plant, or environmental sectors.

Chapter One of this dissertation presents a brief background on our current pandemic era, including driving forces behind some of the most pressing disease threats we face today. After outlining the present state of pandemic preparedness efforts, I then describe what the One Health approach is, and why experts worldwide increasingly recognize the approach as optimal to address the complex and intractable challenge of epidemics and pandemics. In addition to the advantages of a One Health approach, Chapter

One also explores several of the implementation challenges to mounting the integrated and multi-sectoral approach, including reported difficulties at the country-level. Specifically, we consider the case study of Uganda, where research for two of the studies detailed within this dissertation took place.

The subsequent three chapters of the dissertation consist of three empirical studies of One Health timeliness metrics. The first is a study of how timeliness data are being reported at the global level, followed by two studies of One Health timeliness metrics in Uganda which seek to evaluate the feasibility and utility of the framework and assess factors influencing timeliness during multisectoral outbreaks at the country level. Chapter Five draws upon the findings of these three research studies to make recommendations on implementation strategies for the One Health timeliness metrics and pandemic preparedness policy. The dissertation concludes with reflections about the implications of this research on timeliness metrics, One Health and *Disease X*, as well as the field of global health more broadly.

A Pandemic Era

Driven by climate change and a soaring global population with extensive and fast travel and trade networks, our world has entered what many experts call a new "pandemic era."[2] Human behaviors have prompted extensive loss of biodiversity, fundamentally altering ecosystems across the globe. Land use change, such as deforestation, urbanization, and shifts from small- to large-scale, industrialized agricultural practices, have resulted in increased and more intense contact between humans, livestock, and wildlife. Consequently, land use change is a leading driver for disease emergence, accounting for approximately one third of emerging zoonoses, most often through vector-borne and direct animal contact transmission pathways.[3] Simultaneously, sociopolitical challenges such as civil unrest and violence further drive disease by weakening health systems and economies, increasing levels of poverty and undernutrition, and inflicting damage on public health services, infrastructure, and the environment.[4] Whether due to civil unrest or other factors, such as famine or climate-related events, forced migration also leads to increased risk of cross-border transmission of disease within particularly vulnerable and hard-to-reach populations. Importantly, these complex drivers of disease are rarely siloed; researchers are exploring associations between challenges such as climate change and conflict,[5] or loss of habitat and increased viral shedding due to stress in bats.[6]

Between 2022 and 2023 alone, the world saw multiple outbreaks of priority diseases considered high risk for epidemic or pandemic potential.[7] These priority diseases, for which there are few to no effective medical countermeasures, include viral hemorrhagic fevers (VHF) such as Sudan Ebola virus in Uganda and Marburg in Equatorial Guinea and Tanzania. Multiple outbreaks of Lassa virus, another VHF, occurred in Liberia (2022), Guinea (2022), Ghana (2023), and Nigeria (2023). A Public Health Emergency of International Concern was also declared between these years for mpox (formerly monkeypox). All of these outbreaks occurred against the backdrop of one of the largest pandemics ever recorded, with an estimated 19-22 million excess deaths associated directly or indirectly with the COVID-19 pandemic between January 2020 and April 2023.[8]

The novel coronavirus (SARS-CoV-2), which devastated health systems, economies, mental health, and daily life across the globe, is the newest pathogen to be added to the World Health Organization's Research and Development (R&D) Blueprint of Priority Diseases.[9] Due to their epidemic potential, this shortlist of diseases has been classified by experts as posing the greatest public health risk. In addition to 12 known zoonotic viruses, which can be transmitted between animals and humans and vice versa, the WHO R&D priority list also includes a placeholder for an unknown pathogen, termed "Disease X". Though *Disease X* represents an unknown disease, it is likely that this pathogen would also be a zoonotic, possibly RNA virus.[10] Efforts to prevent a potentially catastrophic pandemic caused by any one of these pathogens must therefore engage experts across a variety of disciplines and institutions to identify and reduce risk factors for disease emergence.[11]

The State of Pandemic Preparedness

As COVID-19 quickly revealed that countries worldwide were not prepared for a pandemic, including the economic and societal consequences resulting from the required interventions to slow disease transmission, the WHO commissioned an Independent Panel for Pandemic Preparedness and Response (IPPPR) to evaluate the state of pandemic preparedness prior to the emergence of SARS-CoV-2 and make recommendations on how to avert future pandemic crises.[12] Based on in-depth analyses of what went wrong at critical moments, the panel made seven recommendations to better position both country and international systems to prevent outbreaks from evolving into protracted pandemics. The recommendations are: 1) to elevate leadership for global health to ensure just, accountable, and multisectoral action; 2) to strengthen WHO; 3) to invest in pandemic preparedness now; 4) to establish a new international system for surveillance, validation and alert; 5) to establish a pre-negotiated platform for tools and supplies; 6) raise new international financing for global public goods; and 7) establish effective national coordination for pandemic preparedness and response.[13] Based on reform efforts, in May of 2023, the IPPPR developed a roadmap of six essential functions for pandemic preparedness and response: technical leadership, financing, medical countermeasures, international rules, political leadership, and independent monitoring.[14]

A multitude of other initiatives and efforts focused on pandemic preparedness are underway by multi- and bi-lateral agencies (e.g., the WHO's Preparedness and Resilience for Emerging Threats Initiative),[15] philanthropic organizations (e.g., the Rockefeller Foundation Pandemic Prevention Initiative),[16] foundations (e.g., the Coalition for Epidemic Preparedness Innovations [CEPI], established in 2017), as well as a number of public and private academic institutions. Pandemic preparedness activities through these initiatives are largely focused on surveillance and early detection of outbreaks, laboratory capacity for diagnostic testing and confirmation, public health infrastructure strengthening, simulation exercises and risk assessments, capacity building and workforce training, risk communication and community engagement, and R&D for new drugs and vaccines.

There are additionally a number of platforms and frameworks aimed to strengthen disease surveillance and response capacities for pandemic preparedness at the global, national, and local levels. These include the Global Health Security Agenda, the Integrated Disease Surveillance and Response (IDSR) platform, the Centers for Disease Control and Prevention Pandemic Preparedness and Response Framework, and the Pandemic Influenza Preparedness Framework.

Several preparedness assessment tools are being used to evaluate global health security and preparedness, particularly at the country level, such as the WHO Joint External Evaluation (JEE) tool, an evaluation process conducted by external experts designed to identify gaps in a country's capacity to prevent, detect, and respond to public health threats, and the Global Health Security Index (GHSI). The later received criticism following the pandemic, as high GHSI scores were not associated with reduced COVID-19 cases.[17,18] In fact, the country with the highest GHSI score of 75.9 was the USA, which ended up being one of the worst performing countries during the pandemic with an observed case fatality ratio of 1.1% and the second highest number of deaths per 100,000 population after Peru.[19]

In their 2023 Road Map report, the IPPPR highlighted that political will had visibly waned following COVID-19, resulting in fragmented implementation of the Panel’s recommendations made in 2021. Without sufficient political will, sustained funding for pandemic preparedness remains a major challenge. This phenomenon, often referred to as a vicious cycle of panic and neglect, is not new. As seen during the 2014-2016 Ebola virus epidemic in West Africa and again during the 2016 Zika epidemic, funders are quick to provide emergency funding during a health crisis, and quick to let funding lapse as soon as the emergency is contained.[20] However, pandemics ultimately cost economies more money than the comparatively modest investments to prevent and prepare for epidemic and pandemics. Recent estimates project the COVID-19 pandemic will have cost economies worldwide trillions of dollars, costing the US economy alone $14 trillion between January 2020 and December 2023.[21] In contrast, experts estimate that pandemic prevention, specifically efforts to reduce spillover of zoonotic viruses from animals to people, would cost an estimated $22 to $31.2 billion annually.[22]

Despite the economic, social, and human cost of COVID-19, pandemic preparedness may yet again fail to make it high on policy agendas worldwide. This is in part because public attention, including that of policy makers, is a scarce resource, with competing societal problems being highlighted by the media and dominating public discourse. However, in 2022, the World Bank launched a new pandemic fund, supported by the WHO and civil society organization, aimed to strengthen pandemic preparedness and response capacity in low-and middle-income countries and regions using horizontal, integrated approaches.[23] The first round of funding (to be released in 2023) has prioritized funding for disease surveillance and early warning systems, laboratory systems, and human resources/public health workforce capacity "consistent with a One Health approach."[23]

A One Health Approach

In response to the complex and intractable challenge of epidemics and pandemics, stakeholders worldwide from a multitude of disciplines have embraced an interdisciplinary One Health approach, recognizing the interdependence of human, animal, plant, and environmental health. In addition to working across health sectors, One Health emphasizes the crucial importance of collaborating across the public and private sectors at local, national, regional, and global levels, to achieve optimal health outcomes for all. Through strong collaboration and community engagement, experts are using a One Health approach to address complex global issues beyond disease threats and epidemic preparedness, to include environmental contamination, antimicrobial resistance, food safety and security, destruction of biodiversity, and occupational health and safety.

Though One Health has gained much of its momentum in the past two decades, the concept behind the approach is not new; as early as the fifth century BCE, the father of modern medicine, Hippocrates, described the implications of environmental factors on human health in his book "On Airs, Waters and Places." In the 17th and 18th centuries, Italian physician Giovanni Lancisi made the correlation between the presence of mosquitos in the environment and intermittent fevers (malaria).[24] By the late 19th century, German physician and pathologist Rudolf Virchow coined the term "zoonosis," embracing the connection between human and animal health and encouraging collaborations with practitioners of veterinary medicine.[25]

One Health has roots in the One Medicine approach, which was advanced by public health veterinarians in the 1940s and focused largely on zoonotic diseases.[26] Though zoonoses are a major challenge that are optimally addressed using a cross-sectoral approach, One Health collaborations must go far beyond partnerships across the animal and human health sectors. Indeed, One Health risks being oversimplified as a collaboration between human health clinicians and veterinarians. To optimally understand and address such complex and multi-sectoral problems, One Health efforts must additionally engage social and cultural scientists, political scientists including policy makers and economists, as well as community-based organizations, to employ cross-cutting tactics to conduct surveillance for diseases and tackle them using novel and innovative strategies more holistically. When this occurs, this collaborative approach has been evaluated as an effective method of studying and responding to health events and reducing the economic burden of diseases.[27,28]

In May of 2021, the Food and Agriculture Organization of the United Nations, the United Nations Environment Programme, the World Health Organization [29], and the World Organisation for Animal Health (WOAH, originally the OIE), announced the launch of a One Health High-Level Expert Panel

(OHHLEP).[29] The panel now advises the four organizations, which now form the "Quadripartite," aiming to mainstream the approach, moving beyond the concept to institute concrete One Health policies. The OHHLEP established the following definition of One Health in 2021:

> *"One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment (including ecosystems) are closely linked and inter-dependent. The approach mobilizes multiple sectors, disciplines and communities at varying levels of society to work together to foster well-being and tackle threats to health and ecosystems, while addressing the collective need for clean water, energy and air, safe and nutritious food, taking action on climate change, and contributing to sustainable development."*
> -(OHHLEP 2022)[29]

A 2022 report from the World Bank endorsed One Health as the future of global health security, citing the approach as the best method by which to stop spillover from animals to humans and curbing outbreaks from evolving into pandemics.[30] Despite such endorsement by many leading and global organizations as the most advantageous strategy to address the complex threat of epidemics, in practice, there are critical gaps and structural challenges that impede practitioners from mounting a truly One Health approach. The following section explores the adoption of One Health in Uganda, where research for two of the studies in this dissertation was conducted, including several identified challenges to operationalizing the approach.

One Health and Pandemic Preparedness in Uganda

In 1998, the World Health Organization-Regional Office for Africa and the U.S. Centers for Disease Control and Prevention (CDC) launched the IDSR program across Africa to facilitate the coordination of outbreak response, including surveillance and reporting, across formerly fragmented health systems. The program arrived in Uganda in 2000 and was revitalized in 2012. The following year, in 2013, Uganda's Ministry of Health (MoH) established the National Public Health Emergency Operations Centre (PHEOC) as the central coordinating authority for all health emergencies, including outbreaks.

The PHEOC was established in recognition of Uganda's vulnerability to a number of public health threats, including several emerging and re-emerging diseases. Uganda, which has a uniquely rich biodiversity, is at particular risk for spillover of pathogens from animals to humans. This is in large part due to the country's rapidly growing population, which has led to increased agricultural demands (i.e., loss of biodiversity due to agricultural practices) and increased contact between humans and wildlife. Cross-border migration of refugee populations further compounds the risk of disease spread. Consequently, Uganda has experienced a number of outbreaks of zoonotic diseases of high consequence. For instance, from 2017 to 2018, eight significant outbreaks were reported in Uganda, three of which were prioritized viral hemorrhagic fevers.[31] Uganda has experienced five documented Ebola Virus Disease (EVD) outbreaks and faces additional risk of cross-border EVD transmission.[32] These disease threats are further exacerbated by climate change, with variable climate patterns such as more frequent and intense rains leading to increased vector activity and compromised food and water safety and security.[33,34] In 2022 alone, according to the United Nations Children's Fund, over 21,000 people were displaced due to flooding events in Uganda, and 126,000 had their livelihood activities, homes, crops and infrastructure destroyed.[35]

Given these challenges, Uganda has long used a One Health approach, beginning as early as the 1980s when a Veterinary Public Health division was established within the Ministry of Health to address and control zoonotic diseases.[36] In 2013, a Memorandum of Understanding was established during a One Health conference convened by the Ugandan Veterinary and Medical Associations. In 2016, four government ministries or agencies, namely the Ministry of Health; the Ministry of Agriculture, Animal Industries, and Fisheries; the Uganda Wildlife Authority; and the Ministry of Water and Environment, collaborated with the U.S. Agency for International Development (USAID) Emerging Pandemic Threats 2 Program, to establish and endorse a One Health Framework to formally guide the collaboration.[37] In November of 2016, these four entities formed and launched the National One Health Platform (NOHP), comprised of a One Health Technical Working Group and a Zoonotic Diseases Coordination Office.[38]

Under the leadership of the NOHP, several major One Health milestones have been accomplished in Uganda, including the 2017 Zoonotic Disease Prioritization workshop,[39] in collaboration with the US CDC, and the launch of the 2018-2022 National One Health Strategic Plan, which focuses on seven prioritized zoonotic diseases, One Health communication, biosecurity threats, and antimicrobial resistance.[38]

One Health has also been integrated into education in Uganda, largely through a network of universities which form the Africa One Health University Network (formerly One Health Central and Eastern Africa).[40] Established in 2010, the network supports educational training for a multidisciplinary workforce across ten countries in East, Central, and West Africa, through collaborations across 19 universities and 27 public health, veterinary medicine, and environmental health institutions.[40]

A 2020 exploration of barriers to operationalizing One Health in Uganda found challenges related to inefficient collaboration and coordination across sectors, including the absence of an agreed-upon information-sharing platform between sectors, insufficient political will, including late release of funds, the lack of national One Health policy and laws, and the lack of awareness about One Health and mechanisms to operationalize the approach.[37] Furthermore, the analysis points to insufficient engagement of community stakeholders, the absence of systematic or sustainable One Health education, training, and career opportunities for the next generation, and insufficient research on non-zoonotic One Health priorities (e.g., climate change, loss of biodiversity, food insecurity, etc.,). Consequently, despite their common goal to control outbreaks as quickly as possible, the many stakeholders at district, regional, national, and international levels working across disciplines and public and private sectors, risk approaching outbreak investigation and response risks through a siloed, uncoordinated approach.

Documented implementation barriers from neighboring countries, including Kenya[41] and Rwanda,[42] point to similar challenges as those seen in Uganda. Success stories from Rwanda describe the effective adoption and operationalization of the One Health approach as contingent on bottom-up community engagement, education, and transnational collaborations.

Timeliness Metrics

In 2021, Uganda was among the five countries to pilot the 7-1-7 timeliness metrics, a framework developed and implemented by Resolve to Save Lives, a New York-based non-for-profit led by former US CDC Director, Dr. Thomas Frieden.[43] The 7-1-7 targets are designed to serve as a performance standard assessment tool for early detection and response systems by setting targets to detect an outbreak within seven days of emergence, notify relevant authorities within one day, and mount an effective response within seven additional days.[44] The framework specifies seven early response actions, which should all be complete within seven days of notification: 1) investigation initiated; 2) epidemiological analysis and initial risk assessment; 3) laboratory confirmation; 4) case management and infection prevention and control measures initiated in health facilities; 5) public health countermeasures in communities; 6) risk communication or community engagement activities; and 7) coordination mechanism established.

The Uganda Ministry of Health joins the Zambia National Public Health Institute, the Nigeria Centre for Disease Control and Prevention, the Ethiopian Public Health Institute, and the South Sudan Ministry of Health, as 7-1-7 Alliance members. Led by Resolve to Save Lives and chaired by Dr. Issa Makumbi, Director of Uganda's National PHEOC, the objective of the Alliance is to support the implementation of the metrics in other countries. Toward this goal, the 7-1-7 Alliance has made resources, such as the 7-1-7 Toolkit, available to the public to help stakeholders determine the dates of key milestones (i.e., emergence, detection, notification, and early response), calculate timeliness metrics based on these dates, and then record bottlenecks and enablers and propose remedial actions.[45]

Several of the milestones and definitions used for the 7-1-7 targets align with previously proposed outbreak milestones used to analyze outbreak timelines.[46-48] In 2018, two non-for-profits, Ending Pandemics and Salzburg Global Seminar, convened a program entitled "*Finding Outbreaks Faster: How Do We Measure Progress?*", gathering experts from around the globe to develop a framework to measure outbreak timeliness metrics. In 2019, the two organizations again convened experts from around the world to build upon the human health metrics developed in 2018, to propose a set of One Health timeliness metrics, thereby expanding the application of these human-centric metrics to outbreaks involving the animal, environmental, and plant sectors.[49]

The One Health timeliness metrics measure the time intervals between any two of eleven key outbreak milestones: 1) *Predict*, a valid alert of a potential health threat (e.g., increased rainfall resulting in higher vector density and activity) ; 2) *Prevent*, enhanced surveillance initiated in response to a predictive alert; 3) *Outbreak Start*, the emergence of the outbreak or earliest epidemiologically-linked symptom onset or death; 4) *Detect*, the date of symptom onset, death, or evidence of circulation in humans or animals; 5) *Notify*, the official report to relevant authorities; 6) *Verify*, confirmation by field investigation or other valid method; 7) *Diagnostic Confirmation* via laboratory or diagnostic test; 8) *Response*, when an intervention was enacted; 9) *Public Communication*, date of the official release of information to the public; 10) *Outbreak End*, when the outbreak is declared closed by a responsible authority; and 11) *After-Action Review*, when a joint review of the outbreak occurred by relevant One Health authorities.

Successful execution and tracking of several of these proposed milestones, namely *Predict*, *Prevent*, and *After-Action Review*, requires fundamentally coordinated and cross-sectoral collaborations. For instance, identification of predictive alerts of potential outbreaks often depends on early warning signals from environmental monitoring, meteorological forecasting, and satellite imagery to understand when epidemiologically suitable conditions for a disease outbreak occur (e.g., rainfall and temperature anomalies which result in suitable habitats for mosquitos to lay eggs, thus resulting in an increase in vector-borne illnesses).[50]

Unlike the 7-1-7 metrics, which have been piloted and now considered for scale-up in other settings, the One Health timeliness metrics have not yet been formally implemented in any setting. However, given the complex nature of emerging epidemic threats, and the likelihood that a One Health approach will be crucially important to prevent and address this threat, it seems necessary to integrate more of a multisectoral approach to timeliness metrics. However, empirical work must be done to better understand what can be learned from the One Health outbreak timeliness metrics, as well as whether or not this tool is suitable for implementation within country-specific contexts. Uganda is an ideal setting in which to study the One Health timeliness metrics: given the frequency of outbreaks of diseases of high consequence, the country's long-standing appreciation for the One Health approach, and the successful pilot of the 7-1-7 targets, we believe that Uganda may represent a best-case scenario for countries considering adoption of timeliness metrics as a tool for epidemic intelligence. Countries worldwide have the opportunity to learn from Uganda, which routinely mobilizes to respond to high-consequence diseases that have been identified as high-risk for epidemic potential.

Before examining the use of these metrics in Uganda in Chapters Three and Four of this dissertation, the following chapter will first introduce readers to the One Health timeliness metrics as we explore the reporting of these milestones on a global level. Together, the findings of the subsequent three chapters paint a comprehensive picture of timeliness metrics as a tool for epidemic preparedness and prevention, allowing us to make recommendations about the use and scale-up to other settings, and consider the implications of these metrics in the field of global health.

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Chapter 2. One Health timeliness metrics to track and evaluate outbreak response reporting: a scoping review

INTRODUCTION

As our global population rapidly approaches eight billion, driving forces, such as globalization, climate variability, and changing use of land, have contributed to increasingly complex, intractable risks to the health of humans, animals, plants, and our ecosystems. For decades, experts have warned of the threat of emerging diseases, driven in large part by human behaviours. For example, increasing frequency and speed of travel has resulted in a record number of people, animals, and goods circulating the globe and coming into contact with one another.[1] As disease outbreaks occur with increasing frequency and intensity,[2,3] what begins as a geographically-isolated health event can quickly evolve to become a regional epizootic, epidemic, or pandemic. One Health is a multi-sectoral, transdisciplinary approach that recognizes that the health of animals, humans, plants, and our shared environment are interdependent.[4] Successful control of diseases across these sectors requires a coordinated effort to shorten the time between outbreak milestones, such as the start of an outbreak or even predictive alerts signalling a potential outbreak and all subsequent milestones that occur during the investigation and response. Speed in outbreak detection and etiology identification is essential to executing more successful responses, potentially averting unnecessary morbidity and mortality in human and animal populations, while additionally reducing the economic and societal consequences of an outbreak and necessary control measures.

To understand trends in how quickly we detect and respond to disease outbreaks and human, animal, environmental, and plant health alerts, countries must have established baseline metrics to measure timeliness in outbreak detection and response. Such metrics have been proposed to systematically capture human outbreak timeliness data;[5] however, no standardized benchmarks have been universally adopted to-date. Building upon these metrics, a multidisciplinary team of experts from around the globe gathered in 2019 to develop a set of One Health timeliness metrics for epidemic preparedness to serve as standardized measures during outbreaks involving the animal, environmental, human, or plant sectors.[6] These timeliness metrics, outlined in the Salzburg Statement, are defined as the intervals between two respective outbreak milestones that occur during an outbreak.[7] Examples of timeliness metrics include the interval between the date an outbreak starts and the date of an official release of information to the public, or, similarly, the interval between the date relevant authorities are notified of an outbreak and the date of a diagnostic test or laboratory confirmation. The One Health timeliness metrics, along with 11 clearly defined outbreak milestones, were released in May 2020, coinciding with increasing awareness worldwide of the critical need for a One Health approach to epidemic preparedness.[7]

While the One Health timeliness metrics were devised before the global arrival of COVID-19, the pandemic has exemplified the threat of emerging infections and reinforced the need to leverage a collaborative, multidisciplinary approach to preventing and responding to disease outbreaks.[8] Countries worldwide have seen the effect of speedier detection and response times to COVID-19 manifested as cases averted and lives saved.[9,10] Too many regions have also witnessed the consequence of slow detection and response, which contributes to high case numbers and mortality. We can and must do better to improve the preparedness, prevention, detection of, and response to outbreaks. For this reason, we sought to analyse the use of key One Health outbreak milestones for responses reported between 2010-2020 to establish an important evidence base for future outbreak response recommendations.

METHODS

Scoping Review

Given the breadth and diversity of One Health-related outbreaks and surveillance reports, we opted to synthesize the body of literature using a scoping review.[11,12] The methodology and process of this review have been documented per the Preferred Reporting Items for Systematic Reviews and Meta-Analysis guidelines Extension for Scoping Reviews.[13,14]

Inclusion and Exclusion Criteria

The initial literature screening included reports published between January 1, 2010, and March 15, 2020. All outbreaks meeting selection criteria involved two or more One Health sectors (human, animal, environmental, or plant health) or, particularly for outbreaks of unknown aetiologies, prompt investigation due to concern regarding two or more sectors. Reports included peer-reviewed publications on outbreak events and outbreak reports published by internationally recognized agencies or organizations, namely the U.S. Centers for Disease Control and Prevention's (CDC) Morbidity and Mortality Weekly Report (MMWR),[15] the World Health Organization's (WHO) Disease Outbreak News (DON) reports, and the International Society for Infectious Diseases' Program for Monitoring Emerging Diseases (ProMED) posts.[16] We also included outbreak reports from a United States Agency for International Development (USAID)-funded project as a programmatic case study.[17] Within each reporting outlet, if there were multiple reports of the same outbreak event in any given year, only the last comprehensive report published on that outbreak was included in the analysis. If an outbreak spanned several years, the last report from each of those years was included in the final analysis. Additional details on inclusion and exclusion criteria can be found in the Supplemental Appendix.

Peer-Reviewed Literature Search Strategy

We conducted a search of outbreak reports published in peer-reviewed journals on PubMed and Embase databases. Pre-identified outbreak reports were used to validate the search, which required the term "outbreak" appear in the title and "research report", "research", "report", "describe", or "summarize" in the article abstract or body (Supplemental Appendix). All publications deemed eligible based on titles were reviewed in full for inclusion and exclusion to determine the final set of eligible outbreak reports to be included in the analysis.

Agency and Organizational Reports Search Strategy

Using the archives of the MMWR Weekly Past Volumes and WHO's DON reports, titles were screened to identify all potentially One Health-related outbreak events. Reports were then reviewed in full for eligibility to be included the final review. To access the archives of ProMED reports, we used R[18] to programmatically search and retrieve URLs of posts published with the term "outbreak". All potentially One Health-related topics, including diseases (e.g., "brucellosis"), pathogens (e.g., "E. coli" or "EHEC") and health conditions (e.g., "encephalitis"), were included for the eligibility review. Additionally, all "undiagnosed" or "unexplained" diseases and "die-off" events were included for the eligibility review. Due to the volume of posts on the ProMED platform, an additional set of inclusion and exclusion criteria was applied for foodborne illnesses, as described in the Supplemental Appendix.

PREDICT Case Studies

To understand how outbreak investigations occurring at a project level have reported timeliness metrics and how future projects can improve upon the use of these metrics, our scoping review included a case study of the USAID-funded 11-year global effort aimed at building and strengthening One Health collaborations to detect, diagnose, and respond to epidemic threats.[17,19,20] These PREDICT Outbreak or Health Event Rapid Reports were deemed eligible for full review based on the same inclusion and exclusion criteria as all other reports. For purposes of consistency, we included and analyzed reports written from 2017 onward, the year that the project developed a new reporting template for outbreak investigations. These reports detail outbreak or health events for which the country involved requested active support and events for which PREDICT provided support or was on standby.

Data Management

Data from all outbreak reports, including report year and source, were extracted and organized using REDCap version 10.0. Outbreaks were categorized as taking place in a single country, multiple (two to five) countries, occurring widely (across more than five countries but not globally), or worldwide. The WHO region of the outbreak described was also recorded. Outbreak reports were classified as a national investigation (i.e., investigated by the country's ministry of health or agriculture and livestock, a research institute, university, etc.), an international investigation (i.e., by a foreign institution), an international response assisted by an outside organization in collaboration with the affected country, or vague if the origins of the investigation were unclear.

During data extraction, we documented which sectors were involved in the outbreak. For all outbreaks of known etiology, we documented the transmission route and type of pathogen or parasite implicated in the outbreak as virus, bacteria, parasite, fungus, prion, or toxin. Additionally, we captured whether the report utilized the term "One Health," either by name or implied due to the inherent nature of the investigation.

For each report, we recorded the use of each of the 11 One Health outbreak milestones:[7] 1) *Predict*, a valid alert of a potential health threat; 2) *Prevent*, enhanced surveillance initiated in response to a predictive alert; 3) *Outbreak Start*, the earliest epidemiologically-linked symptom onset or death; 4) *Detect*, the date of symptom onset, death, or evidence of circulation in humans or animals; 5) *Notify*, the official report to relevant authorities; 6) *Verify*, confirmation by field investigation or other valid method; 7) *Diagnostic Test* or lab confirmation; 8) *Respond*, when an intervention was enacted; 9) *Public Communication*, date of the official release of information to the public; 10) *Outbreak End*, when the outbreak was declared closed by a responsible authority; and 11) *After-Action Review*, when a joint review of the outbreak occurred by relevant One Health authorities.

We captured whether a milestone was described with a specific date (a day within a month of a year) or a vague date, such as an epidemiological week. We also captured if a milestone was mentioned but without a date, or if the milestone was not mentioned at all. All milestones reported, however specific or vague, were recorded during data extraction. For the *Diagnostic* milestone, we additionally recorded if an outbreak report described a specific date for diagnostic testing that was unsuccessful, recognizing that even for those outbreaks with unconfirmed etiology, the milestone was addressed. All data were exported to STATA version 16.0 (StataCorp, College Station, TX) for descriptive analyses and to calculate timeliness metrics, which we defined as the median time in days between two respective milestones.

RESULTS

Across all reporting outlets, a total 1014 outbreak reports were included in the final analysis (**Figure 2.1**). Peer-reviewed publications constituted 14.4% (n=146) of included reports, WHO reports 12.0% (n=122), MMWR 10.3% (n=105), PREDICT 3.2% (n=32), and ProMED 60.1% (n=609) (**Figure 2.1**). Over three quarters of the reports (77.0%, n=781) were on single-country outbreaks, 15.9% (n=161) involved multiple countries, 4.0% (n=41) more widely, and 2.7% (n=27) worldwide. Though outbreaks could occur across multiple WHO regions, 381 of the reported outbreaks included in the analysis occurred within the Region of the Americas (PAHO; 37.6%), followed by 225 in the European Region (EURO; 22.2%), 199 in the African Region (AFRO; 19.6%), 152 in the Western Pacific Region (WPRO; 15.0%), 94 in the South-East Asia Region (SEARO; 9.3%), and 64 in the Eastern Mediterranean Region (EMRO; 6.3%; **Figure 2.2**). Two thirds (67.4%, n=684) of the outbreaks were national investigations, and most other reports (21.3%, n=216) described national investigations supported by collaborative international response assistance.

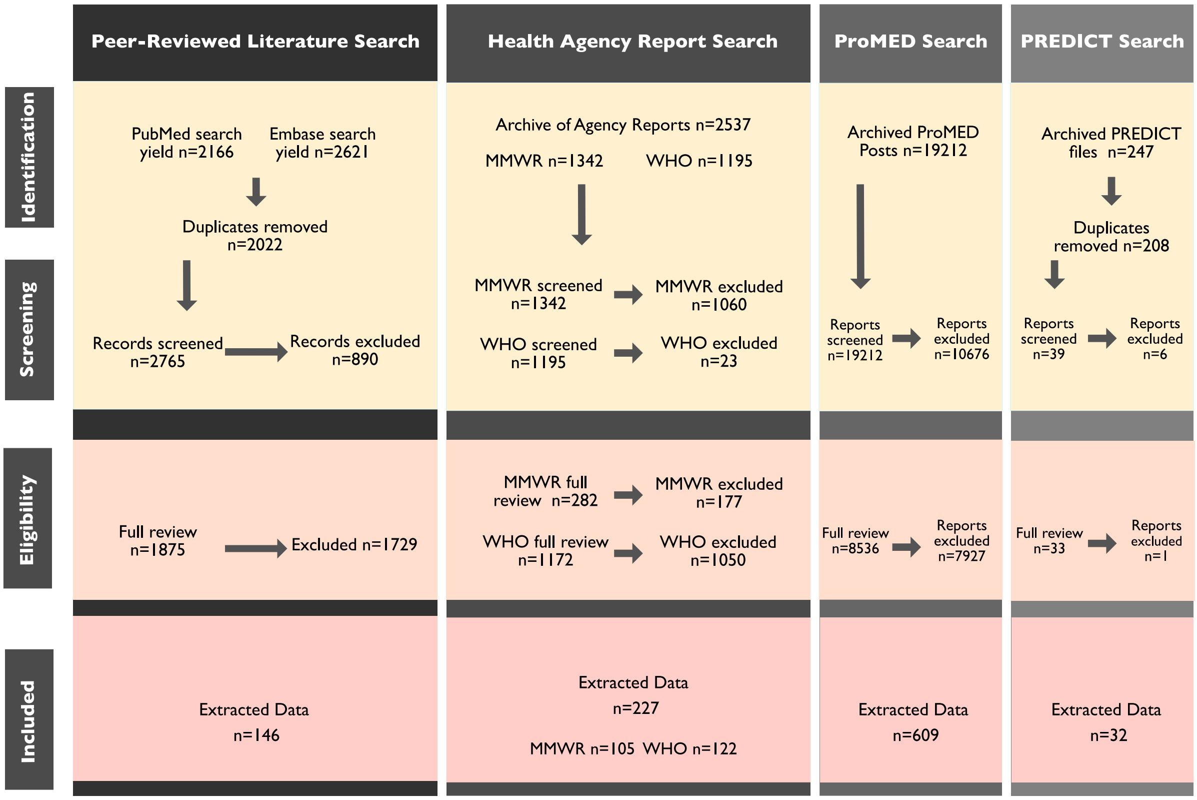

Figure 2.1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis[13] flow diagram of search and selection strategy for scoping review of timeliness metrics. All outbreak reports identified, screened, and considered for inclusion in the scoping review were published January 2010-March 2020.

The most common combination of sectors involved in the outbreak reports was animal, environment, and human (35.3%, n=358), followed by animal and human (29.8%, n=302; **Figure 2.2**). The most common route of transmission was direct contact (48.3%, n=490), followed by foodborne (26.9%, n=273), vector-borne (19.3 %, n=196), waterborne (18.0%, n=183), or airborne (10.4%, n=105) transmission. Eighty-two (82) of the outbreak reports described an outbreak of unknown etiology (8.1%). Thirty-seven (37) of these 82 (45.1%) noted a presumed etiology, which we used to categorize the pathogen. Over forty percent (41.5%, n=421) of included outbreaks were caused by viruses and 35.4% (n=359) by bacteria. Parasites (7.1%, n=72), toxins (6.2%, n=63), fungi (4.7%, n=48), and prions (0.6%, n=6) constituted the rest. Just under 4% (n=38) of analyzed reports specifically mentioned One Health by name.

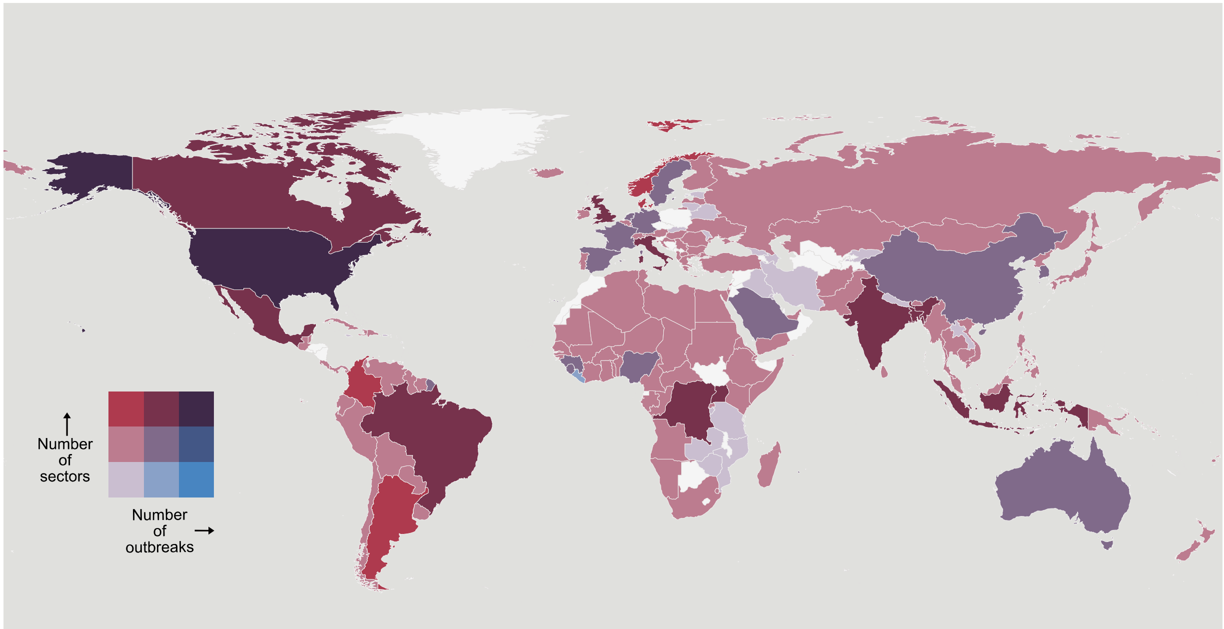

Figure 2.2. Map of outbreaks reports included in final scoping review analysis by number of One Health sectors involved in outbreaks. Map color gradient depicts the number of outbreaks as well as the number of sectors involved in each outbreak ranging from two to four of the One Health sectors: animals, the environment, humans, and plants.

Analysis of Timeliness Metrics

The least reported milestone was *After-Action Review*, a metric included in the Salzburg Statement with the intent to "inspire the necessary collaborations among sectors for operationalizing One Health."[7] Five reports (0.5%) provided a specific date when a joint review of the outbreak occurred, but over 96% (n=978) of reports made no mention of such a collaborative review (**Figure 2.3, Supplemental Table 2.1**). A quarter of all reports described a *Predict* milestone, with 49 reports (4.8%) providing a specific date of a predictive alert of a potential outbreak. Only 6% (n=59) of reports mentioned the *Prevent* milestone, with 1.1% (n=11) providing a specific date of enhanced surveillance or another intervention in response to a predictive alert.

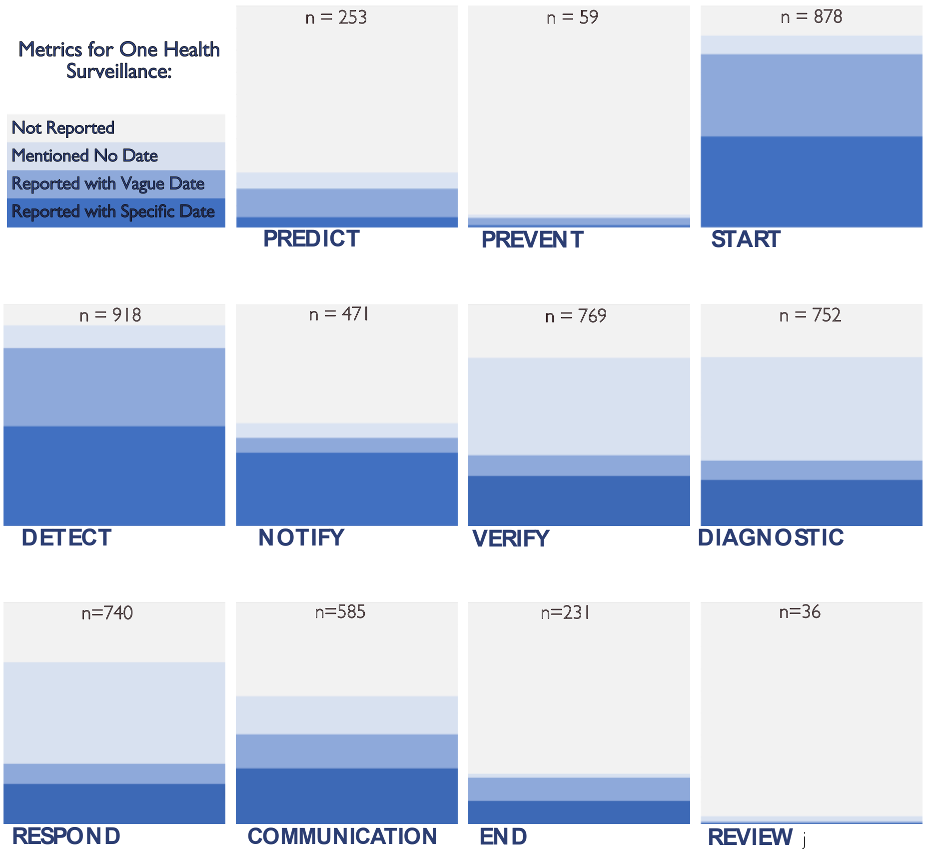

Figure 2.3. Stacked bar chart of milestones reported in the outbreak reports included in the scoping review analysis where n= milestones reported with either a specific date, vague date, or a mentioned but with no date. Each square represents 100% of the 1014 reports, for which the stacked bar chart is proportional to the frequency of the reported milestones.

The milestone most frequently described was *Detect* (90.6%, n=918) with 45.1% (n=457) of all reports providing a specific date of symptom onset or death, 35.2% (n=357) providing a vague date, and 10.3% (n=104) just mentioning the milestone (**Supplemental Table 2.2**). The *Outbreak Start* milestone dates frequently aligned with *Detect* dates with 41.1% (n=417) of all reports providing a specific outbreak start date, 37.1% (n=376) providing a vague date, and 8.4% (n=85) mentioning the *Outbreak Start* (**Figure 2.3**). Fewer reports described the *Outbreak End* milestone, with 77.2% (n=783) of all reports making no mention of when the outbreak was declared over. Because we did not capture whether the outbreak had ended at the time the report was disseminated or published, we do not know what proportion of these reports omitted *Outbreak End* because the outbreak was ongoing. Approximately three quarters of all reports described the *Verify* (75.8%, n=769) and *Diagnostic Test or Lab Confirmation* (76.9%, n=780) milestones, either specifically, vaguely, or in mention without a date. Under half of all reports described the *Notify* milestone (46.4%, n=471), while 57.7% (n=585) of reports described the *Communication* milestone (**Figure 2.3**). Of note, several outbreak reports included in our analysis explicitly justified the exclusion of a specific outbreak milestone (Supplement 1).

When reports provided specific dates for multiple milestones, we calculated timeliness metrics, the median time in days between two respective milestones (**Figure 2.4**). The two milestones most frequently reported together with specific dates were *Detect* and *Outbreak Start* (38.4%, n=390), for which the median time between milestones was zero days, followed by *Detect* and *Notify* (23.6%, n=239), for which the median time was 12 days. For the 96 (9.5%) reports which included both a specific *Outbreak Start* and *Outbreak End* date, the median time between the milestones was 43.5 days. Other timeliness metrics of note included the time between *Detect* and *Respond* (16 days; 10.4%, n=105), between *Start* and *Notify* (14 days; 20.6%, n=209), *Start* and *Communication* (22 days; 9.1%, n=92), and *Notify* and *Diagnostic* (-1 day; 13.2%, n=134) (**Figure 2.4**).

Milestone	Predict	Prevent	Start	Detect	Notify	Verify	Diagnostic	Respond	Communication	End	Review
Predict		3 (0-9) n=3	18 (0-116) n=32	18 (2-278) n=35	27.5 (4-117) n=24	42 (3-117) n=15	30 (4-117) n=15	20 (2-85) n=13	15.5 (0-117) n=12	44 (27-82) n=5	n=0
Prevent			5 (1-109) n=8	6 (1-109) n=8	10 (3-109) n=4	3 (2-106) n=4	3 (2-17) n=3	5 (0-267) n=7	1.5 (0-3) n=2	38 n=1	n=0
Start				0 (0-47) n=390	14 (0-481) n=209	11 (0-242) n=167	13 (0-231) n=155	20 (0-304) n=99	22 (-40-299) n=92	43.5 (0-1010) n=96	55.5 (17-94) n=2
Detect					12 (0- 481) n=239	10 (0-242) n=175	10 (0-242) n=168	16 (0-304) n=105	21 (-40-287) n=93	41 (-33-1010) n=91	55.5 (17-94) n=2
Notify						0 (-131-42) n=150	-1 (-131-35) n=134	3 (-79-75) n=95	3 (-70-235) n=75	15 (-22-912) n=63	39 (34-44) n=2
Verify							0 (-70-63) n=147	0 (-25-64) n=74	1 (-42-34) n=64	23.5 (-9-908) n=40	30.5 (17-44) n=2
Diagnostic								1 (-63-205) n=56	1 (-15-201) n=50	26.5(-33-900) n=42	(n=0)
Respond									0 (-30 – 68) n=85	20.5(-264-425) n=34	10 (0-20) n=2
Communication										14 (-7-899) n = 27	10 (0-20) n=2
End											18 n=1
Review											

Figure 2.4. Timeliness metrics, defined as the median time in days between two outbreak milestones, where n = number of outbreak reports reporting specific date of both milestones. Range of dates in parentheses. Milestones have been organized in sequential order, from left to right, recognizing that several milestones between *Detect* and *Communication* may not always occur in the exact order of events.

Though not defined as an outbreak milestone, we additionally calculated the years between an outbreak start and year the report was disseminated or published. For the 654 organizational reports with a vague or specific start date, report dissemination occurred between zero to six years after the start year, with a median time of zero years. The 130 reports in peer-reviewed journals that provided an outbreak start year were published between 0-11 years after the outbreak start with a median of two years between start year and publication year.

DISCUSSION

Despite consensus among stakeholders on the need to improve outbreak response, observed gaps in milestone reporting suggest the need for more universal agreement on outbreak reporting, including the definitions of milestones, such that robust tracking of critical time points in outbreak detection and response can occur and the efficiency of responses be compared. That said, we recognize that it may not be possible to delineate each milestone for all outbreaks, since reports are generated at various stages of an outbreak's progression. Furthermore, there are several inherent nuances, given the nature of organizational reports and peer-reviewed publications, which may determine which and how milestones are reported. For example, organizations and agencies are more likely to report on early investigations of suspect outbreaks, which may then be discontinued due to lack of follow-up or as outbreaks resolve on their own. Similarly, our evidence suggests that outbreaks are less likely to be written up and published in the peer-reviewed literature if the etiology of the causative agent is not established, which would explain our observation that nearly all (95.2%, 139 out of 146) of reports in peer-reviewed journals described the *Diagnostic* milestone, compared to 73.8% (641 out of 868) of organizational reports. With an additional two years in median time to dissemination, we would also expect to see specific *Outbreak End* milestone dates described more often in reports in peer-reviewed journals than organizational or agency outlets that are most often prepared and conveyed in real-time. In fact, we found that 62.0% of the peer-reviewed reports (90 out of 146) provided or at a minimum mentioned an *Outbreak End* date compared to 16.4% of the organizational reports (142 out of 868) (**Supplemental Table 2.3**). Our finding that only a quarter of all reports specified the conclusion of the outbreak leads us to recommend that reports explicitly state the date the outbreak was declared over. If the outbreak has not yet ended, we recommend reports explicitly state the outbreak is ongoing. Without specification about the conclusion of the outbreak, we cannot track or assess outbreak response improvements over time.

In addition to *Outbreak End*, we believe that several milestones, in particular, should be reported without fail with a specific date whenever possible, including the *Outbreak Start*, *Detect*, *Notify*, *Respond, and Communicate* milestones. Dates for these milestones should be reported as specifically as possible (i.e., a day within a month of a year), as the frequency of the reporting we found suggests these milestones occur across the majority of outbreaks and are feasible to capture. The median time between *Notify* and *Diagnostic* milestones, which was -1 day, illustrates how formal notification to authorities may often occur only after diagnostic or laboratory confirmation of etiology. Waiting for diagnostic confirmation may cause a response delay, which may grow problematic if it further affects mobilization of public health resources. This finding suggests that responders and investigators may be reluctant to signal any unnecessary alarm to authorities until the pathogen is confirmed. In the case of emerging pathogens, this desire to confirm etiology prior to raising a warning can be deadly, as seen in the COVID-19 pandemic.

By restricting this analysis to English language publications, we realize there are outbreak reports, including those generated at the ministerial level, which were not captured in this analysis. However, we did use platforms, such as ProMED and the WHO's DONs, which are third-party aggregators that summarize outbreak information from a variety of sources, including non-English reports. While we did not try to capture every outbreak in every country, we recognize that country-specific considerations, such as varying reporting thresholds or cultural contexts, may affect reporting bias.

At a country level, timeliness metrics can help guide governments in setting their own targets or highlight where efforts must be directed to achieve goals such as the "7-1-7" targets described by Dr. Tom Frieden,[21,22] to identify new suspect outbreaks within seven days of outbreak start, report on and initiate investigation within one day of identification, then implement an effective response within seven additional days. Based on the observed timeliness metrics from our study, however, it is conceivable that the seven-day target between reporting or initiating an investigation and the effective response might be best set even shorter (i.e., a targeting a median time of 3 days between *Notify* and *Respond* and targeting a median time of 0 days between *Verify* and *Respond* may be feasible during outbreaks).

The interdependence of the *Predict* and *Prevent* milestones, whereby a predictive alert prompts a preventive response, may explain the less frequent reporting of the *Prevent* milestone; it is conceivable or even likely that outbreaks may have been averted following a preventive response therefore never written up for dissemination.

In a comparison of timeliness metrics for those reports providing a specific date for both the *Predict* and *Prevent* milestones (n=3) versus those reports providing a *Predict* date but no *Prevent* date (n=42) or neither a *Predict* nor *Prevent* date (n = 761), we found the median time in days to most milestones was on average shorter for outbreaks reporting a *Prevent* milestone (**Supplemental Tables 2.4-2.6**). One such example was a 2012 PLoS ONE publication by Dechet et al. describing a 2005 leptospirosis outbreak in Guyana following particularly heavy rainfall.[23] In response to major flooding, the government of Guyana requested assistance from the U.S. CDC on January 24th to increase surveillance for waterborne diseases. Several days later, on January 29th, investigators detected symptoms in a previously healthy individual, with a microscopic agglutination test confirmation of leptospirosis on February 1st. One day later, on February 2nd, Guyana began a massive chemoprophylaxis campaign to individuals exposed to flood waters.

In this example, the time in days between the *Outbreak Start* and *Respond* milestones was 4 days, (a median of 2.5 days for both [n=2] reports in the study that provided specific *Predict* and *Prevent* milestone dates) compared with 22.5 days for reports with only a *Predict* milestone mentioned (n = 4) and 22 days for those reports with no *Predict* milestone mentioned (n = 73). Though the small sample size is a limitation, we believe the comparatively shortened median times between most milestones is a compelling argument for increased attention to these two milestones, both of which were relatively inconsistently reported at the time of this analysis. Efforts to identify and respond to predictive alerts will necessitate a One Health approach across fields, as well as an emphasis on event-based surveillance. By shifting away from a passive 'wait-and-see before responding' approach and toward a more vigilant alert and response system, countries may be better able and more likely to pick up signals of outbreaks, allowing for more rapid control of outbreaks at their source. Even if investigators over-alert on potential outbreaks then find that a scaled-back response or no response is needed, fewer outbreaks that could potentially grow to be protracted epidemics or pandemics will slip through the cracks, thereby averting cases and socioeconomic disruptions.

A few studies, including Chan et al. (2010), Kluberg et al. (2016), and Impouma et al. (2020), have begun to use timeliness metrics to assess how the time to different outbreak milestones have changed over time.[24-26] These analyses have focused on outbreaks occurring among humans, rather than multisectoral One Health outbreaks which are increasingly more often the case in emerging infectious diseases and diseases with pandemic potential.[27] In addition, previous studies have used slightly different milestone definitions from the eleven we tracked because there has yet to be a concerted effort to standardize outbreak reporting. Before timeliness metrics can be meaningfully utilized and interpreted across different contexts and settings, definitions of milestones must be universally agreed upon and implemented. For example, the Impouma et al.[24] study, which adapted milestones defined by Chan et al.,[25] considered date of notification as the date the outbreak event was first reported to the WHO. Our definition of *Notify* was broader, to include any notification from local to national authorities, notification across relevant sectors, or notification to international authorities. If definitions are to be standardized to allow for cross-country comparisons, we must consider the trade-off that narrow milestone definitions may prohibit stakeholders from capturing these dates altogether, given the differing realities and contexts in which outbreaks occur. Given the findings of this scoping review, particularly those findings related to the *Predict* and *Prevent* events, we believe milestones should be a feasible, flexible, and useful tool for multiple One Health sectors and thus should include a broader set of key outbreak activities in order to be most useful.

This study additionally provided an opportunity to better understand the landscape of outbreak reports across different platforms. Of note, we identified seven peer-reviewed journal reports which were authored by external, international authors with no representation of authors from the country in which the outbreak took place. This absence of local co-authorship is a reminder of the power dynamics that need to be redressed in global health research as we work to decolonize and democratize the field and practice.[28] Through programs that engage future global health workforces, such as the Field Epidemiology Training Program or the USAID One Health Workforce-Next Generation project, we believe that further socialization of these One Health milestones and timeliness metrics, along with accompanying skills related to analysis, writing, and leadership, may contribute to efforts to address this gap. Indeed, when the Salzburg Global Seminar session was convened in 2019 to establish the One Health timeliness metrics, the 38 contributing participants represented organizations across 17 countries worldwide of varying economic strengths.

The COVID-19 pandemic has also demonstrated the utility of timeliness metrics in comparing disease detection and public health response times among reporting units. For instance, California (USA) confirmed the state's first COVID-19 case in Orange County on January 25, 2020, 32 days before the county's Health Officer declared a Local Health Emergency and 39 days before the Governor of California declared a State of Emergency for the entire state.[29,30] San Francisco was the first county in California to respond to the pandemic, even before the first local case was detected; Mayor London Breed declared a State of Emergency on February 25, nine days before the Department of Public Health announced the county's first confirmed cases on March 5.[31] Additionally, in a comparison of all timeliness metrics calculated from the scoping review versus just the COVID-19 reports included in the review, the median time in days was shorter between *Diagnostic* and *Respond* milestones for COVID-19 (-1 day, n= 3 reports) compared to other One Health outbreaks (1 day, n=53 reports). Though a response occurred on average before diagnostic confirmation during the COVID-19 pandemic, timeliness metrics were comparatively longer between all other milestones, including a median time of 19 days between *Detect* and *Notify* for COVID-19 compared to 15 days across other One Health outbreak reports. Despite the small sample size, these metrics illustrate that early reporting of both predictive alerts and of detected outbreaks contribute to faster response and more optimal outcomes. If we consider the December 30th ProMED alert[32] as the predictive alert of the pandemic, 57 days passed between the *Predict* and *Prevent* milestones in San Francisco, California. Such timelines need to be shortened in order to protect populations from protracted lockdowns and other severe interventions that occur once a severe disease has been able to spread.

Of note, while the *After-Action Review* milestone is ostensibly not yet being described in outbreak reports, we believe this a motivational milestone that, if adopted, would serve to remind stakeholders to engage in cross-sectoral discussions with professionals from diverse disciplines to collectively learn from and better understand the evolution and timeliness of an outbreak investigation, and prepare for the next investigation and response, if necessary. Institutions such as the WHO, the World Organisation for Animal Health, and the Food and Agriculture Organization are already advocating the practice of *After Action Reviews,* with guidelines and manuals for *After Action Reviews* as an essential practice to learn from and improve responses during emergencies.[33-35] Training curricula for future public health leaders provide the opportunity to further promote this motivational milestone.

Discussions on preventing the next pandemic are fully underway.[36-39] Despite complex politics surrounding COVID-19, the pandemic has provided policymakers a window of opportunity to invest in and strengthen all aspects of epidemic preparedness and response, recognizing the importance of a multisectoral One Health approach.[8] We recommend the adoption of universal outbreak milestones and definitions, such that baseline metrics on outbreak timeliness performance can be uniformly measured and objectively evaluated. More specifically, we recommend increased attention to and reporting of predictive alerts and preventive action in response to these alerts to maximize efforts to shorten timeliness metrics, including time to the end of an outbreak, thus reducing cases of disease. Furthermore, we believe that early communication to the public during an outbreak facilitates community support and personal action during an outbreak, contributing to optimal health and societal outcomes for all.

Our recommendations for the adoption of these milestones and timeliness metrics echoes the conclusions of other authors that have previously analyzed timeliness during outbreaks. Impouma et al. recommended the use of metrics to monitor timeliness, concluding that momentum for this effort should be supported to ensure systematic tracking of milestones to continually monitor and assess outbreak response performance.[24] Routine and consistent reporting of milestones in outbreak reports published across agencies, organizations, and peer-reviewed journals may decrease the need to triangulate dates across reports and source types, allowing stakeholders to more readily quantify and objectively assess timeliness metrics. Furthermore, given the frequency of outbreaks occurring at the human, animal, plant, and environmental interface, we believe outbreak timeliness metrics should be One Health in nature, ultimately facilitating collaborations and information sharing across disciplines and sectors at the local, national, and regional levels with the long-term objective of improving and speeding up outbreak response in the future.

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Chapter 3. How feasible or useful are timeliness metrics as a tool to optimize One Health outbreak responses?

INTRODUCTION

As the threat from viral spillover and other emerging infectious diseases grows increasingly evident, countries are ramping up efforts to develop and implement innovative tools for pandemic preparedness and response. Toward this objective, the World Health Organization (WHO) developed a *Research and Development (R&D) Blueprint for Action to Prevent Epidemics* to strengthen the global capacity to curb emerging epidemics faster.[1] During a 2017 R&D prioritization exercise, the WHO added “Disease X” to the shortlist of diseases with the highest epidemic potential and greatest public health risk. While this placeholder name represents a pathogen currently unknown to cause disease among humans, the likelihood that the disease will be zoonotic[2] reinforces that cross-cutting R&D efforts must focus on integrated and flexible pathogen-agnostic tools.

Timeliness metrics, or the analysis of speed in detection and response during health events, have been proposed as one such tool to promote monitoring and evaluation of performance during outbreaks and other health emergencies in order to optimize future outbreak surveillance and response.[3,4] In addition to studies of timeliness metrics to assess progress and identify bottlenecks in disease surveillance and response performance,[5-9] several stakeholders have proposed evaluative frameworks for timeliness metrics. Resolve to Save Lives, the New York City-based not-for-profit organization, has proposed the “7-1-7” targets, to identify an outbreak within seven days of emergence, notify health authorities within one day, and complete the initial response within seven additional days, as a timeliness framework and implementation tool.[10] The World Health Organization Regional Office for Africa (WHO AFRO) has formally adopted the 7-1-7 indicators as a target for timeliness in their 2022-2030 Regional Strategy for Health Security and Emergencies.[11]

The same 2022-2030 WHO AFRO strategy report also calls for the adoption of a One Health preparedness and response plan informed by multidisciplinary teams across the public and private sectors.[11] Recognizing that a collaborative approach across environmental, human, animal, and plant health is optimal for detecting and mounting coordinated responses to outbreaks, experts convened in 2019 to expand upon human health timeliness metrics by proposing a set of One Health outbreak milestones.[12] The 11 milestones outlined in the *Salzburg Statement on Metrics for One Health Surveillance* include response components similar to those set forth by other timeliness frameworks while also proposing several additional metrics, reflecting the importance of a multisectoral approach. The One Health timeliness metrics framework specifically proposes that (where possible) dates be captured for predictive alerts of potential outbreaks, preventive responses to early signals, and joint after-action reviews among relevant stakeholders (**Figure 3.1**). Adoption of these additional metrics would necessitate a truly integrated, cross-sectoral approach to disease surveillance, implemented at the national, regional, district, and community levels. As a tool for pandemic preparedness, it is essential that timeliness metrics utilize an integrated One Health approach if they are to support the ongoing effort to anticipate and respond to *Disease X*.[13]

Figure 3.1. The One Health outbreak milestones defined by the Salzburg Global Seminar.[12] NB: Milestones do not necessarily occur in this order or for every outbreak.

Uganda: An opportunity to assess One Health Metrics

While previous studies have sought to evaluate how One Health timeliness metrics are being reported at the global level, it is not well understood how feasible it is to track these outbreak milestones and metrics at the country level. As one of the countries currently implementing the 7-1-7 targets,[14] Uganda is an ideal setting in which to study One Health timeliness metrics. In addition to stakeholders' familiarity with the objectives of timeliness metrics, the Government of Uganda (GoU) has embraced a One Health approach for epidemic preparedness, given the prevalent risk of emerging infectious diseases in the country.[15,16] Uganda's growing population combined with increased demand for agricultural practices has resulted in encroachment into wildlife and other naturally existing ecosystem habitats. Such human behaviors ultimately lead to increased risk of spillover events, a challenge compounded by globalization and environmental drivers of infectious diseases. [17]

As timeliness metrics continue to attract the attention of international organizations as a viable tool and framework for global health security, insights into the perspectives of the stakeholders adopting these frameworks will help provide the critical feedback needed to optimize these approaches for implementation and scale-up. We therefore sought to describe how the One Health outbreak timeliness milestones have been reported during recent multisectoral outbreaks in Uganda, as well as to characterize the perceived feasibility and utility of a more integrated, collaborative approach to tracking timeliness metrics as a tool to systematically and quantifiably assess outbreak performance.

METHODS

This study followed a convergent parallel mixed methods study design, with quantitative and qualitative data collection and analysis occurring concurrently. Quantitative analyses were conducted using outbreak reports to assess reporting frequency of One Health outbreak milestones, and qualitative interviews were conducted to explore the perceived feasibility and utility of tracking the One Health milestones and timeliness metrics among expert stakeholders. Analysis focused on areas of convergence and divergence between findings.[18]

Quantitative Study

Data Sources

Investigators from Uganda's Public Health Emergency Operations Center and the Infectious Diseases Institute (IDI) at Makerere University collaborated with researchers from the University of California in the United States of America to develop a database of documented outbreak events in Uganda that began or were ongoing between January 2018 and December 2022. We created an electronic folder for each event as a repository for all available Situation Reports, outbreak investigation reports, and Spot Reports. Reports were provided by the Ministry of Health's (MoH) Public Health Emergency Operations Center (PHEOC), the coordinating body responsible for managing all information, resources, and operations related to public health emergency response within Uganda.[19] Other formal GoU documentation was also compiled for review, including press releases from ministries and agencies such as the Uganda Wildlife Authority or the Ministry of Agriculture Animal Industries and Fisheries, International Health Regulations Notification reports, and National Task Force (NTF) meeting presentations. Our database was cross-checked against records of all PHEOC activations between 2018 and 2022 to assess completeness.

Inclusion and Exclusion Criteria

This study aimed to include health events which prompted PHEOC activation and were documented by the responsible government body. PHEOC activation is determined on an event-by-event basis by the Director General of Health Services based on the existing guidelines on Integrated Diseases Surveillance and Response (IDSR) thresholds.[19] These activations could occur at the alert or response level, depending on the perceived severity and magnitude of the public health event. Outbreaks had to be multisectoral, defined as involving two or more of the One Health sectors, namely humans, animals, plants, or the environment. In accordance with Uganda's IDSR guidelines, an outbreak was defined as the occurrence of disease beyond normal expectancy with epidemiologically related cases within a confined period of time and space.

Given these inclusion criteria, non-multisectoral outbreaks of diseases, such as those arising from a human reservoir, including surges in measles cases, were excluded from our analysis. Disease preparedness activities for Ebola virus disease and mpox were excluded, as were natural disasters, given these events did not meet our definition of an outbreak.

Data Management and Analysis

A study team member reviewed all records available to find the earliest date for each of the 11 One Health outbreak milestones (**Figure 3.1**).[12] In addition to recording the milestone date, we documented if a milestone was described without a date or was not mentioned at all. If different sources reported conflicting dates for a milestone, we deferred to the date recorded in the latest available PHEOC-provided report.

Other variables captured included the district and region in which the outbreak occurred, if Uganda had experience with similar outbreaks in the past and, if so, the relative frequency of the occurrence, defined as "frequent" (>10 in the past decade) or "infrequent" (≤10 in the past decade). Transmission route, pathogen type, and status as an IDSR priority disease were recorded.[20] Data were exported to STATA version 16.0 (StataCorp, College Station, TX) for descriptive analysis to determine the frequency of reporting of the 11 milestones as well as a bivariate screening to assess the association between covariates of interest and the outcome of a milestone date being reported. Chi-square and Fisher's exact tests of independence were conducted, followed by logistic regression to assess predictors of milestone reporting.

Qualitative Study

Sampling and Participants

Informants with expertise in public health emergencies in Uganda were identified and invited via email for a Key Informant Interview from a list of professionals that previously participated in 7-1-7 timeliness workshops, convened by IDI. Purposive sampling was applied to ensure informants represented the human, animal, and environmental sectors and had knowledge of different levels of the health system. Participants were contacted directly by email by a study team member. Invited contacts that agreed provided written consent to participate in a recorded interview with a trained researcher. No compensation was provided to participants.

Public Involvement

Stakeholders, beyond those represented by the coauthors and anonymous interviewees, were not involved in setting the research question or data development; however, results will be disseminated to the expert participants and additional stakeholders during a PHEOC-led NTF meeting.

Interview Content

Thirty- to forty-five-minute interviews were conducted and transcribed in English, using a semi-structured interview guide. Topic domains included feasibility and utility of tracking One Health milestones and timeliness metrics. Interviews were conducted either in-person or remotely via teleconferencing software, depending on the preference of the informant. Mid-way through each interview, informants were shown the 11 One Health outbreak milestones with definitions and a description of timeliness metrics calculations. Participants were asked: “In your experience, how feasible would it be to report a specific date for these milestones during an outbreak?” and “Do you think tracking the timeliness of different outbreak steps or events could be useful in improving outbreak responses in the long term?” (Supplement 2).

Framework Analysis

Following familiarization with interviews, two study team members developed a working analytical framework based on open coding of the first four interview transcripts. We then compared, revised, and re-coded all transcripts using a cyclical approach. In addition to inductive coding, several deductive codes were pre-defined based on interview questions about feasibility and utility. Codes, grouped by category, were applied to all interviews using Dedoose Version 9.0.90 (SocioCultural Research Consultants, Los Angeles, CA, 2023). Data were charted into a framework matrix for each transcript, summarized by category along with noteworthy quotes. Data were mapped and interpreted using the framework table in Microsoft Excel, and memos were generated to describe codes of particular interest and highlight deviant cases.

Ethics

This study was reviewed and received approval by the IDI Research and Ethics Committee in Uganda (#IDIREC REF077/2022), and the Uganda National Council for Science and Technology (#HS2255ES). The study was deemed exempt by the University of California, Davis Institutional Review Board (IRB ID1778303-1).

RESULTS

Quantitative Results

Outbreak Events

Between 2018 and 2022, the PHEOC was activated 302 times for 282 epidemiologically distinct public health emergencies. Of these activations, 129 events met our inclusion criteria, constituting 21 types of health emergencies (**Figure 3.2**); however, complete documentation was unavailable for 47 events (**Supplemental Table 3.1**). Thus, we analyzed One Health outbreak milestones for 82 outbreak events occurring in Uganda between 2018 and 2022 (**Figure 3.2**). Thirteen different types of disease events were represented, including undiagnosed illnesses (n=5). Cholera was the most frequent outbreak, with n=22 reports included in the analysis, followed by anthrax (n=14), Crimean-Congo hemorrhagic fever (n=12), and Rift Valley Fever (n=12).

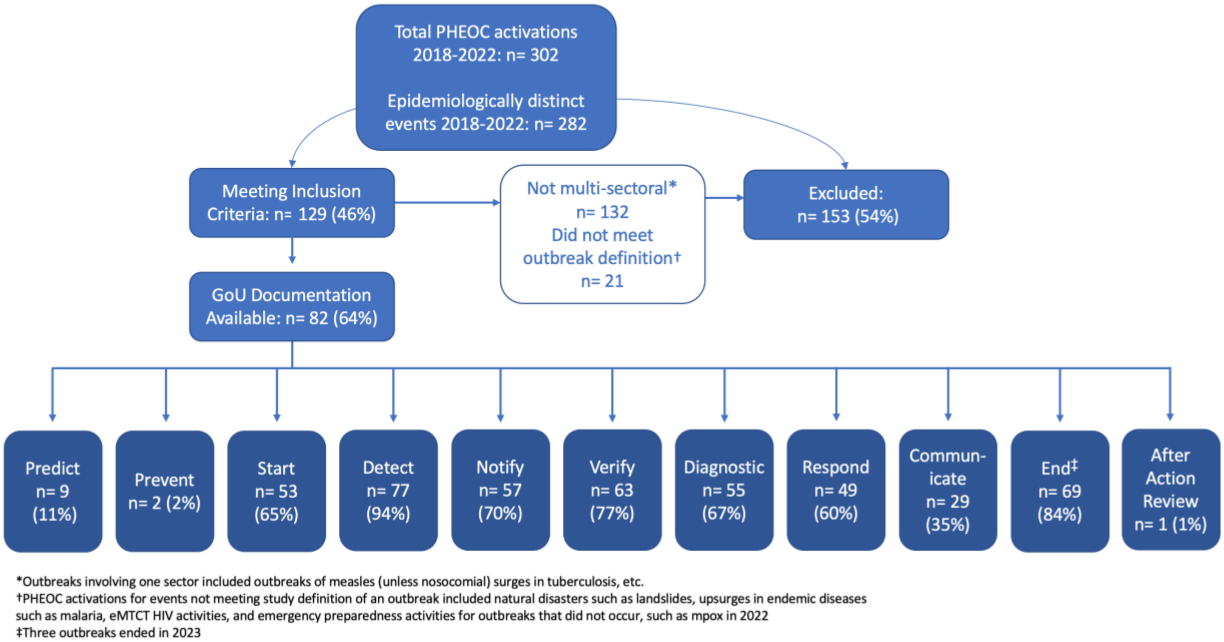

Figure 3.2. Flow diagram of the Uganda Ministry of Health Public Health Emergency Operations Center activations, by frequency of reporting One Health outbreak milestones

Reporting of Outbreak Milestones

Among the documented events, the three milestone dates reported most consistently were *Detect*, with 94% of reports providing the milestone date; *Outbreak End*, with 84%; and *Verify,* with 77%. Of the dates captured for *Outbreak End,* only five were documented in the outbreak reports themselves while 93% of these dates came from the PHEOC activation database. *Respond, Start, Notify,* and *Diagnostic* milestones were all reported with an approximate frequency of 60-70%. Thirty five percent (35%, n = 29) of reports provided a specific date of official communication to the public about the outbreak, though 33 additional outbreaks mentioned this milestone without a date, highlighting that this step is being executed but reported with low frequency (**Table 3.1**).

The least reported milestones were *After-Action Review* and *Prevent*, with one report describing a date when a review meeting took place and two reports describing a date that a preventive action in response to a predictive alert occurred. (**Table 3.1**) *Predict* was also infrequently reported, with 11% of reports from the GoU providing a specific date of an alert signaling a potential outbreak. Of the 82 outbreaks analyzed, approximately 80% (n=65) of events could have theoretically had a predictive alert based on epidemiologic considerations (e.g., climate-related predictors for cholera, anthrax, and vector borne illnesses). Eight additional PHEOC reports described predictive alerts of outbreaks without providing a specific date, though none described any additional preventive actions.

Tests of association between covariates of interest and reporting of outbreak milestone dates found that outbreaks of viral hemorrhagic fevers had 5.3 times the odds of reporting the *Diagnostic* milestone date compared to outbreaks of non-viral hemorrhagic fevers (95%CI 1.4-20.9, p-value 0.02), 3.4 times the odds of reporting the *Start* date (95%CI 0.98-11.69, p-value 0.05), and 4.7 times the odds of reporting the *Verify* date (95%CI 1.1-20.3, p-value 0.04).

Qualitative Results

Key Informant Interviews

Of the 23 experts invited to participate in interviews, 15 agreed to an interview and 11 scheduled one. Half of the individuals that did not respond to our request were senior ministerial officials; however, several senior officials from other institutions participated. One remote interview was interrupted due to internet connectivity and was not rescheduled. Therefore, 10 informants, one female and nine males, were interviewed from seven institutions at the regional, national, and international levels of the Ugandan health system. Four informants worked primarily with the human health sector, two primarily with the animal health sector, two in laboratory sciences, one at the human-environmental health interface, and one explicitly in One Health. Findings across the expert informants was highly consistent with very few deviant cases, helping to assure data saturation given the range of expertise and responsibilities captured (Supplemental Appendix). In the following section, we present results of our framework analyses by feasibility and utility.

Feasibility

Capturing specific dates for the One Health outbreak milestones was perceived as desirable across participants; however, certain milestones were described as more easily captured than others. Broadly, participants generalized it to be very feasible to capture a specific date for the *Detect, Notify, Verify, Diagnostic Confirmation, Respond,* and *Public Communication* milestones. *Outbreak Start* was perceived by some as feasible and by others as challenging to identify the date of emergence. *Outbreak End* and *After-Action Review* were generally described as less feasible to capture, but possible in theory. The *Predict* and *Prevent* milestones were perceived as difficult to capture. Still, participants described ongoing efforts by the GoU to actively build the capacity to capture these two milestones, namely through tracking seasonal, weather, and geographical patterns of diseases.

Table 3.1 below describes the feasibility of capturing the specific One Health outbreak milestones, beginning with those milestones that are described by informants as easy and feasible to routinely capture (shaded green) and ending with those milestones perceived as challenging to routinely capture (shaded red).

Table 3.1. Analysis of feasibility of capturing specific dates and tracking timeliness metrics for One Health outbreak milestones as reported by ten key informants*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
Detect: symptom onset, death, or evidence of circulation observed or	Specific date n=77 (94%) Mentioned, no date n=3 (4%)	Existing infrastructure facilitates capturing the date of detection, including the 6767 SMS alert notification platform under eIDSR; however, additional	*"First of all, it is feasible and doable [to report a specific date]. The way we've been doing it here, is in such a way that once there's an alert that comes from the*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
suspected in humans or animals	Not mentioned n=2 (2%)	digitalization of reporting forms may increase tracking of this date.	*community, whether it is an animal health alert or a human health alert, or a community disaster… These are events that are reported through our eIDSR channels, especially the 6767 SMS platform." (KII 11)* *"Detect, of course that is something to do with how the system was able to say, 'You know what? This is something'. You can put a date on that." (KII 7)*
Notify: outbreak reported to relevant authorities	Specific date n=57 (70%) Mentioned, no date n=3 (4%) Not mentioned n=22 (27%)	As relevant authorities must be informed to prompt a response, the *Notify* milestone necessarily always occurs and should be recordable. Several factors have improved the ease of notification and documentation, including the advent of new technology (e.g., mobile phones, network accessibility, email).	*"Notification, I must say that one has been occurring faster enough, because as soon as get to know about [the outbreak] then the notification has always been first because people have access to phones, people have access to emails. So that [milestone], notification, has always not been an issue." (KII 1)*
Verify: outbreak confirmed by field	Specific date n=63 (77%)	Existing infrastructure including regional EOCs and rapid deployment of District Task	*"One of the things that has helped us in tracking of the dates, or the duration of these events, is the*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
investigation or other valid method	Mentioned, no date n=10 (12%) Not mentioned n=9 (11%)	Forces to investigate rumors facilitates verification and consistent tracking of this milestone, among others through the reporting mechanisms of spot reports and situation reports.	*existence of the original public health emergency operations center in West Nile which sits in Arua. And the center is able to have all this information, sieve them out… 'Spot reports' are written if the event has been verified and teams have been sent to go and respond… And thereafter, a situation report is written as the event is being contained. So that the durations or the dates in between there from when the alert came and up to when response teams go to the ground or intervening, are all tracked." (KII 11)*
Diagnostic Confirmation†: outbreak confirmed by diagnostic test or laboratory confirmation	Specific date n=55 (67%) Mentioned, no date n=20 (24%) Not mentioned n=4 (5%)	Existing infrastructure facilitated tracking dates for diagnostic confirmation through the hub system, which requires documentation at every step of transportation and delivery of specimens to laboratories.	*"There is now…chain of custody tools around. Almost at every step a sample goes though, somebody signs. Handing over the sample, okay, picking the sample, somebody signs. Handing it over to the transport, somebody signs. You bring it to Kampala you hand it to*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
			somebody else? Sign. Until it reaches the gate." (KII 7)
Respond: intervention enacted in response	Specific date n=49 (60%) Mentioned, no date n=25 (30%) Not mentioned n=8 (10%)	Though the response is dependent upon type of intervention required, this milestone date is considered feasible to routinely track.	*"Respond, that deserves a date because our SOPs is that people respond with… in coordination with the public health administration, so the time they say yes to something is the date." (KII 7)*
Communication: official release of information to the public	Specific date n=29 (35%) Mentioned, no date n=33 (40%) Not mentioned n=20 (24%)	Government press releases and readily available radio airtime facilitate this milestone and easy tracking of the date for public communication.	*"You can write a date for these public communications. You write a date, because there will be a press release." (KII 7)*
Outbreak Start: earliest epidemiologically linked symptom onset or death	Specific date n=53 (65%) Mentioned, no date n=4 (5%)	Reporting for this milestone could be increased if frontline workers, especially those at the facility or clinic, are trained to ask and record date of symptom onset.	*"If a health worker at facility X is informed that, actually, if you have a suspect measles patient in front of you, please note for me the date when they first showed symptoms or something like that. If that is part what the data piece they have to*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
	Not mentioned n=25 (30%)		*collect, and angle it into the system, I think that will go a long way in helping us to capture these data pieces." (KII 4)*
Outbreak End: date that outbreak is declared closed by a responsible authority	Specific date n=69 (84%) Mentioned, no date n=1 (1%) Not mentioned n=12 (15%)	Formal declaration of the end date occurs more often for outbreaks perceived as high consequence (e.g., VHFs declared over in a press release). The end date may be more difficult to capture for other outbreaks of diseases which are perceived as less urgent, due to some ambiguity as to when the outbreak is declared closed.	*"Many of the outbreaks, at least they normally declare the end of the outbreak, especially the VHFs, but other diseases they have ben not so much declaring the outbreak end… [W]hen you're still in that very first phase in that outbreak you find that you're meeting daily, eventually that meeting after a few days may be weekly, then monthly, then you find that the risk is no longer there or whatever, then you find… the NTF is deactivated… that seems, that marks the end." (KII 1)* *"Outbreak end - it will be on paper, even though that is on paper, but it doesn't really mean the end of outbreak in the field. Let's call it outbreak end for logistic reasons." (KII 7)*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
After-Action Review: joint review of outbreak by relevant One Health authorities	Specific date n=1 (1%) Mentioned, no date n=2 (2%) Not mentioned n=79 (96%)	To-date, *After-Action Review* is an inconsistent practice which is therefore a difficult date to capture; however, international involvement has recently facilitated reviews.	*"[W]e can follow [milestones] chronologically until the outbreak ends and even take the After-Action Review. But we have not in fact been doing this one, we have been now like, it is just coming up. (KII 5)"* *"So at least but at least the issue of AAR we've been doing it. Even last year…through facilitation and from TDDAP and FAO, were able to do after-action review of RVF or anthrax." (KII 1)*
Predict: a valid predictive alert of a potential outbreak	Specific date n=9 (11%) Mentioned, no date n=8 (10%) Not mentioned n=65 (79%)	Difficult to capture dates of predictive alerts of outbreaks but increasingly possible with geographical and seasonal mapping. The feasibility of capturing this milestone will differ from outbreak to outbreak depending on context.	*"Like these predict milestones, you know there are particular disease outbreaks for which this can be applied, like the cholera outbreak which often come along with heavy rain and flooding in some parts of the country. But for a couple other outbreak conditions… it's a little difficult to track…So for the more often incidents like cholera, maybe*

Milestone	Reporting Frequency (Total n=82)	Cross-cutting Themes of Perceived Feasibility	Illustrative Quotes
			yes, but for the vast majority of the other diseases, no." (KII 6)
Prevent: date that preventive action is initiated in response to the predictive alert	Specific date n=2 (2%) Mentioned, no date n=0 (0%) Not mentioned n=80 (98%)	Informants describe that it is not always possible to capture a date because dependent on *Predict* milestone, which is also not possible to consistently record a date for.	*"Yeah you can [ensure the date is reported]. Always. Except the first two. Predict and Prevent, you can't put a date, you can't put a consistent date." (KII 2)* *"[T]he same for prevention, the milestone to prevent. Well, to be able to have surveillance after a predictive alert, that's in line with my first response that for the vast majority of outbreaks you don't have all that information, you know, available to facilitate such a decision." (KII 6)*

* AAR, After-Action Review; eIDSR, electronic Integrated Disease Surveillance and Response; EOC, Emergency Operations Center; FAO, Food and Agriculture Organization; NTF, National Task Force; RVF, Rift Valley fever; SMS, short message service; SOP, standard operating procedure; TDDAP, Tackling Deadly Diseases in Africa Project, UK Aid; VHF, viral hemorrhagic fever
†Dates of unsuccessful diagnostic tests were additionally described for three of the unknown illness

Key. Outbreak milestones were described by participants based on feasibility of capturing a specific date as:

Easy and feasible to routinely capture	Feasible but more difficult to routinely capture
Easy and usually feasible to capture	Challenging to routinely capture

Utility

Unanimously, participants characterized timeliness metrics as a useful tool to inform and optimize future outbreak detection and response. Descriptions of how timeliness metrics are useful fell into three broad categories: 1) learning from past outbreaks to be more prepared for future outbreaks; 2) improving communication and accountability; and 3) serving as a motivator and educational tool (**Table 3.2**).

Table 3.2. Thematic analysis of the perceived utility of One Health timeliness metrics by ten key informants

Theme	Sub-Theme	Illustrative Quotes
Learning from past outbreaks to position the health system to be more prepared for future events	Allowing stakeholders to identify gaps, barriers, and enablers in the current system	*"We're able to also note what were the gaps between vet and also the human health side... So, we noticed that there had been actually a training on community-based surveillance that involved both the vet and also the human health rapid response teams that enabled them to share information promptly. So, looking at the timeliness, it actually helps us to track our enablers, the enabling factors for us to be able to detect the outbreak and also respond."(KII 9)*
	Providing evidence on how to best allocate and mobilize resources	*"[T]imeliness is key to response. And the earlier you respond, the less the cases, or the faster you take action when you know what is happening. So, it will also help us mobilizing resources where we need them. And maybe in case we need extra support we can always use the data that we have as evidence." (KII 10)*
	Generating data for comparative studies and evaluation of implementation projects	*"[W]e will learn from it and then… say, 'Hey, in 2018 this is what happened, in 2019 this is what happened, and then we make this kind of comparative research and findings to make us better.'" (KII 2)* *"Then it will also help us to be able to track the progress in terms of implementing the proposed recommendations because at the end of*

Theme	Sub-Theme	Illustrative Quotes
		the day, we are able to look back and know what has been proposed… So, timeliness will actually be very key to help us track our successes in terms of our detection, tracking the different remediations that we have proposed, and also to be able to appreciate how fast we are." (KII 9)
Improving communication and accountability	Providing a platform to elevate messages between levels of the health system and internationally	*"Those at the national level [messages] often reach because we often have a platform to present and share with them… So maybe something that you could probably include at the national level, is often a follow-up meeting with the district staff that's where the outbreak has occurred, so that they can take on some of the response, understand what have been their weaknesses, to be able to now prepare for the next outbreak." (KII 9)* *"Uganda is what I want to call a hub because so many countries are learning from us." (KII 2)* Stated in the context of how timeliness metrics can contribute to the outbreak landscape.
	Increasing communication and coordination between health sectors	*"[T]he issue of the mandates will come in. If I am from the animal side, I am mandated to report mainly on them. I might keep a blind eye [to the human side]… But now with this open One Health approach, we need to report on similar issues. And even share the findings." (KII 5)*
	Serving as a mechanism for increased accountability, including accountability in reporting	*"[Tracking timeliness is] very, very, very, very useful. Why? Because if you do not have as a system, you don't have monitoring, you can't monitor yourself that I took so many days before responding to signals A, B, C, then there's no accountability. So, if*

Theme	Sub-Theme	Illustrative Quotes
		the question is usefulness, then the actual answer is a very big plus. It's very useful." (KII 4) *"It's supposed to flag what has not been done within the timelines, so in a sense it kind of begins to enforce or help people get used to the need to routinely report certain types of information in a timely manner." (KII 8)*
Serving as a motivator and educational tool	Providing a learning opportunity for investigators and the next generation of health leaders	*"Yeah, people or the responders really need to see the reason why you know certain action needs to be taken when events are detected. So keeping track of those timelines targets and metrics is vital to ultimately contributing or even turning around, implicating better response in terms of timeliness." (KII 6)* *"There are those learners who are still in school, studying their master's in public health, doing PhD programs. Now [timeliness metrics] will give them an opportunity also to come and learn." (KII 2)*

While timeliness metrics are seen as a useful long-term investment in outbreak preparedness, the benefits of tracking milestones may not be immediately evident. One informant cited that the implementation of these metrics will also add work for investigators:

> "In the short term a benefit may not be seen…Because it's kind of adding work onto the reporter's side. But in the long term if we want to improve our system, this will be very, very handy… So short term might not be very visible, but long term the benefits are enormous." (Public Health Information Analyst)

Additionally, informants cautioned that steps to improve timeliness during outbreaks ultimately depend on a multitude of other on-the-ground priorities:

> "Even if you tracked [timeliness] there are so many barriers... If you've planned and you say that the team will leave for the field tomorrow, the team cannot leave without resources and the process to receive the money… So, I mean it is important to set the timeliness tracker and see how things are done but you need to be cognizant of the reality." (Epidemiologist)

Participants also described a perceived need for integrated reporting channels. One informant described that, at present, reporting channels are not yet designed to streamline data for use or analysis across sectors:

> "I think the major thing is how feasible is it for us to match all these reporting channels. So there is what you might consider as inoperability of the different channels for reporting…Already there are two parallel channels, but can we have interoperability of the two or three…So that in the end there's somewhere they're amassed, and everyone sees the events as they come in." (Medical Lab Scientific Officer)

Despite the perceived ease of capturing seven of the eleven milestones (**Table 3.1**), participants also acknowledged that routine tracking of timeliness data is not yet happening. As such, timeliness metrics are not yet being measured or analyzed:

> "What has been happening, is that [timeliness] is something that we have not been focusing much on, about. When an outbreak happens, we just swing into action to go and support investigating, responding, but not trying to measure the timeliness for each of the key components." (Public Health Officer)

DISCUSSION

Feasibility

The consensus among expert informants that most One Health outbreak milestones are feasible to track is supported by the frequency of milestones documented in reports of the 82 events in this study.

Given the relatively new focus on the use of the One Health milestones, there were some reporting variations. There was a similar reporting frequency on the *Notify*, *Diagnostic*, and *Respond* milestones and their perceived ease of being routinely documented. In contrast, although *Outbreak Start* was described as usually feasible to capture, participants felt slightly less confident in their documentation. If countries want to assess whether efforts to shorten the duration of an outbreak translate to better outcomes, then the *Start* and *End* outbreak milestones are two of the more critical dates to capture.

However, most informants expressed that the *Outbreak End* milestone is difficult to document. As an example, the *End* date for the 2022 outbreak of *Sudan ebolavirus was formally announced* 42 days after the last admitted case tested negative and the last confirmed death was buried.[21] This date follows objective criteria per WHO recommendations for declaring the end of an outbreak based on interrupted human-to-human transmission.[22] Conversely, the end date for outbreaks of other diseases, including cholera and anthrax, is linked to deactivation of the response, a date not often described in outbreak reports. Even if identified retrospectively, if both *Start* and *End* dates are defined per symptomology (onset and last observed), these standardized metrics could be consistently used by countries to track their own progress in the duration of outbreaks.

A few participants expressed uncertainty about the definitions of several other milestones, including *Public Communication*, given that this step will likely occur more than once during an outbreak.

Concern regarding the subjective interpretation of milestone dates reflects the possibility of measurement bias in timeliness analyses. Indeed, the quantitative data review for this study was performed by one study member from the University of California, increasing the risk that our milestone reporting frequency is subject to measurement bias. However, the study member had previously reviewed thousands of outbreak reports for a scoping review on One Health timeliness metrics for which validation exercises for interpretation of milestone reporting and dates took place.[8] As timeliness metrics continue to be adopted globally, implementation tools such as the 7-1-7 toolkit should provide guidance and examples of milestone definitions.[23]

Descriptions of *After-Action Review* meetings during two interviews suggests that this milestone has taken place more than it was reported in the past five years. It is possible that when outbreaks slowly subside without formally being declared over, it is more difficult to set a date to convene for a review meeting. The infrequent reporting of *After-Action Reviews* may also reflect observations by informants that they are often overwhelmed by the ever-present, and sometimes concurrent, threat of outbreaks, which keep responders too busy to take advantage of calm periods (if they exist) between outbreaks to fully learn from previous crises. These lost opportunities for quality improvement may result in the same performance patterns being repeated over time.

As reflected in both our qualitative and quantitative findings, dates for *Predict* and *Prevent* milestones are not yet being documented. Most informants described these milestones as challenging or not possible to capture, or only possible for certain outbreaks. Though participants describe steps in Uganda to increase tracking disease seasonality, the non-reporting of these metrics reflects the absence of documented dates due to a lack of public health action for these domains. For all countries, *Predict* and *Prevent* actions provide an opportunity to minimize human, animal, and economic losses arising from outbreaks and other hazards. Greater efforts to strengthen work in this area are needed, particularly due to climate change. A 2022 study investigating transmission pathways of climate hazards found that nearly 60% of pathogenic diseases that affect humans are or can be exacerbated by climate change.[24] In Uganda, increased rain, floods, landslides, mudslides, and changes in seasonality and drought, may serve as predictors of outbreaks and should be tracked as such.

Beyond barriers to milestone reporting, informants also highlighted that the feasibility of using these data for timeliness metrics analysis is dependent on integrated health information systems. If reporting channels are to be integrated, these systems must be easy to operate and accessible "on-the-go", with training opportunities and clear instructions for system users.

Lastly, despite the perceived importance of tracking timeliness metrics and feasibility of documenting milestones dates, participants cited on-the-ground realities that pose practical challenges to tracking and improving timeliness. Our findings of increased odds of reporting *Start*, *Diagnostic*, and *Verify* milestone dates for outbreaks of viral hemorrhagic fevers (VHFs) may reflect one such country-specific reality: certain outbreaks may receive heightened attention compared to others given their perceived threat. VHFs are highly fatal and most have no known treatments. Past experience has also illustrated difficulties in bringing these outbreaks under control. We believe that contextual influences such as these warrant further investigation.

Utility

Several categories of utility that emerged in our framework analysis align with the general objectives of the 7-1-7 targets. Necessarily, we recognize that informants may have a biased perspective of the utility of timeliness metrics, given that we recruited participants who had previously been invited to participate in 7-1-7 workshops. Key informants interviewed for this study also did not represent all levels of the health system. However, the study participants were heterogeneous across different sectors. Their responses may be more transparent than those by senior leaders, and their perspectives may represent individuals better positioned to report on perceived strengths and limits of the framework given their first-hand experience. Due to their understanding of the proposed framework, these individuals are most likely to be early adopters of timeliness metrics, representing the best-case scenario for implementation. Those not yet exposed to the timeliness metrics framework may be less quick to embrace this change opportunity. Additional considerations for capacity building and training should consider how to incorporate evidence illustrating the effectiveness of these metrics. By naming the metrics of interest as "One Health" during the interview, it is also possible that participants were more inclined to describe timeliness metrics in terms of coordination between health sectors.

Indeed, informants invariably expressed an interest in and appreciation for the One Health approach to both timeliness metrics and outbreak investigations more broadly. In particular, the integrated approach was described as an opportunity for increased communication and collaboration across sectors. As a tool, One Health timeliness metrics can serve as a platform to elevate messages not only between levels of the health system, but also between disciplines and the public and private sectors. The *After-Action Review* milestone seems the ideal opportunity to convene stakeholders across relevant sectors and the national, regional, and district levels. While beyond the scope of this assessment, the WHO has also encouraged countries to conduct intra-action reviews for protracted outbreaks when significant changes to response plans could be needed.[25]

Other timeliness metrics frameworks similarly consider review meetings as an essential component of the implementation of timeliness metrics. By incorporating the *Predict* and *Prevent* milestones into the framework, we believe that stakeholders are more likely to approach the investigation and response with a coordinated approach in mind across environmental, animal, and human sectors from the outset, rather than identifying missed opportunities for collaboration after the fact.

The more robust and complete the data on milestone dates, the richer and more accurate our understanding of timeliness trends will be. Our study relied on data from a country with a great deal of experience in responding to public health emergencies and one that has already adopted timeliness targets as a monitoring and evaluation tool. Generalizability to other settings may therefore not be feasible. However, Uganda's experience makes it an ideal context in which to test the feasibility and explore the perceived utility of the One Health timeliness metrics. Additional testing and piloting of the framework is necessary to understand if information is captured consistently and how adaptable it is to other localities with different contexts.

This study provides evidence of consensus among a group of key stakeholders in Uganda that timeliness metrics are recognized as a beneficial tool to assess past performance in outbreak detection and response. It also points to the importance of such data for quality improvement initiatives that engage each level of outbreak responder, from community members and "on-the-ground" frontline workers to policy makers and health leaders at the national and international levels. Additionally, several outbreak milestones need to be reported on more frequently to allow optimal utility of these metrics, including quality improvement efforts.

IMPLICATIONS AND CONCLUSIONS

These initial results hold promise for a variety of future steps. First, with consideration within the country where the study was conducted: Uganda is prone to WHO R&D priority diseases including Crimean-Congo hemorrhagic fever, Ebola and Marburg virus diseases, and Rift Valley fever. It is also at risk for *Disease X* being an animal-sourced virus.[26] Consequently, Uganda would benefit from leveraging a One Health approach to address future epidemic and pandemic threats, as well as the impacts of climate change, and continuously monitor its performance in predicting, preventing, detecting, and responding to these threats.

Secondly, findings from this study have led us to make the following recommendations regarding timeliness metrics in Uganda and more broadly for other countries positioned to adopt timeliness into existing surveillance and response frameworks:

- Timeliness metrics frameworks would potentially benefit from a collaborative and transdisciplinary One Health approach that is inclusive of animal, environmental, and human sectors, and cross-cutting in both scope and implementation.
- Global actors need to identify additional ways by which to develop guidance and toolkits that formally engage eventual consumers of these tools to help advance a coherent strategy. This implies that such resources incorporate the context and realities of countries which seek to strengthen their country-wide efforts in predictive alerts and preventive action of outbreaks.
- Using principles of community engaged research, stakeholder trainings and other capacity-building opportunities, for example virtual or in-person technical assistance on how best to incorporate these metrics, will need to be developed and implemented. Over time, this infrastructure can help assess, capture, and share best practices for wider distribution among countries using such frameworks.
- Reminders, in the form of field prompts or reporting templates to capture timeliness milestones, can be introduced to enhance documentation of relevant metrics.
- To ensure metrics are standardized, stakeholders should agree upon the most appropriate proxy dates to use for the *Start* and *End* milestones. The date of symptom onset is the most reliable available proxy date for *Outbreak Start* and therefore, we recommend that this milestone date, as well as *Outbreak End*, be based on symptomology.

- Current outbreak reporting channels are siloed, posing challenges to tracking timeliness during outbreaks involving multiple sectors. By integrating reporting channels to create a single repository for milestone dates, which is easily accessible to all possible investigators across all ministries, agencies, and institutions, may result in more complete data and facilitate analysis and use of these metrics.
- To ensure dates are reported transparently and in every instance possible, timeliness targets must be feasible to investigators given on-the-ground realities. Therefore, we recommend targets be flexible given contextual factors which may vary on a country-by-country basis.
- Beyond capturing data, planning for how to incorporate system oriented, quality-improvement initiatives, where the individual is not blamed for a particular action, but rather seen within the broader context is also necessary to fulfill the "last mile" of implementation.

Recognizing the increased training and work required on behalf of outbreak investigators to implement this framework, additional engagement with expert stakeholders at the district and community level will be useful in implementing the next set of programmatic efforts.

As shown in this study, Uganda has exemplified how timeliness metrics can be utilized during outbreaks through the implementation of the 7-1-7 targets. However, to achieve these targets, relevant milestones must first be routinely tracked. Furthermore, we believe that Uganda is well positioned to incorporate surveillance for predictive alerts into these efforts. There is also a need to continue to support staff in their efforts to assure that they have the time to devote to incorporating the lessons learned and to build in quality improvement efforts based upon these local lessons. Given the expertise of coordinating bodies, such as the National One Health Platform and the PHEOC, Uganda is likely to continue to play a leadership role as an early adopter of these additional metrics, which are critically important to a global model needed to prepare for and prevent pandemics.

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Chapter 4. Learning from One Health Timeliness Metrics: An Analysis of Multisectoral Outbreaks in Uganda

INTRODUCTION

As the Public Health Emergency declaration for the COVID-19 pandemic ends, the world once again risks perpetuating a cycle of panic followed by neglect for pandemic preparedness.[1,2] Given the probability of extreme epidemics increasing in frequency,[3] however, efforts to bolster national and global preparedness for and performance during outbreaks remain more crucial than ever to detect and respond rapidly to outbreaks, thereby averting future pandemics.

Estimates of increased intensity and frequency of epidemics in the future are largely attributable to the heightened risk of disease emergence from animal reservoirs associated with climate variability, change in land use, and loss of biodiversity.[4,5] Experts worldwide recognize that a coordinated and integrated One Health approach, which emphasizes that the health of humans, animals, and our ecosystems are interdependent, is optimal to tackle this complex and interdisciplinary global challenge. The Quadripartite, comprised of the Food and Agriculture Organization of the United Nations (FAO), the United Nations Environment Programme, the World Health Organization (WHO), and the World Organisation for Animal Health (WOAH), have issued an urgent call to action to strengthen collaboration and commitment to One Health, including enhanced intersectoral health governance and the implementation of One Health strategies to prevent pandemics and health threats at their source.[7]

To strategically inform policies and activities aimed to prevent pandemics, countries must first be able to objectively evaluate past and present performance to identify strengths and weaknesses in the outbreak landscape. Faster performance in outbreak detection and response allows stakeholders a greater window of opportunity to slow or prevent disease transmission, ideally translating to lives saved and a reduced socioeconomic toll associated with protracted outbreaks. Timeliness metrics, an objective measure of the time between key outbreak milestones,[8] have been proposed as a tool to quantitatively assess where detection and response times have historically lagged or been fast and to optimize future responses. Several timeliness metrics frameworks have been proposed, including the 7-1-7 approach developed by Resolve to Save Lives, targeting detection of an infectious disease outbreak within 7 days, notification of relevant public health authorities within 1 day, and deploying an effective response within 7 days from notification.[9]

Similarly, the One Health timeliness metrics have also been proposed as a framework designed to assess performance in timeliness in 11 key outbreak milestones (**Figure 4.1**).

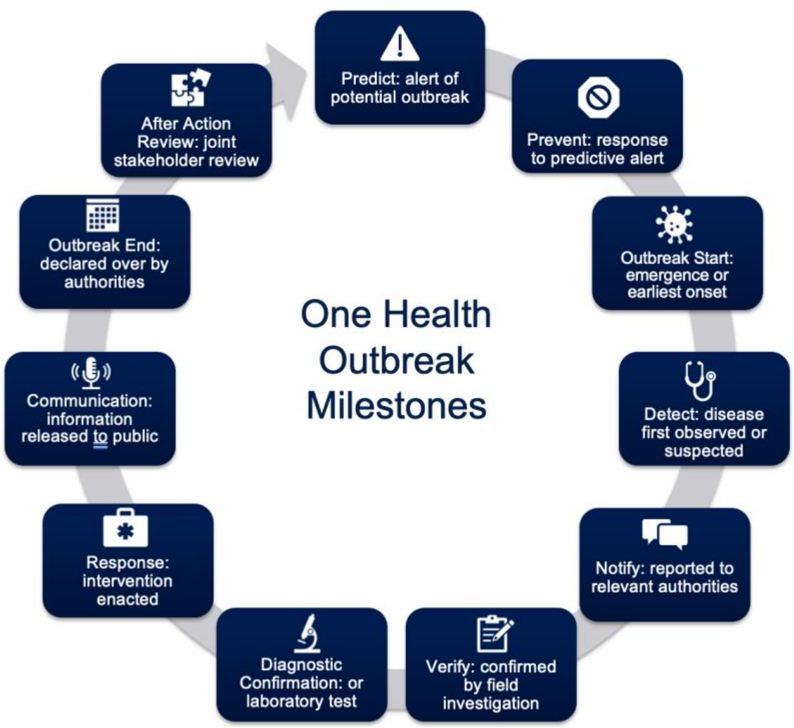


Figure 4.1. The One Health outbreak milestones defined by the Salzburg Global Seminar.[7] Timeliness metrics are calculated as the time in days between any two respective milestones. Note: Milestones do not necessarily occur in this order or for every type of health event

With an emphasis on community engagement and coordination across human, animal, and environmental sectors, the One Health timeliness framework extends analysis to metrics related to predictive alerts of outbreaks and preventive responses, when possible. Though it is not an exhaustive list, of the eleven diseases prioritized in the WHO Research & Design Blueprint, ten are zoonotic viruses and the eleventh, "Disease X", represents a currently unknown pathogen which is also likely to also be zoonotic.[10] Epidemiologically, at least five of these diseases, which includes COVID-19, could have predictive alerts, such as climate-related predictors for vector-borne illnesses, which signal potential outbreaks. Given these known and unknown threats, a truly integrated One Health approach is optimal to ensure that epidemic policy action, including monitoring and evaluation for outbreak metrics, is transdisciplinary and unified.

While analyses have demonstrated timeliness metrics as a useful tool for identifying where performance is fast and where there are lags in detection and response times,[8,11,12] these quantitative findings leave stakeholders to speculate as to why bottlenecks occur and what factors promote speed. This study therefore seeks to use a mixed methods approach to explore timeliness during multisectoral outbreaks in Uganda, a country prone to outbreaks of diseases of epidemic and pandemic risk and one of the six countries in which the 7-1-7 targets have been successfully piloted.[13] Though our analysis excludes COVID-19 timeliness data given the pandemic was an outlier in duration, scope, and geographic spread, Uganda's response to the pandemic was objectively fast, with preventive actions (e.g., public gatherings suspended, quarantines enforced for travelers arriving in Uganda) taken three days before the first case was detected.

METHODS

As described in Chapter Three, we conducted a convergent mixed methods study with quantitative and qualitative data collection and analysis taking place concurrently.[14] This study was conducted in parallel to the study described in Chapter Three, which reported on the feasibility and utility of implementing timeliness metrics as a tool to assess and inform outbreak preparedness. This manuscript analyzes timeliness metrics during multisectoral outbreaks in Uganda, focusing on factors influencing speed during an outbreak.

Quantitative

As previously reported in Chapter Three, collaborators from Makerere University's Infectious Diseases Institute, Uganda's Public Health Emergency Operations Centre, and the University of California (at Davis and San Francisco) developed a database of One Health outbreak milestones for public health events prompting activation of Uganda's Public Health Emergency Operations center between 2018 and 2022. Outbreak events, which were organized in Excel, were compared against a list of all PHEOC activations to check for completeness. Events had to meet our definition of an outbreak, per Uganda's Integrated Disease Surveillance and Response (IDSR) guidelines,[15] and involve two or more of the One Health sectors (i.e., animals, humans, plants, or the environment). Diseases arising from a human reservoir were therefore excluded from our database, as were natural disasters and activations for disease preparedness activities.

The earliest date reported for each One Health milestone (**Figure 4.1**) was extracted from original outbreak investigation reports, Situation Reports, Spot Reports, and other formal reports, which were compiled from PHEOC electronic records. To ensure maximum completeness of milestone dates, we additionally conducted a literature review of outbreaks in Uganda. Databases included reports from the U.S. Centers for Disease Control and Prevention's[16] Morbidity and Mortality Weekly Reports (MMWR),[17] the World Health Organization's Disease Outbreak News (DON) reports,[18] the World Organization for Animal Health (WOAH, formerly OIE) Information System reports,[19] and the International Society for Infectious Diseases' Program for Monitoring Emerging Diseases posts.[20] We also conducted a literature review of outbreaks reported in peer-reviewed journals published on the PubMed database between January 1, 2018 and December 31, 2022. Reports of outbreaks in Uganda for which the PHEOC was activated were reviewed for milestone dates. In instances of conflicting dates, we deferred to those in reports from the Government of Uganda. As previously described in Chapter Three, milestone date extraction was conducted by one study team member from the University of California. This study member build upon previous experience interpreting One Health milestone dates based on a study of thousands of outbreak reports, for which exercises were conducted across three investigators to validate interpretation of dates.[26]

In addition to extracting milestone dates (a day of a month of a year), a study team member captured the following variables: the district(s) and region(s) in which the outbreak occurred; if the outbreak had crossed borders to or from another country; if Uganda had experience with similar outbreaks in the past either at the district or national level and, if so, the relative frequency of the occurrence in the country; transmission route and pathogen type; the surveillance method by which the outbreak was detected; and if the outbreak was an IDSR priority disease, condition, or event.[15] For the *Notify* milestone, we also made note of which authority was notified on the date recorded.

QGIS Version 3.12.3 (QGIS Geographic Information System, Open Source Geospatial Foundation Project) was used to map outbreaks by district. Statistical analyses were conducted in STATA version 16.0 (StataCorp, College Station, TX). Descriptive statistics of the outbreak characteristics were generated, along with the median time in days and interquartile ranges (IQR) between all respective milestones. Metrics were stratified by report year, region, disease, pathogen type, transmission route, surveillance type, One Health sectors involved, and whether the outbreak affected multiple countries, was a prioritized zoonotic disease,[21] or was a viral hemorrhagic fever. Outbreaks spanning multiple regions were categorized and analyzed by the region in which the outbreak began, where earliest milestone dates were most likely to have occurred. Outbreaks of suspect illnesses were categorized and analyzed by presumed etiology. We also stratified by frequency of past experience with a similar outbreak at the country level, categorized as “frequent” (PHEOC activation >10 for a disease in the past decade), “infrequent” (PHEOC activation ≤ 10 for a disease in the past decade), or “unknown” for outbreaks of undiagnosed illnesses.

Uni- and multivariate Cox proportional hazards regression analyses were conducted to assess changes in speed over time between two respective milestones. For outbreaks in which the predictor milestone (e.g., *Outbreak Start*) and outcome of interest milestone (e.g., *Detect*) occurred on the same date, we adjusted the second milestone to 0.3 days, or the equivalent of 8 hours. Based on the outcome of interest, missing dates were imputed based on the logic of subsequent milestone dates. For example, missing *Detect* dates were imputed with the next available milestone date (e.g., date of notification, verification, diagnostic confirmation, etc.) given the assumption that detection must necessarily have occurred for the subsequent milestones to transpire. Missing *Diagnostic Confirmation* dates were imputed using the *Public Communication* date if the outbreak reports indicated a confirmed diagnosis had occurred at some point in time. Missing *Response* dates were also imputed using *Public Communication* dates.

Predictor variables included outbreak report year, relative frequency of experience with similar outbreaks, and whether the event was an outbreak of a viral hemorrhagic fever. Multicollinearity was assessed using a variance inflation factor (VIF) test. Survival curves were plotted to evaluate for proportional hazards assumptions. Findings are reported as estimated hazard ratios with 95% Confidence Intervals (CI). We used proportional hazards models after checking the potential violations of the proportional hazards assumption using log-minus-log survival plots and scaled Schoenfeld residual statistics. All predictors satisfied the proportional hazards assumption via graphical and test evaluation.[22]

Qualitative

As previously described in Chapter 3, key informant interviews were conducted with Ugandan experts in health emergencies. Purposive sampling methods were used to ensure perspectives of informants from different One Health sectors and levels of the health system. A study team member contacted 23 potential informants directly via email from a list of participants previously engaged for 7-1-7 stakeholder meetings. Ten (10) experts who agreed to participate provided written consent to a 30- to 45-minute recorded interview. No compensation was provided.

Interviews were conducted by a trained researcher either in-person or remotely, per the interviewee's preference. Interview questions were open-ended, and a semi-structured interview guide was used to explore factors affecting outbreak detection, investigation, or response timeliness. Participants were broadly asked to describe the latest outbreak they were involved in investigating or responding to, after which we asked: "What kinds of challenges can investigators encounter when responding to or reporting on outbreaks?" and "Are there any factors that contribute to more successful or more expedient responses to outbreaks?" (Supplement 2).

Interviews were analyzed using a framework analysis developed by two study members who, following familiarization with the transcripts, identified a thematic framework based on the open-coding of the first four transcripts using Dedoose Version 9.0.90 (SocioCultural Research Consultants, Los Angeles, CA, 2023). Over a series of meetings, the study team compared, revised, and re-coded all transcripts, using a cyclical approach to coding. Codes, grouped by category, were then charted into the framework table in Excel for each transcript. Iterative exploration was conducted in the visual collaboration platform, Miro (2023), to explore big-picture relationships and guide further explanations.

As described in Chapter Three, this study was reviewed and received ethical approvals from two institutions in Uganda, namely the Infectious Diseases Institute Research and Ethics Committee (#IDIREC REF 077/2022) and the Uganda National Council for Science and Technology (registration number HS2255ES). Additionally, this study was reviewed and deemed exempt by the University of California, Davis Institutional Review Board (IRB ID 1778303-1).

RESULTS

Quantitative

As described in Chapter Three, the PHEOC was activated 302 times for 282 epidemiologically distinct public health emergencies between 2018 and 2022. Of these events, 129 were outbreaks meeting our inclusion criteria, and complete documentation was available for 82 events (64%). After removing COVID-19 from the dataset, 81 outbreaks remained in our analysis. Though most dates included in our analysis were captured from the PHEOC-provided reports, we included 23 milestone dates found through our literature review, including 10 dates from peer-reviewed publications found on PubMed, 6 from ProMED, 4 from the CDC, and 3 from the WHO.

The most frequent outbreak included in the dataset was cholera, constituting 28% (n=22) of events, followed by anthrax (18%; n=14), Rift Valley fever (15%, n=12), and Crimean-Congo hemorrhagic fever (15%, n=12); (**Table 4.1, Supplemental Table 3.1**). Missing dates for reported outbreak milestones are outlined in Chapter 3.

Our analysis of timeliness metrics found an overall median time of 3 days (IQR 1-5) between outbreak *Start* and date of *Detection,* 2 days (IQR 0-9) between *Detection* and *Notification,* and 5 days (IQR 2-16) between *Detection* and *Diagnostic Confirmation* (**Table 4.1**). The median time from *Detection* to *Outbreak End* was 57 days (IQR 37-95). A complete list of overall timeliness metrics is available in Supplement 3 (**Supplemental Table 4.1**).

Results from the multivariate Cox proportional hazards model found report year to be a statistically significant predictor of timeliness for the *Start* to *End* interval (**Table 4.2**). Timeliness also improved in 2019 for the *Detect* to *Diagnostic* interval (HR 2.58, 95% CI 1.12-5.96) and the *Detect* to *End* interval

(HR 3.30, 95% CI 1.47-7.41). In 2020 and 2022, timeliness decreased between the *Detect* and *Respond* interval (HR 0.18, 95% CI 0.07-0.48 in 2020 and HR 0.29, 95% CI 0.12-0.74 in 2022).

Cox proportional hazard models found that, across most timeliness intervals, having frequent past experience with similar diseases and being a viral hemorrhagic fever (VHF) outbreak were the greatest predictors of improved timeliness (**Table 4.2**). VIF test values for all regression models were ≤ 2.35, suggesting any correlation between past experience and VHFs was moderate and unlikely to result in unreliable regression findings.

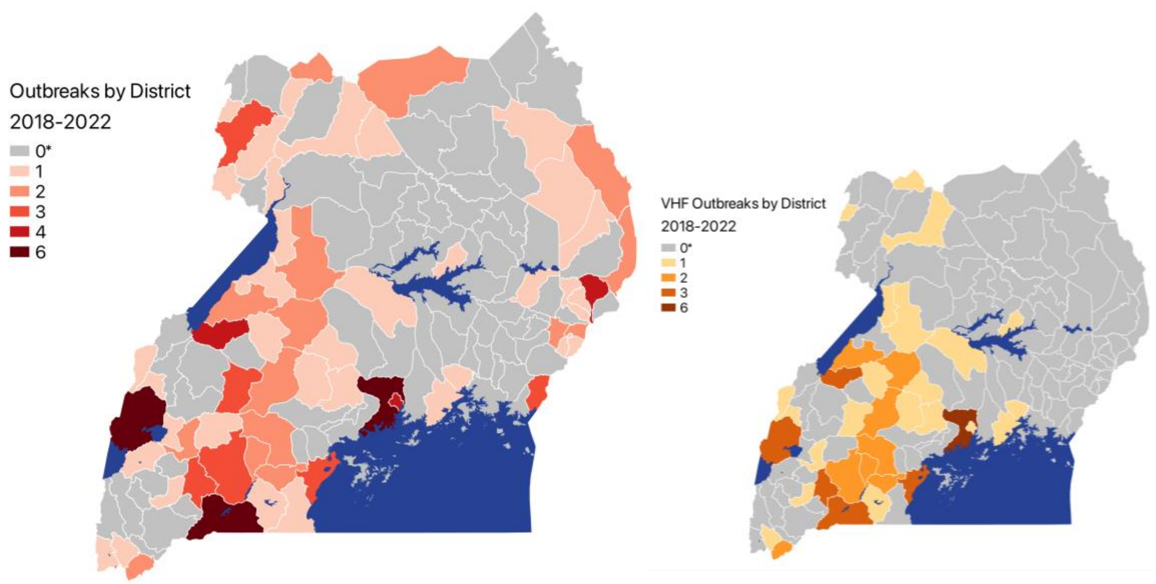
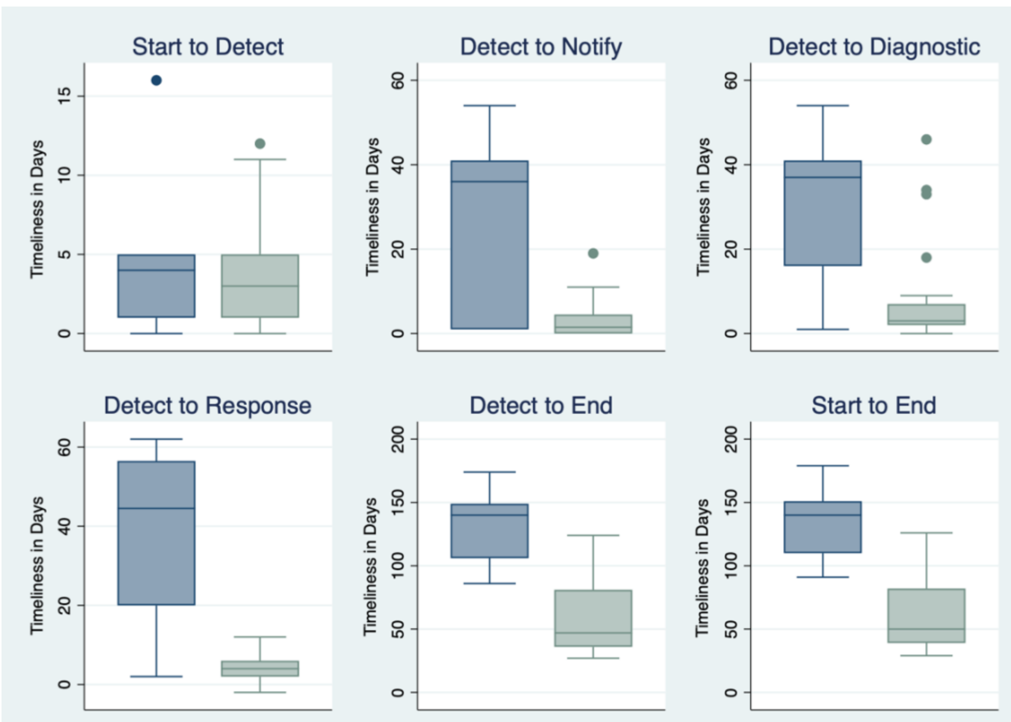


Figure 4.2. Maps of the distribution of all 81 outbreaks included in our timeliness metrics analysis (left) and the distribution of the 31 viral hemorrhagic fever outbreaks (right) across the 135 districts of Uganda. *No outbreaks in these districts were included in our analysis; however, outbreaks could have occurred in these districts between 2018-2022 that did not prompt activation of the PHEOC or were excluded from our database for not meeting inclusion criteria.

For most intervals, timeliness was faster for frequent outbreaks (>10 PHEOC activations in the past decade) compared to infrequent outbreaks (≤ 10 PHEOC activations in the past decade) (**Figure 4.3**). This finding remained true regardless of the outbreak year or if the outbreak was a VHF, with hazard models finding timeliness increased between *Detect* and *Diagnostic*, *Start* to *End*, and *Detect* and *End* intervals.

Compared to outbreaks of non-VHFs, timeliness from *Start* to *Detect* was slower for outbreaks of VHFs, with a timeliness decrease of 56% (HR 0.44, 95% CI 0.21-0.90). Following detection, however, response intervals were significantly faster, with timeliness improving 173% from the *Detection* to *Diagnostic Confirmation* (HR 2.73, 95% CI 1.37-5.46) and 167% from *Detection* to *Outbreak End* (HR 2.67, 95% CI 1.33-5.35).



Key: Infrequent Outbreaks Frequent Outbreaks

Figure 4.3. Box plots of the median time in days between two respective milestones, by outbreaks that have occurred infrequently (≤10 outbreaks prompting PHEOC activation in the past decade) versus frequently (>10 outbreaks prompting PHEOC activation in the past decade). Extreme outliers are not shown. Unknown frequency of five undiagnosed outbreaks excluded.

In an analysis by disease, median days from *Start* to *Detect*, *Detect* to *Diagnostic*, and *Detect* to *End* were longest for Yellow Fever compared to all other diseases, except for the *Notify* to *Diagnostic Confirmation* metric. The median time for the latter metric is 0 days (n=3) but in each instance, the earliest date of notification on record was the Uganda Virus Research Institute notifying various responsible parties of the positive diagnostic confirmation (Vignette).

Table 4.1. Select One Health Timeliness Metrics, defined as time in days between respective milestones, during multisectoral outbreaks in Uganda 2018-2022, stratified by predictor variables

Predictor	**Total no. (%)**	**Start to Detect**		**Detect to Diagnostic**		**Detect to Respond**		**Start to End**		**Detect to End**	
		No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)
Overall	**81 (100)**	54 (67)	3 (1-5)	52 (64)	5 (2-13)	50 (62)	4 (2-9)	50 (62)	61 (43-110)	67 (84)	57 (37-95)
Report Year											
2018	19 (23)	14 (74)	4 (2-4)	13 (68)	5 (2-18)	14 (74)	2 (1-4)	10 (53)	118 (64-130)	15 (79)	90 (53-124)
2019	15 (18)	9 (60)	1 (0-3)	7 (47)	1 (1-2)	8 (53)	4 (3-7)	10 (67)	44 (29-57)	14 (93)	42 (28-71)
2020	20 (25)	12 (60)	4 (2-5)	13 (65)	9 (4-30)	12 (60)	9 (3-45)	11 (55)	82 (42-106)	14 (70)	83 (36-104)
2021	11 (14)	6 (54)	4 (2-5)	7 (63)	2 (2-5)	4 (36)	5 (3-25)	6 (54)	46 (39-56)	9 (82)	43 (37-53)
2022	16 (20)	13 (81)	4 (2-12)	12 (75)	5 (3-8)	12 (75)	7 (4-13)	13 (81)	86 (50-126)	15 (94)	53 (40-116)
Region											
Western	32 (40)	23 (72)	4 (3-5)	22 (69)	5 (2-9)	18 (56)	4 (1-8)	22 (69)	90 (52-130)	27 (84)	84 (46-121)
Northern	20 (25)	14 (70)	2 (0-4)	10 (50)	7 (4-33)	13 (65)	4 (3-9)	11(55)	50 (38-106)	15 (75)	50 (35-96)
Central	16 (20)	12 (75)	3 (3-6)	13 (81)	3 (2-18)	11 (69)	4 (2-14)	12 (75)	51 (41-102)	13 (81)	39 (36-61)
Eastern	13 (16)	5 (38)	1 (1-5)	7 (54)	2 (1-5)	8 (62)	5 (2-8)	5 (38)	30 (26-81)	12 (92)	68 (29-80)
Multi-Country											

Predictor	**Total no. (%)**	**Start to Detect**		**Detect to Diagnostic**		**Detect to Respond**		**Start to End**		**Detect to End**	
		No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)
Yes	11 (14)	7 (63)	4 (1-5)	8 (73)	11 (3-39)	9 (82)	8 (2-43)	6 (55)	118 (91-140)	9 (82)	89 (57-124)
No	70 (86)	47 (67)	3 (1-5)	44 (63)	4 (2-8)	41 (59)	4 (2-7)	44 (63)	56 (41-97)	58 (83)	53 (37-91)
Prioritized zoonotic disease											
Yes	47 (58)	36 (77)	4 (2-6)	36 (77)	4 (2-13)	28 (60)	5 (2-11)	34 (72)	57 (43-110)	40 (85)	55 (40-111)
No	34 (42)	18 (53)	2 (1-4)	16 (47)	5 (2-13)	22 (65)	4 (2-8)	16 (47)	77 (28-109)	27 (79)	61 (31-91)
Disease* (incubation)											
Cholera (2hr-5d)	22 (28)	12 (55)	3 (1-4)	14 (64)	4 (1-7)	17 (77)	4 (2-6)	11 (50)	94 (57-112)	20 (91)	77 (41-96)
Anthrax (1-7d[†])	14 (17)	9 (64)	4 (2-5)	9 (64)	8 (5-30)	7 (50)	3 (0-12)	8 (57)	88 (50-143)	12 (86)	85 (59-153)
RVF (2-6d)	12 (15)	11 (92)	5 (3-10)	11 (92)	4 (2-7)	5 (42)	6 (4-9)	10 (83)	54 (43-82)	11 (92)	47 (36-81)
CCHF (1-13d)	12 (15)	8 (67)	3 (3-4)	10 (83)	2 (1-3)	9 (75)	4 (2-7)	8 (67)	39 (38-44)	9 (75)	37 (35-41)
Foodborne[‡]	5 (6)	5 (100)	1 (0-1)	0	--	2 (40)	3 (3-3)	4 (80)	23 (19-35)	4 (80)	23 (19-34)
Undiagnosed	5 (6)	1 (20)	93	0	--	1 (20)	14	1 (20)	126	2 (40)	38 (33-43)
	5 (6)	4 (80)	5 (3-11)	3 (60)	41 (16-54)	3 (60)	51 (41-62)	4 (80)		4 (80)	

Predictor	Total no. (%)	Start to Detect		Detect to Diagnostic		Detect to Respond		Start to End		Detect to End	
		No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)
Yellow Fever (3-6d)									144 (124-165)		135 (114-162)
VHF											
Yes	31 (38)	25 (81)	4 (3-6)	26 (84)	3 (1-5)	19 (61)	6 (2-10)	24 (77)	54 (41-102)	26 (84)	45 (36-84)
No	50 (62)	29 (58)	3 (1-4)	26 (52)	7 (2-24)	31 (62)	3 (2-8)	26 (52)	86 (44-112)	41 (82)	70 (43-95)
Past experience[§]											
Frequent	65 (80)	45 (69)	3 (1-5)	44 (68)	4 (2-7)	40 (62)	4 (2-7)	41 (63)	52 (39-94)	56 (86)	53 (37-87)
Infrequent	11 (14)	8 (73)	5 (2-11)	8 (73)	31 (9-46)	9 (82)	38 (2-43)	8 (73)	139 (101-155)	9 (82)	116 (90-140)
Unknown	5 (6)	1 (20)	93	0	--	1 (20)	14	1 (20)	126	2 (40)	38 (33-43)
Pathogen Type											
Bacteria	39 (49)	23 (59)	3 (1-4)	24 (62)	6 (2-17)	26 (67)	3 (1-6)	21 (54)	90 (50-112)	35 (90)	76 (46-104)
Virus	33 (40)	26 (79)	4 (3-6)	28 (85)	3 (2-8)	21 (64)	6 (4-11)	25 (76)	55 (42-94)	27 (82)	47 (36-86)
Toxin	4 (5)	4 (100)	1 (1-3)	0	--	2 (50)	3 (3-3)	3 (75)	21 (17-44)	3 (75)	21 (16-43)
Unknown	5 (6)	1 (20)	93	0	--	1 (20)	14	1 (20)	126	2 (40)	38 (33-43)

Predictor	Total no. (%)	Start to Detect		Detect to Diagnostic		Detect to Respond		Start to End		Detect to End	
		No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)
Transmission Route											
Direct or mixed	35 (43)	25 (46)	3 (1-6)	28 (80)	5 (2-13)	19 (54)	4 (2-9)	23 (66)	55 (43-86)	29 (83)	53 (40-90)
Water/food-borne	28 (35)	18 (64)	2 (1-4)	14 (50)	4 (1-7)	19 (68)	3 (2-6)	16 (57)	77 (28-109)	25 (89)	67 (31-95)
Vector-borne	13 (16)	10 (77)	4 (3-5)	10 (77)	5 (1-37)	11 (85)	7 (4-41)	10 (77)	93 (39-137)	11 (85)	84 (37-121)
Unknown	5 (6)	1 (20)	93	0	--	1 (20)	14	1 (20)	126	2 (40)	38 (33-43)
Surveillance Type											
Indicator-based	50 (62)	37 (74)	3 (2-5)	33 (66)	3 (2-7)	32 (64)	5 (2-9)	34 (68)	57 (39-106)	44 (88)	53 (35-93)
Event-based	8 (10)	4 (50)	3 (1-49)	5 (63)	8 (5-16)	4 (50)	8 (2-14)	4 (50)	88 (49-111)	6 (75)	85 (33-147)
Wastewater	1 [22]	0	--	1 (100)	50	1 (100)	43	0	--	0	--
Unknown	22 (27)	13 (59)	2 (0-5)	13 (59)	5 (2-7)	13 (59)	3 (1-6)	12 (55)	74 (47-135)	17 (77)	70 (43-90)
One Health Sectors											

Predictor	Total no. (%)	Start to Detect		Detect to Diagnostic		Detect to Respond		Start to End		Detect to End	
		No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)	No. (%)	Median # Days (IQR)
Hum-Anim-Enviro	48 (59)	37 (77)	4 (2-6)	35 (73)	4 (2-9)	29 (60)	5 (2-11)	35 (73)	58 (43-124)	40 (83)	53 (39-100)
Hum-Enviro	26 (32)	13 (50)	2 (1-3)	16 (62)	5 (2-13)	19 (73)	4 (2-8)	12 (46)	92 (44-109)	23 (88)	70 (39-95)
Hum-Enviro-Plant	5 (6)	4 (80)	1 (1-3)	0	--	2 (40)	3 (3-3)	3 (60)	21 (17-44)	3 (60)	21 (16-43)
Animal-Environment	2 (2)	0	--	1 (50)	16	0	--	0	--	1 (50)	147

Median and IQR calculations were rounded to the whole number given the analysis unit of days.
*Most frequent diseases reported here, whereas outbreaks occurring twice or less not analyzed here (including outbreaks of EVD, meningitis, plague, West Nile virus, and circulating vaccine-derived poliovirus type 2)
†Cutaneous and gastrointestinal anthrax
‡Foodborne illnesses range from 1hr – 30 days depending on the bacterial, chemical, parasitic, or viral etiology
§Country-level past experience categorized as frequent: >10 in the past decade; or infrequent ≤10 in the past decade.

Table 4.2. Multivariable Cox proportional hazards regression analysis Hazard Ratios (HR) with report year, past experience, and VHF as predictor variables for select timeliness metrics intervals

	Start to Detect (n=55)		Detect to Diagnostic (n=52)		Detect to Respond (n=52)		Start to End (n=50)		Detect to End (n=67)	
Predictors	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**
Report Year										
2018	14 (25)	Ref.	13 (25)	Ref.	14 (27)	Ref.	10 (20)	Ref.	15 (22)	Ref.
2019	10 (18)	1.87 (0.74-4.70)	7 (13)	2.58 (1.12-5.96)*	10 (19)	0.56 (0.25-1.27)	10 (20)	10.51 (3.11-35.61)*	14 (21)	3.30 (1.47-7.41)*
2020	12 (22)	1.33 (0.56-3.12)	13 (25)	0.58 (0.26-1.31)	12 (23)	0.18 (0.07-0.48)*	11 (22)	7.03 (2.17-22.83)*	14 (21)	1.67 (0.76- 3.68)
2021	6 (11)	1.41 (0.50-3.94)	7 (13)	1.26 (0.47-3.39)	5 (10)	0.39 (0.13-1.18)	6 (12)	10.83 (2.71-43.29)*	9 (13)	2.69 (0.99-7.34)
2022	13 (24)	1.27 (0.45-3.59)	12 (23)	0.55 (0.21-1.42)	11 (21)	0.29 (0.12-0.74)*	13 (26)	5.64 (1.62-19.64)*	15 (22)	1.30 (0.58- 2.92)

	Start to Detect (n=55)		Detect to Diagnostic (n=52)		Detect to Respond (n=52)		Start to End (n=50)		Detect to End (n=67)	
Predictors	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**	**N (%)**	**Hazard Ratio per year (95% CI)**
Experience										
Unknown	1 (2)	0.0	0	--	1 (2)	1.00 (0.11-9.3)	1 (2)	2.17 (0.21-22.60)	2 (3)	19.20 (2.6-141.60)
Infrequent	8 (15)	Ref.	8 (15)	Ref.	9 (17)	Ref.	8 (16)	Ref.	9 (13)	Ref.
Frequent	46 (84)	1.45 (0.59-3.59)	44 (85)	2.96 (1.33-6.59)*	42 (81)	2.13 (0.86-5.27)	41 (82)	11.27 (3.39-37.44)*	56 (84)	5.57 (2.17-14.27)*
VHF										
No	29 (53)	Ref.	33 (55)	Ref.	32 (62)	Ref.	26 (52)	Ref.	41 (61)	Ref.
Yes	26 (47)	0.44 (0.22-0.91)*	27 (45)	2.73 (1.37-5.46)*	20 (38)	1.33 (0.70-2.53)	24 (48)	1.34 (0.62-2.89)	26 (39)	2.67 (1.33-5.35)*

CI: Confidence Interval
*Statistically significant findings ($\alpha = 0.05$).

Qualitative

As previously described in Chapter Three, 10 of 23 invited experts agreed to participate in a recorded interview with a study member. Participants, only one of whom was female, represented seven institutions at the regional, national, and international levels of the health system in Uganda. Four of the informants had backgrounds in epidemiology (all levels), two in veterinary science, two in laboratory science (all levels), and two in health information analytics (national and international).

Below, we describe the sub-themes for three broad themes emerging from our framework analysis of factors influencing timeliness: 1) factors related to the outbreak event itself; 2) contextual influences on the outbreak; and 3) considerations related to personnel experiences (**Table 4.3**).

Table 4.3. Analysis of factors related to timeliness of outbreak detection and response in Uganda, organized by theme and sub-theme.

Theme	Sub-Theme	Description	Illustrative Quotes
Outbreak factors	Past experience (novel vs. repeat)	Participants describe learning from experience with past outbreaks of the same disease as an enabling factor because Uganda has established health systems specifically prepared for outbreaks of given diseases. Informants also gave examples of how first-of-kind outbreaks are particularly challenging to manage, in terms of novel pathogens at both the district and	*"My experience was that we, this outbreak was the very first of its kind in this area… where it happened. So, it was a bit of a challenge for the people, because it had never happened in this area, so we had to ensure that many things are done, for them to go ahead, to manage."* *"I think a good example would be the West African Ebola outbreak, and having not had Ebola and these viruses*

Theme	Sub-Theme	Description	Illustrative Quotes
		national level. There is awareness that the current systems are best suited to respond to geographically limited outbreaks, whereas COVID-19 caught systems off guard in part because it was country-wide but also because it was an unknown disease with potential major unequal repercussions.	*caught them completely off guard with the systems that were in place, they were delayed to detect, delayed to report on time. And as compared to… how Uganda has had several outbreaks of Ebola in the past from that experience and the systems that were put in place have ensured that we've not had Ebola significantly spread and become a Public Health Emergency of International Concern. So I think it's always going to be a 'what do we do in the this -- in the now, rather than what do we do in the time of an outbreak'."*
	Perceived threat (VHF)	Informants described that outbreak response is heightened for certain viruses, namely Ebola and Marburg, due to perceived risk of these diseases. However, not all viral hemorrhagic fevers are considered of equal consequence. Risk communication materials have been developed in advance for	*"[W]hen it comes particular other diseases… like the Marburg and Ebolas, those ones you find that the response is different I think because of the threat with which people look at it. You find that again everyone should be scared about it, you find that the attention that that one deserves- gets is far, far, far higher, yes, so you find that the stakeholders are quickly mobilized to*

Theme	Sub-Theme	Description	Illustrative Quotes
		several prioritized diseases, including Ebola, facilitating faster response following detection.	*make sure that they give support to really respond to that. So that one, the attention deserved has always been higher for Ebola, you can compare the two how it happens when you have like anthrax or RVF. And RVF of course because the human to human is very limited or not there yet, you find that the attention it deserves is not so much as the others like the Ebolas and some of the others."*
	Diagnostic & lab considerations	Laboratory capacity continues to be built across the country as this has been identified as a priority to curb delays given lessons learned from past outbreaks. While the Hub System acts as an enabler to timely diagnostic confirmation, informants cautioned that laboratory methods required to confirm an outbreak can vary based on the pathogen, both in time and supplies required. It is therefore	*"[W]hen there is a problem we usually intervene as if it is actually an outbreak, even before being declared. Why? Instituting preventive measures is much better than waiting to have it confirmed as the transmission continues to occur in the community…Though of course there is a delay. You realize we don't have laboratories for some of these tests that need to be done? So, the samples have to be shipped, for example from the East to the Central. And sometimes if the reagents are missing from the*

Theme	Sub-Theme	Description	Illustrative Quotes
		understood as difficult to use a universal target for confirmation. Furthermore, not all laboratories country-wide have the same diagnostic capacity, with most well-supplied laboratories situated in Central Uganda. Veterinary laboratories were described as often having reduced capacity (e.g.., fewer supplies and equipment) compared to laboratories under the auspices of the Ministry of Health. Lastly, laboratories cannot run samples if the accompanying reporting forms are incomplete, which has historically led to delays.	*Central lab, then they have to ship to another lab!"* *"There will be outbreaks for which Uganda doesn't have any diagnostic capacity. Like monkeypox! We don't have the diagnostic capacity. It has been around for the last one month. In terms of saying, 'Hey, can you start doing something… we may be having something here'. The last one month or two we are trying to put things together. Maybe by the end of this week we may have something in this country, to test for monkeypox."* *"[O]ne of the limitations we have often faced, has been with the diagnostic confirmation as sometimes depending on the type of test to be undertaken. If it's anthrax you may see that it requires PCR. Or if it's yellow fever it has specific primers that are required. And also, the whole process. So maybe we*

Theme	Sub-Theme	Description	Illustrative Quotes
			may either have to measure … diagnostic confirmation as per the expected time of that particular outbreak."
Contextual Influences	Existing infrastructure and health system structures	Public health infrastructure is described as facilitating timely detection, notification, and response. Specific systems cited include: the national sample transport system (Hub System) for diagnostic confirmation; the short message service (SMS) 6767 platform which facilitates notification and prompts rapid verification, coordination, and distribution of resources; Integrated Disease Surveillance and Response (IDSR) guidelines; national and regional EOCs and other personnel structures of the	*"We rely on the local structure… A case and point: the current anthrax outbreak in Bududa … it was [identified by] the Animal Husbandry Officer while she was doing her routine work. So, she reported to the DVO and since some human cases had been observed, they connected with the DSFP, the District Surveillance Focal Person, who reported the case to the DHO, that is the District Health Officer... Who later notified the hospital director who also got in touch with the EOC. So having the local structure is really, really helpful."*

Theme	Sub-Theme	Description	Illustrative Quotes
		health system. While infrastructure is described overall as facilitating timeliness, several informants described imperfect or inconsistent use of these systems, due in part to insufficient training, as well as gaps in their rollout caused by policy and funding limitations.	*"[S]tructures have been put in place, like sample transport system. Wherever an event occurs, there is almost free transport…that can bring the sample up to the testing laboratories…So there is that system throughout the country… samples can get to Kampala free of charge. It's one of the main factors that makes this... [easier] to work with than before."*
	One Health collaborations	One Health collaborations were universally described as important to a coordinated outbreak investigation and response, as well as efforts to increase tracking of predictive alerts of potential outbreaks. While informants described several significant milestones in One Health implementation in Uganda, the approach is still not yet fully integrated into health systems. Inequities across the	*"[A]nother thing that facilitated… Mbale EOC and then the regional vet lab, they have gone through One Health training. So they appreciate the value of a multisectoral coordination in such an outbreak setting, so it was easy for them to really quickly.. help out and coordinate things together. But the district where it had happened, they had not received that training…[W]e've actually prioritized that at some time this year, those very districts and the*

Theme	Sub-Theme	Description	Illustrative Quotes
		One Health sectors, including discrepancies in access to resources and funding, inhibit a fully integrated, collaborative approach. Several informants acknowledged that coordination across sectors requires constant and intentional effort.	*neighboring ones, they should ensure they're trained in One Health as well."* *"It took us very long to transform our district epidemic committees, or response committees, into a One Health committee. Because the animal sector, the agricultural sector, the water and environment sector, the wildlife sector, were … not yet having buy-in. Until we…engaged them further – first of all individually– and said, you are part and parcel of this to have a multisectoral approach to some of the challenges we face as a population, as a community. And so yes, we can only achieve that through rigorous and constant engagement of these different actors or players."*
	Community engagement	Informants agreed that prevention and response efforts, including educational approaches, must incorporate	*"For any outbreak or disease outbreak or any other public health emergency if the responders for example do not engage the community through their*

Theme	Sub-Theme	Description	Illustrative Quotes
		social and cultural understandings of community practices to be effective. There was recognition that community engagement needs to include and prioritize responder engagement with community leaders, including religious and cultural leaders.	*leadership or through their existing structures… some of these interventions are very sensitive. Their acceptance, their willingness to participate or get involved is actually the major factor that we rally on, or that we ride on. Once the community is engaged through their leadership structures, through the stakeholder structures it is always a little easier…you can actually combat challenges effecting or facing the communities just because the ground has been kind of leveled for you to move into the community."*
	International engagement and political involvement	International partner involvement was described as closely tied to resources needed to investigate and respond to outbreaks; however, while funding facilitates investigation and follow-up, international partner involvement may also contribute to uncoordinated or siloed investigations because of disease-	*"Most of these outbreaks that we are investigating in Uganda, are mostly driven by partner support, which is very fine… [I] guess what we need to do, is to make sure that partners supporting us also move uniformly. Because if partner A has funds to investigate anthrax in District B and because they have these funds they just send in directly without the Ministry of Health or Ministry of*

Theme	Sub-Theme	Description	Illustrative Quotes
		specific interests of different partner groups. Additionally, the interests and decisions of international multilateral agencies were cited as influential in the priorities (namely funding decisions) made at the country-level, including when it comes to One Health collaborations.	*Agriculture knowing, and then another team, then another team, that creates confusion. So, I think what we can do is to create what we call a bucket fund, where all investigation funds can be deposited. And that can also allow teams to be deployed in a One Health coordinated manner."* *"The top, the giants up there, the need to embrace [One Health]… if WHO can give money to the Ministry of Agriculture to do work in animals, I think no one will say no. Even [the] Ministry of Agriculture can give money to the Ministry of Health to investigate Rift Valley cases [laughter]. Then it will happen!"*
Personnel experiences and needs	Motivation	Informants reported that stakeholders are motivated by different goals. For example, certain individuals who would be required to notify authorities about a suspect outbreak may be	*"[W]e have even the other leaders – say the CAO, the chief administrative officer… As the district [head] they may not want to report maybe a disease because of some reasons, a loss of revenue or yeah."*

Theme	Sub-Theme	Description	Illustrative Quotes
		unmotivated to report due to the socioeconomic consequences of the response. Several informants linked motivation among outbreak investigators with the need for increased training on the value of reporting on outbreaks. One informant suggested that by tracking timeliness metrics, frontline workers will grow increasingly motivated if they witness progress in their own performance.	*"I'm sorry to tell you but we have some of our colleagues, for them they don't see the value of reporting. 'Why should I report, eh?' I mean, they have to be self-motivated to report. It doesn't see the immediate outcomes or immediate tangible results of reporting… so you have those kinds of attitude you know kinds of challenges, personal problems."* *"People or the responders really need to see the reason why, you know, certain action needs to be taken when events are detected."* *"When an outbreak occurs, of course it might be from the farmers' side of it, they may fear to report, thinking that you may now impose a quarantine or you're now going to stop them from trading some of those products. So there is that delay in the information."*

Theme	Sub-Theme	Description	Illustrative Quotes
	Perceptions of power or powerlessness	This sub-theme largely describes perceived dynamics between 1) the One Health sectors; and 2) national and international agencies and priorities. Several stakeholders expressed concern over perceived preferential treatment of the human health sector over animal, environmental, and plant health sectors, calling for a leveled playing field. Informants also described power dynamics relating to decision-making authority and influence related to outbreaks, while also acknowledging the consequences of dependency upon external, international stakeholders for funds to execute outbreak investigation and response activities.	*"In fact, the Office of the President should be the place where we should be going [for National Task Force meetings] that can bring us all together so that there is no feeling of superiority of a particular sector over the other."* *"The World Health Organization would never intervene in any outbreak until there is a human case. You know that? Until there is, a human, confirmed case. That's when WHO will say 'yes, now we're on the table, talk to us.' OIE, or FAO, Food and Agricultural Organization, OIE, will only get involved if there is an animal case confirmed or acutely infected animal case. Now, without those giants, nothing happens. Without those giants say, blessing the activity, then, our people will not get involved."*
		Participants described the need for funds to be released quickly	*"You find that most of the outbreaks do occur or start from the community level,*

Theme	Sub-Theme	Description	Illustrative Quotes
	Resources and funding availability	in order to rapidly mobilize for field investigation. Disrupted supply chains were cited as problematic, with informants recognizing delays in detection and response due to lack of personal protective equipment and supplies to collect biospecimens, challenges securing transport for field investigation and verification, laboratory supplies and equipment, and funding for One Health activities.	*meaning the lower units that have the push system may not have adequately some of the things that they would need to quickly pick and go and respond to these emergencies. And so…the challenge of logistics is real and it does affect our response mechanisms across the board. It's not only the logistics of supplies to use but also logistics in terms of transport, in terms of time allowance, you're waiting to go out there…all of that."* *"[You] go to the Ministry of Agriculture and say 'hey, we have Rift Valley in some district – can you rush there?' They don't have that money. And then it has to come from funders… availed outside the mainstream government funds. So you rush to MAAIF and say we're having an outbreak…it's CCHF, a One Health disease. Can you go there? There is a case, a human case. They say, 'No, we don't have money*

Theme	Sub-Theme	Description	Illustrative Quotes
			now, maybe you go, we shall find you there in the field'. You can't go in one vehicle, because of those funding issues. Eventually it happens, but the human centric people, the medical people will go because they have money to do something. But while they are there they are not dealing with the environmental sector or the animal sector. Those will come later on, when they get their money."

*CCHF, Crimean-Congo Hemorrhagic Fever; DVO, District Veterinary Officer; EOC, Emergency Operations Center; FAO, Food and Agriculture Organization; MAAIF, Ministry of Agriculture, Animal Industries and Fisheries; OIE, World Animal Health Organization; PCR, polymerase chain reaction; RVF, Rift Valley fever; WHO, World Health Organization

DISCUSSION

Analyses of timeliness during multisectoral outbreaks in Uganda occurring between 2018-2022 suggest that overall national performance in detection and response time is relatively strong. Uganda performed faster than the 7-1-7 targets for two intervals: from outbreak emergence (i.e., start) to detection and from detection to response. Though the observed median time from detection to notification (2 days) was slightly slower than the target of one day, a recent analysis of the 7-1-7 implementation in five countries, including Uganda, found the median time to notification of public health authorities was also two days for events outside the human sector versus zero days for outbreaks involving the human sector. Additionally, in a comparison of timeliness metrics calculated from our study with those from an analysis by Impouma et al. (2020)[11] of timeliness during outbreaks between 2017-2019 in 41 out of 47 WHO AFRO member states, Uganda had shorter median times to events for all intervals (start to detection, detection to notification, and start to end dates) except for *Start* to *End* in 2018 (**Supplemental Table 4.2**).

Our findings that timeliness has remained relatively steady over the five-year study period, neither significantly improving nor worsening, may be a result of the challenges arising from the COVID-19 pandemic. The increase in timeliness observed in 2019 compared to 2018 may suggest that improvements were made then derailed in 2020 when human and financial resources were (re)directed to the pandemic response.

Despite Uganda's fast response to the pandemic, our findings highlight not surprisingly that systems perform faster for diseases that they have had comparatively more experience for similar outbreaks in the past. Given Uganda has seen repeat outbreaks of the same disease, sometimes even on an annual basis, this finding points to a positive or improved timeliness trend for familiar outbreak types in Uganda; however, timeliness may be problematic in the face of novel disease outbreaks, including *Disease X*. As described by one informant, even knowing that mpox was a public health emergency in 2022, it took a month for Uganda to establish diagnostic capacity to conduct surveillance for it. Delays in diagnostic confirmation are particularly concerning if any subsequent key steps, including notification, public communication, or other response measures, are contingent upon laboratory or diagnostic confirmation.

A convergence of qualitative and quantitative findings illustrates that, at present, there is a somewhat non-agnostic approach to outbreaks in Uganda. The perceived threat of certain types of outbreaks, namely VHFs, results in heightened preparation for outbreaks of these diseases, such as the development of risk communication materials for Marburg and Ebola virus disease (EVD), as well as a faster overall response. This finding is supported by our previous analysis in Chapter Three of frequency of One Health milestone reporting, which found that more timeliness data was reported for VHFs compared to outbreaks of non-VHFs. Preparedness for and rapid response to diseases of a high threat ultimately contributed to the successful control of the 2022 outbreak of Sudan EVD, which was brought under control before it grew into an event of significant enough spread to warrant declaration of a Public Health Emergency of International Concern. While timeliness during outbreaks of VHFs may save lives and even prevent a pandemic, the comparative lags in response to non-VHFs, or diseases perceived as less of a threat than Ebola and Marburg virus diseases, or with ones that staff have less experience with, could be problematic by resulting in longer delays between key milestones if there is an outbreak of a novel, unknown disease.

The sub-themes emerging from our key informant interviews align closely with the most commonly described bottlenecks and enablers identified in the 2023 study of the 7-1-7 implementation in five countries.[13] This includes bottlenecks and enablers related to the availability of resources or resource mobilization, transport of specimens, inoperable reporting channels, low community knowledge or trust in public health system, and challenges related to laboratory and diagnostic capacity. Interestingly, One Health information sharing or collaboration (or presumably the lack thereof) was described exclusively as a bottleneck to detection, notification, and response for 4% of events in the 7-1-7 implementation analysis.[13]

Informants in our study characterized One Health collaborations as an enabler to detection and notification; however, delays were cited due to the disproportionate allocation of resources to the human health sector. If funding is released more slowly to all non-human sectors, these bureaucratic bottlenecks inhibit responder's ability to mount a truly coordinated and collaborative One Health response to outbreaks. In some instances, illness or die-off events first observed within animal populations may even serve as a predictive alert of an outbreak of human illness. For example, in 2012, staff trained in wildlife disease surveillance through the USAID PREDICT project discovered six howler monkeys dead near a wildlife sanctuary in Bolivia.[24] Post-mortem diagnostic tests confirmed infection by flavivirus, later confirmed as yellow fever virus. The MoH was immediately notified of the findings, enabling prompt implementation of public health prevention measures such as human vaccination campaigns, education and outreach, and mosquito control measures. Consequently, no human cases of yellow fever occurred during this outbreak.[25]

Furthermore, inequities in resource allocation to different health sectors contributes to perceptions of power imbalances across disciplines, as described by informants. These power imbalances are detrimental to efforts to build trust across sectors, which can be devastating to efforts to work across the necessary stakeholders required to prevent and control outbreaks.

Discrepancies between when funds and supplies are released to human versus animal health sectors illustrates a qualitative finding that could not be explored in depth through our quantitative analyses. This limitation is due in large part to our sampling strategy for our database, which was linked to the Public Health Emergency Operations Center, under the Ministry of Health. Consequently, our data is biased toward human diseases as opposed to those diseases affecting exclusively the animal, environmental, and plant sectors.

The limitations of our database underscore broader shortcomings of timeliness metrics as a tool: quantitative snapshots of timeliness risk missing key findings such as the perceived importance of a collaborative One Health approach in increasing speed during outbreaks. Comprehensive insight into the complex processes during outbreaks requires complementary qualitative work, a step which could logically take place during an *After-Action Review* meeting, when multidisciplinary stakeholders can convene and discuss strengths and challenges encountered. Establishing a systems approach in analyzing bottlenecks and other problems instead of blaming of any one individual or sector, is key in establishing the level of trust necessary to constructively review negative, as well as positive factors.

This analyses also needs to consider that in some instances, timeliness metrics may simply reflect epidemiological characteristics of the disease-causing pathogen, rather than the performance of responders. For example, foodborne illnesses may naturally have a shorter duration from start to end than VHFs or diseases with longer incubation periods. Additionally, timeliness metrics may be subject to measurement bias due to interpretation of outbreak milestone dates.

While useful for identifying trends in timeliness, the One Health timeliness metrics alone are not a panacea and must be utilized alongside other pandemic preparedness and prevention tools to inform epidemic and pandemic policy action. Furthermore, timeliness metrics are premised on an assumption that increased speed between intervals results in improved outbreak outcomes, such as reduced morbidity and mortality in human and animal populations. In our comparison of timeliness metrics calculated for this study in Uganda versus timeliness calculated across WHO AFRO by Impouma et al. (2020),[11] we saw that despite having faster overall *Start* to *Detect* and *Detect* to *Notify* times in 2018, Uganda had a longer overall *Start* to *End* interval. Additional analyses should explore this assumption that increased speed between all intervals means improved outbreak outcomes, as well as other possible explanations for the observed phenomena, such as differences in definitions of outbreak end. Analyses might also explore if certain timeliness metrics, including those with predictive alerts and preventive action, are more or less influential on improved outcomes.

CONCLUSION

As teams of experts worldwide continue to develop innovative strategies to confront our pandemic era, stakeholders must remain cognizant of the need for disease-agnostic outbreak preparedness activities, such that health systems are resilient when faced with an outbreak of a novel disease. Given our finding that timeliness is enhanced when an outbreak is of a disease event frequently encountered or after detection of viral hemorrhagic fever, investments must be made for preparedness and readiness to detect and respond to less frequently seen One Health outbreaks.

Targeted actions are needed for specific barriers related to One Health challenges, including the slow release of funding for cross-sectoral investigations. In countries where it has been a problem to assess both progress and whether timeliness continues to lag because of slow release of funding, we recommend tracking when funds are released for outbreak investigation. Toward this objective, we echo a recommendation made by an informant in this study, that the Quadripartite organizations pool response funds for any agencies that needs to respond to an outbreak, regardless of health sector.

Efforts to achieve truly integrated One Health collaborations for outbreak detection and response may ultimately improve timeliness during outbreaks involving multiple health sectors. Continued tracking and comparisons of timeliness during outbreaks involving versus not involving the human sector are warranted, as are studies of timeliness during outbreaks with predictive alerts, which would inherently necessitate collaborations across One Health sectors to detect and to respond with preventive measures. For all timeliness metrics analyses, a systems approach to evaluate and then monitor successes and challenges for quality improvement will prevent the onus from being placed on any one sector or group of responders.

Ongoing activities to build trust, ensure equitable access to funding, and establish integrated channels for communication and data sharing will better position countries to mount a unified front against epidemics. In addition to building trust between frontline workers from different health sectors, stakeholders have described that fostering trust with communities is paramount to successful control of outbreaks. If partnerships and trust are established between these key stakeholders, becoming routine and expected for all outbreaks, it will be less of a shock to the health system when collaborative relationships are needed to address larger-impact emergencies and the emergence of *Disease X*.

Vignette: Lessons from Yellow Fever in Uganda

In this study, the observed timeliness from outbreak detection to end was longer for outbreaks of yellow fever (YF) than any other disease, with a median time of 135 days (n=4, IQR 114-162) versus 53 days for other diseases (n=63, IQR 36-90). Despite it being a VHF, timeliness decreased 69% between outbreaks of other diseases and outbreaks of YF, regardless of outbreak year (HR 0.31, 95% CI 0.11-0.87).

Our analysis included five outbreaks of YF occurring between 2018 and 2022. Timeliness from outbreak start to detection was similar to that of other diseases; however, timeliness from outbreak detection to diagnostic confirmation was 41 days (n=3, IQR 16-54) compared to a median time of 4 days for all other diseases (n=49, IQR 2-8). Diagnostic confirmation of YF is a particularly long process, and not all laboratories will have the many supplies required. There are also very few validated commercial assays for the virus on the market, a challenge compounded by specific timing requirements for sample collection following disease onset, complex diagnostic testing algorithms for unvaccinated versus vaccinated people, and a host of other laboratory challenges.[27]

Beyond diagnostic considerations, YF may be particularly challenging for responders due to the relative novelty of the virus in the outbreak landscape in Uganda. In November of 2010, Uganda experienced the first detected outbreak of yellow fever since the 1970s, when surveillance activities slowed until the Integrated Disease Surveillance and Response system was introduced in 2000.[28] YF outbreaks have occurred sporadically in Uganda since 2010, until more recently in 2019, when outbreaks began to occur on an annual basis, with one to two outbreaks each year.

The 2010 outbreak was the largest of YF the country had experienced to-date. However, due to the unfamiliarity with the virus, given several decades had passed since the last outbreak of YF, responders were not experienced in detecting and bringing the outbreak under control. Given the challenging case definition, the 2010 outbreak was initially believed to be an outbreak of plague. With no treatment (antivirals) for yellow fever, vaccination and other prevention measures such as vector control are essential to bringing outbreaks under control. Unfortunately, the response was hampered because of need for a diagnosis in order to then determine which pool of funds to release for investigation. This bottleneck highlights the importance of our recommendation to quickly release funds for the investigation of a suspect outbreak, whether or not the etiology has been confirmed yet.

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Chapter 5. Conclusion

Overview of Findings

The body of research described in this dissertation assesses the current reporting of key multisectoral outbreak milestones and explores lessons learned from the One Health timeliness metrics both at the global level and, through a case study from Uganda, the country level. By exploring implementation questions and analyzing trends in outbreak detection and response times, these studies provide empirical evidence that One Health timeliness metrics are a tool that should be considered for scale-up toward the goal of understanding health systems' performance during outbreaks.

Our findings from Chapters Two and Three, which both assessed the frequency of the reporting of One Health outbreak milestones during multisectoral reports, reinforced that the same outbreak milestones are being reported with approximately the same frequency in Uganda as at the global level. *Detect*, the date an outbreak was first observed, was the most frequently reported milestone, while the *Start*, *Verify*, *Diagnostic Confirmation*, *Response*, and *Public Communication* milestones were all reported relatively often, being described in more than half of all outbreak reports both globally and within Uganda. The date for *Notification* was reported more frequently in Uganda than in global reports, and dates for the *Predict*, *Prevent*, *End*, and *After-Action Review* milestones were all reported infrequently across outbreak reports analyzed from Uganda and the scoping review of the global literature.

The infrequent reporting of the *Predict*, *Prevent*, and *After-Action Review* milestones observed in these studies may reflect a lack of coordinated activities related to these milestones. Alternatively, these events may be occurring without being reported, as must be the case for *Outbreak End*, given that the majority of the outbreak events included in our studies had concluded prior to our analyses. Most likely, the low reporting frequency of these dates is a product of both factors, though additional work to understand the extent of public health action to predict and prevent outbreaks would help elucidate where efforts should be focused: to ramp up multisectoral efforts to predict outbreaks, or to increase the reporting of said activities.

Through our qualitative work in Uganda, we learned in Chapter Three that timeliness metrics are perceived by many key stakeholders as feasible to track and useful to inform epidemic intelligence, preparedness, and prevention. However, several implementation challenges remain, which must be addressed to allow successful adoption of these metrics. These challenges are largely related to inoperable and nonintegrated reporting channels, a dearth of guidance for early adopters, and insufficient flexibility in recognition of on-the-ground realities during outbreaks.

Our analyses in Chapter Four demonstrated what we can learn at the country level by analyzing timeliness metrics. Namely, through the case study of multisectoral outbreak events in Uganda between 2018 and 2022, we found empirical evidence that outbreak surveillance and response systems in Uganda may perform faster during outbreaks of diseases that occur more frequently and following detection of outbreaks of viral hemorrhagic fevers (VHFs). Findings were supported by both our quantitative and qualitative analyses, with stakeholders explaining the phenomena of faster performance during outbreaks of VHFs as a result of increased attention to diseases that are perceived as more dangerous or consequential. Other factors influencing performance speed include One Health collaborations, which are viewed as necessary to facilitating collaborations but challenging to achieve in practice. Existing infrastructure, community and international engagement, motivation and perceptions of power, access to resources and release of funding were all described as prominent factors that influenced how quickly stakeholders were able to detect or respond to an outbreak.

Given that COVID-19 was so dissimilar from all other outbreaks in our dataset, we opted to exclude the pandemic from final analyses of timeliness metrics in Uganda. The pandemic was the only country-wide disease event in our database and was unique in its response, given that so many of the country's resources were redirected to the pandemic. However, even though COVID-19 was excluded from our calculations of timeliness metrics, we cannot ignore that over half of the outbreaks included in our analysis occurred against the backdrop of the pandemic, which undoubtedly had implications for those events. Though beyond the scope of this dissertation, there are crucial lessons to be explored regarding COVID-19 in Uganda, including how the pandemic affected timeliness for other health events.

Significance of Work

Implications for Timeliness Metrics

As illustrated by our study of the 81 outbreaks in Uganda in Chapter Four, analyses of aggregate timeliness data have allowed us to interpret trends and lessons about a country's outbreak performance that are distinct from what we could glean from the analysis of a single outbreak (i.e., during an After-Action Review meeting). However, our work also points to several other implications related to methodologies used to assess outbreak detection and response speed. Our qualitative findings complement and offer possible explanations for several of our quantitative findings, such as which factors influence timeliness at the country-level. The strength of our mixed-methods approach demonstrates how measurements of timeliness metrics are more meaningful when considered in tandem with qualitative work that engages the expert community that is most familiar with a country's outbreak landscape, as well as those communities impacted by the outbreaks themselves. Beyond the stakeholders engaged in our study, mixed-method analyses of outbreak timeliness would be even more informed if integrating knowledge from local voices from the district and community levels. Towards a more equitable approach to interventions for epidemic preparedness, this important step would seek to include the perspective of historically marginalized communities that, unlike those stakeholders we interviewed for our study, lack the institutional power that affords them a platform for their voices to be heard.[1]

Furthermore, the One Health timeliness metrics, and even timeliness metrics more broadly, are not a universal or standalone solution to pandemic prevention and preparedness. These metrics can highlight bottlenecks and strengths in timeliness; however, this tool must be used alongside other tools designed to evaluate how equipped we are at the country, regional, or global level to respond to health emergencies. Furthermore, recognizing that metrics are only as strong as the data informing them, timeliness metrics are subject to biases, such as measurement bias when interpreting milestone dates. Especially given our observation that several of the outbreak milestones are reported with low frequency, generalizations based on incomplete or inaccurate data could result in unfounded and misinformed policy recommendations.

For this reason, the One Health timeliness metrics may be more appropriate to assess within-country outbreak performance rather than for use as a tool to compare timeliness between countries. Until we are confident that outbreak milestones are being defined universally, we cannot assume that timeliness metrics are being measured consistently from country to country, thereby making it difficult to make valid comparisons. Moreover, different countries and regions of the world experience routine outbreaks of different diseases with distinct epidemiologic considerations. Ultimately, comparisons of metrics between countries may be meaningless and fail to drive positive performance improvements. To avoid this scenario, we believe that timeliness metrics should always be considered within the context of the country in which the outbreaks occur.

Implications for One Health

It is our hope that by facilitating the adoption of a standardized, collaborative tool for pandemic preparedness, this body of work will positively impact the field of global health by increasing the visibility and actionability of One Health. To successfully track *Predict* and *Prevent* milestones, countries must first establish collaborations across key sectors to enact the public health surveillance methods necessary to detect signals of potential outbreaks. These partnerships must involve the environmental sector, which, at present, seems to be under-represented in ongoing global health security activities in

Uganda. However, a 2021 scoping review of outbreak prediction for the WHO R&D diseases found that outbreak prediction occurred most frequently for diseases transmitted by vectors or other climatic components; conversely, prediction methods for diseases with complex sociocultural considerations (e.g., Ebola and Marburg) were multifactorial.[2] Therefore, partnerships for disease prediction must crucially include teams conducting spaciotemporal modelling and risk mapping (e.g., of mosquito activity, meteorological forecasting, etc.). Of note, none of the publications included in the aforementioned scoping review sought to predict outbreaks of a novel, unknown *Disease X*.

Despite the necessity of a One Health approach to predict possible future outbreaks, the three studies that comprise this dissertation all provide evidence that barriers currently impede the operationalization and implementation of fully integrated One Health approaches for outbreak investigations and response. Despite a genuine willingness among expert stakeholders to collaborate across sectors, as described by one participant in our study, it remains both an implementation challenge and opportunity to integrate a multisectoral approach to detect and respond to outbreaks. Our findings suggest that there are missed opportunities to learn lessons about collaborating for multisectoral outbreaks, which could be explored jointly by key multidisciplinary stakeholders following the conclusion of an outbreak, namely through an After-Action review meeting.

Furthermore, our qualitative finding regarding perceived imbalances in power between the One Health sectors suggests critical work must be done to build, or even repair, interpersonal dynamics between the multisectoral stakeholders working in this arena. To avoid a crisis of trust between sectors when it is most crucial, such as during an emergency response to a multisectoral disease outbreak, it is essential that work is done during post-epidemic periods and prior to the next health crisis to establish channels of communication and foster mutual respect, premised on an understanding of shared objectives.

Relationship strengthening across sectors and with the community, more broadly, will also facilitate the implementation of a One Health approach to address multisectoral problems beyond that of outbreaks. For instance, a One Health approach is similarly optimal for establishing systems to prevent and address antimicrobial resistance (AMR), which poses a major threat to the health of humans, animals, and our shared environment. Though the burden of AMR is not yet well established in animal populations, an estimated 5 million human deaths were associated with AMR in 2019, disproportionately affecting low-resource settings.[3] The complex dynamics driving AMR threaten the health and wellbeing of animals (livestock, wildlife, and aquatic animals alike), as well as water, soil, and plants, thereby affects livelihoods, economies, and food safety and security.

Implications for Disease X

Not only do the findings from these three studies illustrate the utility of timeliness metrics, but this work also highlights important lessons that can inform future epidemic preparedness efforts. Specifically, these findings have important significance considering the Herculean task of preparing health systems for *Disease X*. At present, the Ugandan health system is less prepared to detect and respond to outbreaks of diseases they are unfamiliar with. To prepare for outbreaks of new or rare diseases, including a novel *Disease X*, outbreak preparedness efforts must increasingly be agnostic to disease type. This recommendation stemming from our work reinforces our growing appreciation that the field and practice of global health must move away from a vertical, siloed approach to diseases, and toward horizontal or even ‘diagonal’ approaches to strengthen overall health systems and structures.[4] Specific recommendations on leveraging disease-agnostic epidemic preparedness efforts are described in the following section.

Translating Findings to Action

Next Steps for Timeliness Metrics

Per our findings from Chapter Three, stakeholders view timeliness metrics as an educational tool that can potentially motivate outbreak investigators and responders to improve timeliness once they have seen empirical evidence of how they are currently performing during outbreaks. Particularly given the encouraging timeliness data explored in Chapter Four, it seems an intuitive and necessary next step to disseminate these findings among outbreak responders and frontline workers in Uganda. Conceivably, this information-sharing might positively reinforce and inspire prompt or speedy action during outbreaks, possibly even galvanizing support for timeliness metrics as a tool in the process. It would be particularly meaningful if we were able to show stakeholders a positive association between fast performance during outbreaks and better outcomes related to morbidity and mortality.

Timeliness metrics are premised on the assumption that faster detection and response times are desirable because they result in improved outcomes, such as reduced morbidity and mortality. This assumption is logical given that earlier detection and implementation of control measures would ideally lead to reduced transmission and therefore avert cases of disease. A few studies have established empirical evidence of this association, including that delays in detecting Ebola virus disease is significantly associated with longer duration and more cases of disease.[5] However, evidence of this association across all disease types has not been conducted, and consequently, additional research to establish that speed indeed improves outcomes during outbreaks should be conducted before resources are dedicated to scale up timeliness metrics work and further explore implementation strategies.

With adequate data on timeliness for each of the One Health outbreak milestones, stakeholders can explore if certain timeliness metrics (i.e., speed between any two respective milestones) make more or less of an impact on the extent of the outbreak outcomes. In particular, the findings from Chapter Two of this dissertation would support further investigation into timeliness for those outbreaks with predictive alerts and preventive responses, to understand if timeliness here results in improved measures of morbidity and mortality.

To achieve these goals, it is our hope that our findings will inform the work being done by others that are similarly committed to timeliness metrics, including the impressive implementation of the 7-1-7 targets by Resolve to Save Lives and the 7-1-7 Alliance. Rather than reinventing the wheel, we envision other timeliness metrics efforts might seek to incorporate more fully integrated One Health approaches to their frameworks, including consideration of predictive alerts and preventive responses as two important milestones that should be tracked when possible.

Fortunately, Uganda has already taken several integral steps toward mainstreaming timeliness metrics by integrating the tool into existing surveillance and response frameworks. Excitingly, Uganda recently developed and launched an electronic compendium of public health emergencies (PHE) within the electronic Integrated Disease Surveillance and Response platform.[6] The data dictionary developed for the response milestones to be documented for each PHE was premised on the 11 One Health outbreak milestones defined in the Salzburg Statement on Metrics for One Health.[7] As such, the PHE Compendium seeks to document, among other relevant variables, the predict date ("date occurrence of the PHE was predicted or date an alert of a potential PHE occurrence is availed/given") the prevent date ("date initial preventive interventions were implemented"), and if and when an After-Action Review was completed. Prospectively, these dates are to be collected in real-time, which will facilitate data completeness for these historically under-reported milestones.

Ideally, the Compendium will be accessible and allow tracking of PHEs data by all multisectoral stakeholders, and not just those working within the human health sector. Data that has been consolidated through this platform can also be more easily analyzed through a systems approach that considers timeliness as a product of how the entire health system functions, which alleviates blame from being placed on any one sector or individual component of the response. Without a systems approach, policy makers may find that frontline workers avoid reporting milestone dates during outbreaks altogether so as to avoid being blamed when there are noticeable lags in timeliness, a phenomenon one informant described as already occurring.

Lastly, given recent advances in machine learning and artificial intelligence, there may also be an opportunity to introduce automation into the measurement system, whereby timeliness metrics are automatically calculated and even flagged when metrics deviate significantly from expected trends or targets and warrant follow-up.

Next Steps to Operationalize One Health and Prepare for Disease X

Informants in our studies described overlapping challenges for One Health collaborations across disciplines that were related to cross-sectoral training, funding, surveillance, and policy. Training was described as a challenge only in that Uganda's National One Health Platform is still in the process of scaling up One Health trainings across districts in Uganda; where those trainings have occurred, informants described this as an enabler to rapid detection and response of outbreaks.

With regard to funding, a 2020 case study of One Health activities for global health security in Uganda found that across five technical areas, multisectoral activities under the purview of the national laboratory systems received the most funding (81% of planned work fully funded), whereas of 54% of planned One Health activities workforce development were not funded, as well as 24% of real-time surveillance activities, and 18% of emergency response activities.[8] For the emergency response pillar, the case study found that one in five districts (18%) had established district One Health teams at the sub-national level to assist with outbreak response.

To establish surveillance systems that can detect signals of potential outbreaks, increased and consistent funding must be allocated for coordinated activities between sectors both at the national and sub-national levels. In Uganda, for example, that might look like increased funding to the National One Health Platform, which can than ensure equity in financing across sectors; rather than availing funds predominantly to activities centered on human health, resources must be made available for collaborative projects, but also sector-specific funds for the animal, plant, and environmental sectors so that they can quickly mobilize during an outbreak without depending on another sector. If domestic, public financing within Uganda cannot be availed, then funding from international donors should be explored given the importance of this work; however, to avoid donor-driven projects and priority setting, we have recommended in Chapter Four of this dissertation that the Quadripartite pool resources to create a flexible basket-fund that can be directed to any agency, regardless of sector, which needs to quickly respond to outbreaks.

By financing the integration of systems across health sectors, Uganda can help streamline and facilitate multisectoral communication, which will inherently help prepare their health systems to detect and respond to both emerging, non-endemic diseases with which their health system has had comparatively less experience with, but also for *Disease X*, an entirely unknown pathogen. Efforts to prepare for the latter, which is likely to emerge at the human-animal-environmental interface, require a disease-agnostic approach to epidemic preparedness and response plans. Examples of these efforts include One Health workforce development, where trainees from diverse sectors come together to learn from one another and begin to foster interpersonal relationships and communication channels. Importantly, these training opportunities may help to address the perceived imbalances in power across sectors by establishing rapports and building trust and across these interdependent disciplines. However, efforts to establish mutual respect and appreciation for the importance of each sector’s role require steadfast commitment from all involved and must be an ongoing process.

Other disease-agnostic approaches relate to diagnostic testing, which has historically been established to detect single pathogens. Diagnostics can be diversified through increased use of multiplexing diagnostic technologies and pan-species molecular assays. Integration of multiplexed and pan-species diagnostics into routine surveillance systems, particularly at the human-animal interface, will increase our chances of detecting the emergence of *Disease X* or any pathogen that is novel to a country or geographic region. Perhaps most importantly, basic investments must also be made in public health infrastructure and disease prevention measures, the latter of which must include education, risk communication, and trust-building activities with the community.

Implications for Global Health

As an area of research and practice, this study has implications for the field of global health, particularly with regard to the use of metrics, which are foundational to the discipline. Criticisms highlight the historical use of metrics as a means of power and to perpetuate coloniality.[9] To ensure that standardized metrics are not once again developed by the global North and forced upon the global South as 'universally accepted' gold-standard measurements, global actors must first decide if these metrics are useful and then decide collectively upon what these metrics should entail. Particularly when funding for these tools is availed by the global North, we run the risk of determining that this tool will be adopted by external users, in its current state, whether or not it is the most appropriate intervention.[9] Though our study does provide evidence that several key stakeholders in Uganda do believe this tool to be useful, ethical implementation of timeliness metrics requires that we remain vigilant that this measurement tool is being used in a valuable and fair way.

There are several strategies we must employ to address this significant risk. To begin, timeliness metrics must be driven and informed by community-based research. Next, as timeliness metrics are tracked and analyzed, these metrics should not be divorced from the human story behind them. Qualitative work can complement the quantitative findings of timeliness metrics analyses to explain observed phenomena, but this work also humanizes the outbreak experience, reminding stakeholders of the lives that are affected by the diseases that we are striving to prevent and control.

The findings from our work in Uganda demonstrate the critical lessons that can be learned through collaborations among countries that have routine experience combatting outbreaks, including many diseases of high consequence with pandemic potential. To study One Health timeliness metrics, however, partnerships had to be developed with stakeholders beyond the traditional disciplines and between academic and government institutions. Though many proponents of timeliness metrics are from the global North, the institutional knowledge about detecting and responding to many of the diseases that are consistently considered of the greatest threat for pandemic potential lies with experts in the global South. Consequently, pandemic preparedness efforts must be fundamentally collaborative with those countries with the most knowledge and experience to share.

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Supplement 1: Appendix for Chapter 2

Methods

Inclusion and Exclusion Criteria

Based on the title, the included reports had to appear to describe a multisectoral outbreak event. The event had to meet the following definition of an outbreak: the occurrence of disease cases in excess of normal expectancy with epidemiologically related cases within a confined period of time and space. Consequently, outbreaks describing etiologies in a region endemic or hyperendemic for a specific pathogen were excluded, as were outbreaks of seasonal disease circulation. All non-outbreak related announcements, notices to readers, or errata were excluded. Reports describing disease trends over time, if not immediately apparent by the title during the initial screening phase, were excluded, as were publications reporting on standalone phylogenetic analyses, clinical studies, health laws or policy updates, or vaccine/pharmaceutical intervention updates. If an outbreak spanned several years, the last report from each of those years was included in the final analysis. To be eligible for inclusion in the final analysis, the full report had to be available in English. Poster abstracts were excluded.

Peer Reviewed Literature Search Strategy

Of note, this search took place on the legacy version of PubMed before the platform was updated to the default new PubMed on May 19, 2020. The exact search string used in PubMed was: “outbreak[Title] AND (("research report"[MeSH Terms] OR ("research"[All Fields] AND "report"[All Fields]) OR "research report"[All Fields] OR "report"[All Fields]) OR describe[All Fields] OR summarize[All Fields]) AND ("2010/01/01"[PDAT] : "2020/03/15"[PDAT]) AND ("2010/01/01"[PDat] : "2020/03/15"[PDat])”. The exact search string used in Embase, MEDLINE was: “outbreak:ti AND ((report OR research) AND report OR summary OR describe) AND (2010:py OR 2011:py OR 2012:py OR 2013:py OR 2014:py OR 2015:py OR 2016:py OR 2017:py OR 2018:py OR 2019:py OR 2020:py).”

All citations were exported from the two databases to EndNote version X9, where duplicates were removed.

Agency and Organizational Reports Search Strategy

Two additional platforms were considered, the European Union's European Centre for Disease Prevention and Control (ECDC) Communicable Disease Threats Reports and the World Organization for Animal Health's (OIE) World Animal Health Information System reports; however, these two outlets were frequently captured as sources for the ProMED reports.

To narrow the viral topic list, we used SpillOver: Viral Risk Ranking tool (https://spillover.global), accessed April 16, 2020.[1] All posts under each topic were examined in Microsoft Excel, and all duplicate posts with more than one source were removed.

ProMED Inclusion and Exclusion Criteria

All ProMED posts were visited to extract the publication date, source of information, and outbreak subject. Though foodborne illnesses are broadly a One Health topic, due to the large volume of foodborne outbreak posts in ProMED, we adopted a more specific inclusion and exclusion criteria for ProMED foodborne outbreak posts. Outbreak posts falling under topics such as "*E.coli* EHEC", "foodborne illness", "gastroenteritis", "norovirus" or "salmonellosis" that described point source outbreaks at a single location (e.g., restaurant, prison) or event (e.g., wedding, race, church potluck), were excluded as we assumed the preparation of the food was likely a single source of the outbreak and therefore inherently less of a One Health challenge. All foodborne pathogen-related outbreaks pertaining to food items distributed across a broad geographic area were included, as were point source outbreaks of that necessarily required multiple One Health sectors, such as Trichinellosis. Additionally, all posts with the subject of "recall" were excluded.

Data Management

When classifying of the origins of the investigation, responses to outbreaks occurring on US military bases abroad were considered a national investigation.

When documenting the type of pathogen or parasite implicated in the outbreak, bacterial infections that generated toxins were classified as bacteria. Biosafety levels for pathogens were captured and verified using Stanford University's Biosafety Levels for Biological Agents online tool, which categorizes infectious agents according to the Centers for Disease Control and National Institutes of Health Biosafety in Microbiology and Biomedical Laboratories, 5th Edition.[2] When transmission route was unknown, all possible routes for the pathogen were selected. For example, for a cutaneous anthrax outbreak linked to direct contact during animal slaughter, the transmission route was categorized only as direct contact. If the outbreak was a foodborne illness with no conclusive source, we categorized the transmission route as waterborne, foodborne, or direct contact.

Findings

Scoping Review Reports Identified for Analysis

The peer-reviewed literature search string yielded 2166 results in PubMed and 2621 results in Embase, totalling 2765 publications after duplicates were removed (Supplemental **Figure 3.1**). After titles were screened, 1875 articles were reviewed using the full inclusion and exclusion criteria, of which, 146 reports met the criteria and were included in the final analysis. Across the 2537 Centers for Disease Control and Prevention's (CDC) Morbidity and Mortality Weekly Reports (MMWR) and World Health Organization's [3] Disease Outbreak News (DON) reports published during the study period, 1454 report titles indicated the report described One Health-related outbreaks. Of those, 310 were deemed eligible for a full review based on inclusion and exclusion criteria and 227 were included in the final analysis. Of the 19212 ProMED posts published between 2010 and March 2020, 10676 pertained to One Health related outbreaks. Eight archived posts had URLs that would either not load or had formatting errors. After duplicate reports were removed, we reviewed a total 8022 reports for inclusion and exclusion criteria, of which, 609 were included in the final analysis. Of the 247 archived PREDICT reports, there were 39 outbreak or health events, 38 of which were eligible based on inclusion and exclusion criteria. Of these, 32 reports were written using the new reporting template developed in 2017, all of which were included in the final analysis.

Analysis of Timeliness Metrics

Diagnostic tests or lab confirmation was most frequently mentioned with no date (45.4% of reports), though 20.5% of reports included a specific date of a successful diagnostic confirmation and 8.5% provided a vague date. Over three quarters of reports (76%) described verification of the outbreak by means of field investigation or another valid method, though 57.5% of those reports described an investigation without indicating a date. Just under half of all reports described the notification milestone, with 33% giving a specific date, 7% a vague date, and 7% mentioning notification but without indicating any date. A specific date for public communication of the outbreak was provided in a quarter of all reports, with 42.3% of reports making no mention of if or when information about the outbreak was released to the public by a responsible authority.

Though over half (56.8%) of all ProMED posts included in the analysis were informed by local newspapers, journals, or radio and television reports, there were approximately 20 recurrent reporting sources, including Outbreak News Today (n = 38), the OIE (World Animal Health Information Database n = 33; World Animal Health Information System n = 11), the WHO (non-DON reports n = 20), CDC (non-MMWR reports n = 13), Food Safety News (n = 13), the British Broadcasting Corporation (n = 11), WHO’s Global Alert and Response (n = 12), Agence France-Presse (n = 8), MMWR (n = 8), the University of Minnesota’s Center for Infectious Disease Research and Policy (n = 7), the Canadian Broadcasting Corporation (n = 6), the Associated Press (n= 5), Reuters (n = 5), The New York Times (n = 5), ECDC (n = 4), and EpiCore Global Surveillance (n= 4). In addition, there were 24 (4%) personal correspondences providing outbreak information, ranging from anonymous sources to emails directly from faculty and staff at universities and ministries. The source of 5% of the ProMED posts (n=30) were government agencies, including ministries and departments of health and agriculture.

Supplemental Table 2.1. Characteristics of outbreak reports included in One Health timeliness metrics scoping review and analysis

Report Characteristic	N = 1014 (%)
WHO Region (may be more than one)	
AFRO	202
PAHO	382
SEARO	95
EURO	226
EMRO	65
WPRO	150
Involvement in investigation	
National only	684 (67.4)
National with response assistance	216 (21.3)
Vague	42 (4.1)
National & international	31 (3.1)
National & international with response assistance	27 (2.7)
International only	7 (0.7)
International with response assistance	5 (0.5)
Response assistance only	2 (0.2)

Report Characteristic	N = 1014 (%)
One Health sectors	
Animal / Environment / Human	358 (35.3)
Animal / Human	302 (29.8)
Human / Environment	173 (17.1)
Animal / Environment	68 (6.7)
Human / Environment / Plant	34 (3.1)
Animal/Human/Environment/Plant	28 (2.7)
Human / Plant	18 (1.8)
Animal / Environment / Plant	14 (1.4)
Environment / Plant	12 (1.2)
Animal / Human / Plant	4 (0.4)
Animal / Plant	3 (0.3)
Reportable/notifiable disease	
Yes	122 (12.0)
No	24 (2.4)
Not mentioned	796 (78.5)
Etiology unknown	72 (7.1)

Report Characteristic	N = 1014 (%)
Etiology*	
Virus	421 (41.5)
Bacterium	359 (35.4)
Unconfirmed	82 (8.1)
Parasite	72 (7.1)
Toxin	63 (6.2)
Fungi	48 (4.7)
Prion	6 (0.6)
Transmission route (may be more than one)	
Direct contact	490
Foodborne	273
Vector-borne	196
Waterborne	183
Airborne	105
Other/Unknown	107
Publication year	
2010	78 (7.7)

Report Characteristic	N = 1014 (%)
2011	61 (6.0)
2012	92 (9.1)
2013	88 (8.7)
2014	85 (8.4)
2015	80 (7.9)
2016	89 (8.8)
2017	129 (12.7)
2018	138 (13.6)
2019	133 (13.1)
2020	41 (4.0)

AFRO: African Region; BSL: biosafety level; EMRO: Eastern Mediterranean Region; EURO: European Region; MMWR: Morbidity and Mortality Weekly Report; PAHO: Region of the Americas; SEARO: South-East Asia Region; WHO: World Health Organization; WPRO: Western Pacific Region.

*Where pathogens etiology was unknown but suspect, we selected both the probable pathogen type and unconfirmed.

Supplemental Table 2.2. Frequency of One Health Timeliness Metrics Outbreak Milestones reported across 1014 peer reviewed literature and organizational outbreak reports published 2010-2020

Outbreak Milestone	Yes, specific date N (%)	Yes, vague date N (%)	Mentioned, no date N (%)	Not mentioned N (%)
Predict	49 (4.8)	130 (12.8)	74 (7.3)	761 (75)
Prevent	11 (1.1)	33 (3.2)	15 (1.5)	955 (94.2)
Outbreak start	417 (41.1)	376 (37.1)	85 (8.4)	136 (13.4)
Detect	457 (45.1)	357 (35.2)	104 (10.3)	96 (9.5)
Notify	336 (33.1)	68 (6.7)	67 (6.6)	543 (53.6)
Verify	230 (22.7)	94 (9.3)	445 (43.9)	245 (24.1)
Diagnostic confirmation*	206 (20.3)	86 (8.5)	460 (45.4)	234 (23.1)
Respond	186 (18.3)	91 (8.9)	463 (45.6)	274 (27.0)
Public communication	255 (25.2)	156 (15.4)	174 (17.2)	429 (42.3)
Outbreak end	107 (10.5)	106 (10.5)	18 (1.8)	783 (77.2)
After action review	5 (0.5)	7 (0.7)	24 (2.4)	978 (96.4)

* Diagnostic dates reported but etiology unconfirmed for 28 reports

Supplemental Table 2.3. Frequency of Timeliness Metrics Outbreak Milestones reported by peer reviewed literature and organizational outbreak reports published 2010-2020

Outbreak Milestone	Peer-Reviewed Reports (N = 146)				Organizational Reports (N = 868)			
	Specific date N (%)	Vague date N (%)	Mentioned N (%)	Not mentioned N (%)	Specific date N (%)	Vague date N (%)	Mentioned N (%)	Not mentioned N (%)
Predict	7 (4.8)	33 (22.6)	7 (4.8)	99 (67.8)	42 (4.8)	97 (11.2)	67 (7.7)	662 (76.3)
Prevent	4 (2.7)	10 (6.9)	2 (1.4)	130 (89)	8 (0.9)	23 (2.6)	13 (1.5)	824 (94.9)
Detect	73 (50)	55 (37.7)	8 (5.5)	10 (6.8)	385 (44.4)	302 (34.8)	95 (10.9)	86 (9.9)
Notify	38 (26)	17 (11.6)	14 (9.6)	77 (52.7)	298 (34.3)	52 (6)	53 (6)	465 (53.6)
Verify	35 (24)	29 (18.9)	55 (37.7)	27 (18.5)	195 (22.5)	66 (7.6)	390 (44.9)	217 (25)
Diagnostic confirmation*	36 (24.7)	19 (13)	83 (56.8)	7 (4.8)	170 (19.6)	67 (7.7)	377 (43.4)	227 (26.2)
Respond	25 (17.1)	28 (19.2)	39 (26.7)	54 (36.9)	165 (19)	62 (7.1)	422 (48.6)	219 (25.2)
Public communication	14 (9.6)	2 (1.4)	27 (18.5)	103 (70.5)	241 (27.8)	154 (17.7)	147 (16.9)	326 (37.6)
Outbreak start	61 (41.8)	70 (48)	7 (4.8)	8 (5.8)	356 (41)	307 (35.4)	77 (8.9)	128 (14.7)
Outbreak end	31 (21.2)	54 (36.9)	5 (3.5)	56 (38.4)	76 (8.8)	53 (6.1)	13 (1.5)	726 (83.6)

Outbreak Milestone	Peer-Reviewed Reports (N = 146)				Organizational Reports (N = 868)			
After action review	1 (0.6)	2 (1.4)	7 (4.8)	136 (93.1)	4 (0.4)	5 (0.6)	17 (2.0)	842 (97.0)

* Diagnostic dates reported but not etiology unconfirmed 27 organizational reports, 1 peer-reviewed report

Supplemental Table 2.4. Timeliness metrics for the three outbreak reports where specific *Predict* and *Prevent* Milestone dates were provided

Milestone	Predict	Prevent	Start	Detect	Notify	Verify	Diagnostic	Respond	Communication	End	Review
Predict		3 (n=3)	18 (n=3)	18 (n= 3)	20 (n=1)	106 (n=1)	20 (n=1)	17 (n = 2)	-	47 (n=1)	-
Prevent			15 (n=3)	15 (n=3)	17 (n=1)	106 (n=1)	17 (n=1)	10.5 (n=2)	-	38 (n=1)	-
Start				0 (n = 3)	2 (n=1)	5 (n =1)	2 (n = 1)	2.5 (n = 2)	-	37 (n =1)	-
Detect					2 (n = 1)	5 (n =1)	2 (n = 1)	0.5 (n =2)	-	33 (n =1)	-
Notify						-	0 (n=1)	-1 (n = 1)	-	-	-
Verify							-	-	-	-	-
Diagnostic								-1 (n=1)	-	-	-
Respond									-	33 (n=1)	-
Communication										-	-
End											-
Review											

Supplemental Table 2.5. Timeliness metrics for the 42 outbreak reports where a specific *Predict* date were described but no *Prevent* date was provided

Milestone	Predict	Prevent	Start	Detect	Notify	Verify	Diagnostic	Respond	Communication	End	Review
Predict		-	17 (n= 26)	17 (n=29)	28 (n = 21)	41 (n = 11)	30 (n = 13)	22 (n = 9)	13 (n = 11)	36 (n = 4)	-
Prevent			-	-	-	-	-	-	-	-	-
Start				0 (n = 26)	12 (n = 14)	10 (n = 10)	10 (n = 10)	23 (n = 4)	1 (n = 7)	16 (n = 4)	-
Detect					10 (n = 15)	10 (n = 10)	10 (n = 12)	16 (n = 5)	1 (n = 7)	16 (n = 4)	-
Notify						-2 (n = 10)	0 (n = 10)	6 (n = 7)	0 (n = 6)	8 (n = 4)	-
Verify							0 (n = 8)	-1 (n = 3)	-1 (n = 3)	40 (n = 2)	-
Diagnostic								14 (n = 4)	-6 (n = 2)	3 (n = 3)	-
Respond									0.5 (n = 4)	44 (n = 2)	-
Communication										80 (n = 1)	-
End											-
Review											

Supplemental Table 2.6. Timeliness metrics for the 761 reports for which no *Predict* milestone was given

Milestone	Predict	Prevent	Start	Detect	Notify	Verify	Diagnostic	Respond	Communication	End	Review
Predict		-	-	-	-	-	-	-	-	-	-
Prevent			3 (n = 5)	3 (n = 5)	3 (n = 3)	3 (n = 3)	3 (n = 2)	56 (n = 2)	2 (n = 2)	-	-
Start				0 (n = 282)	15 (n = 160)	13 (n = 122)	15 (n = 109)	22 (n = 73)	29 (n = 62)	44 (n = 74)	94 (n = 1)
Detect					12 (n = 189)	10 (n = 130)	13 (n = 122)	16 (n = 79)	29 (n = 63)	41 (n = 69)	94 (n = 1)
Notify						0 (n = 111)	-1 (n = 100)	3 (n = 73)	5 (n = 54)	14 (n = 49)	39 (n= 2)
Verify							0 (n = 104)	0 (n = 57)	1 (n = 41)	20 (n = 31)	44 (n = 1)
Diagnostic								0 (n =43)	1 (n = 31)	41 (n = 31)	-
Respond									1 (n = 68)	21 (n = 26)	10 (n = 2)
Communication										4 (n = 18)	20 (n =1)
End											18 (n =1)
Review											

Supplement 2: Appendix for Chapter 3

Results

With regard to deviant cases among the expert informants, one informant described the *After-Action Review* milestone as unnecessary, which deviated from patterns observed across the nine other informants who described this milestone as an important learning opportunity.

Key Informant Interview Guide

Background Questions:

1. To start off, could you please tell me a bit about your position or your role at your place of work? And how long you have worked there?
2. In what capacity do you engage with outbreaks in your work? Handle or contribute to outbreak reports?
    1. Probe: Have you contributed to writing an outbreak report previously?
    2. Probe: Have you used outbreak reports to make public health decisions before?

Reporting-Specific Questions:

3. Thinking back on the latest outbreak you investigated, can you tell me about your experience?

4. In your experience, what kinds of challenges can investigators encounter when responding to or reporting on outbreaks?

5. Are there any factors that contribute to more successful or more expedient responses to outbreaks?

1. Probe: How do existing reporting tools affect your/an investigator's ability to report on outbreaks?

6. Do you think tracking the timeliness of different outbreak steps or events could be useful in improving outbreak responses in the long term?

[Share list of 11 outbreak milestones with definitions and explain timeliness metrics, including where milestones align with the 7-1-7 targets, with the addition of the *Predict*, *Prevent*, and *After Action Review* milestones].

7. In your experience, how feasible would it be to report a specific date for these milestones during an outbreak?
    1. Probe: Do you think it is important to capture specific dates for these milestones?

8. Can you think of anything that would make it easier to ensure these specific milestone dates are reported consistently?

9. How do you think these timeliness metrics could contribute to the outbreak response landscape or systems in Uganda?

10. Do you have any thoughts about how systemized or reproducible outbreak reporting is under the current monitoring systems?

11. What else do we need to be thinking about when it comes to reporting on multisectoral One Health outbreaks?

Supplemental Table 3.1. Public health emergencies prompting activation of Uganda's Public Health Emergency Center and meeting our inclusion criteria*

Outbreak	2018	2019	2020	2021	2022	Totals
Anthrax	5/5	1/3	3/3	2/4	3/4	14/19
Brucellosis	0	0	0	0	0/1	0/1
Cholera	9/12	7/8	5/5	1/1	0	22/26
Circulating Vaccine Derived Polio Virus 2	0	0	0	1/1		1/1
COVID19 Pandemic	0	0	1/1			1/1
Crimean Congo Haemorrhagic Fever	3/7	3/8	1/1	1/1	4/8	12/25
Ebola Virus Disease	0	1/1	0	0	1/1	2/2
Food Poisoning	1/1	2/3	0	1/1	1/1	5/6
Influenza	0	0	0	0	0/1	0/1
Malnutrition (famine)	0	0	0	0	0/1	0/1
Meningitis	1/1	0	0	0	0	1/1
Plague	0	1/1	0	0	0	1/1
Rabies	0	0	0	0/2	0	0/2
Rift Valley Fever	1/5	0/4	5/5	2/3	4/5	12/22
Scabies	0	0	0	0	0/1	0/1
Suspect Typhoid	0	0/1	0	0	0	0/1
Suspected methanol poisoning	0	0	0	0	0/1	0/1
Undiagnosed Illness	0/1	0/2	3/3	2/2	0	5/8
West Nile Virus Fever	0	0	1/1	0	0	1/1
Yellow Fever	0	1/2	1/2	1/2	2/2	5/8

Outbreak	2018	2019	2020	2021	2022	Totals
Totals	**20/32**	**16/33**	**20/21**	**11/17**	**15/26**	**82/129**

*Denominators are the total number of events occurring per year and the numerators are the events available for inclusion in the analysis. Outbreaks spanning multiple years are included in the count totals for the year that the outbreak started.

Supplement 3: Appendix for Chapter 4

Supplemental Table 4.1. Overall timeliness metrics defined as the median time in days between two outbreak milestones and Inter Quartile Ranges (IQR) where n = number of outbreak reports reporting specific date of both milestones.

Milestone	Prevent	Start	Detect	Notify	Verify	Diagnostic	Respond	Communi -cation	End	Review
Predict	98 n=1	16 (4-42) n=8	14 (7-60) n= 11	10 (9-117) n= 8	11 (9-61) n= 7	15 (10-119) n= 8	22 (12-59) n= 7	17 (9-28) n=7	82 (62-100) n= 9	n=0
Prevent		215 n=1	215 n=1	216 n= 1	216 n= 1	216 n= 1	217 n= 1	216 n= 1	355 n= 1	n=0
Start			3 (1-5) n=54	7 (3-15) n=42	7 (4-16) n=47	9 (6-20) n=39	8 (5-13) n=37	10 (4-20) n=27	61 (43-110) n=50	n=0
Detect				2 (0-9) n=54	2 (1-7) n=61	5 (2-13) n=52	4 (2-9) n=50	6 (3-9) n=34	57 (37-95) n=67	n=0
Notify					0 (0-3) n=48	1 (0-4) n=38	1 (0-5) n=38	3 (1-7) n=28	56 (36-95) n=47	n=0
Verify						0 (-1-2) n=48	1 (0-3) n=46	2 (0-4) n=31	47 (35-86) n=54	n=0
Diagnostic							1 (-1-3) n=41	2 (0-3) n=26	49 (35-83) n=49	n=0
Respond								0 (-1-4) n=30	52 (33-87) n=47	n=0
Communication									64 (34-89) n=33	n=0
End										

Supplemental Table 4.2. Comparison of timeliness metrics between Uganda and WHO AFRO region in 2018 and 2019 for three timeliness metric intervals

	Start* to *Detect		***Detect* to *Notify***		***Start* to *End***	
	Uganda	**WHO AFRO**	**Uganda**	**WHO AFRO**	**Uganda**	**WHO AFRO**
2018 Median days (IQR) N Reports (%*)	4 (2-5) n=15 (68)	7 (1-27) n = 62 (61)	1 (0-2) n=13 (59)	3 (0-14) n=83 (82)	120 (64-130) n=11 (50)	67 (25–144) n=72 (71)
2019 Median days (IQR) N Reports (%*)	1 (0-3) n=9 (60)	4 (1–11) n=47 (54)	2 (0-5) n=6 (40)	4 (1-9) n=62 (71)	44 (29-57) n=10 (67)	45 (22–90) n=67 (77)

*Total reports for 2018 in Uganda n = 22, WHO AFRO n=101; total reports for 2019 in Uganda n= 15, WHO AFRO n= 87

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