

Characterizing the Global Burden of Hepatitis E Outbreaks

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START
CENTER

STRATEGIC ANALYSIS,
RESEARCH & TRAINING CENTER

Department of Global Health | University of Washington

AGENDA

- Introductions
- Project Overview
- Methodology
- Results
- Synthesis & Recommendations
- Discussion



PROJECT TEAM



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START OVERVIEW



Leverages leading content expertise from across the University of Washington



Provides high quality research and analytic support to the Bill & Melinda Gates Foundation and global and public health decision-makers



Provides structured mentorship and training to University of Washington graduate research assistants

PROJECT OVERVIEW



BACKGROUND

- Hepatitis E virus (HEV) is a leading cause of acute hepatitis globally, transmitted through the fecal-oral route and primarily through contaminated water
- Pregnant women and immunocompromised individuals are at particularly high risk for severe morbidity and mortality
- Despite the availability of a safe and effective HEV vaccine, Hecolin, global use has been limited

MOTIVATIONS

- Summarize ways in which outbreaks have been measured and associations have been determined to inform future study designs
- Identify gaps in knowledge around HEV outbreaks to inform prevention and control initiatives
- Articulate the potential value of Hepatitis E vaccines to policy and decision makers



PROJECT REQUEST

- To undertake a [literature \(peer-reviewed and gray\) review](#) of the occurrence of Hepatitis E outbreaks globally to help quantify the burden of Hepatitis E disease
- A written report and slide deck based on a literature (gray and white) review and interactions with experts in the Hepatitis E disease and epidemiology field, [including a tabular summary of outbreaks](#) and key variables
- A [publication in the peer-reviewed literature](#) is highly encouraged

METHODS

SUBJECT MATTER EXPERT CONSULTATIONS



SUBJECT MATTER EXPERTS



Dr. Philipa Easterbrook: Senior Scientist, Global Hepatitis Program

Dr. Alexander Rosewell: Technical Officer, Vaccine Preventable Disease Outbreaks

Dr. Melanie Marti: Technical Officer, Immunization Policy Unit, Department of Immunizations, Vaccines, and Biologicals (IVB)

Dr. William Augusto Perea Caro: Coordinator for Control of Epidemic Diseases



Dr. Iza Ciglenecki: Doctor and medical and emergency coordinator based mainly in sub-Saharan Africa, a medical advisor for outbreak response and epidemiology

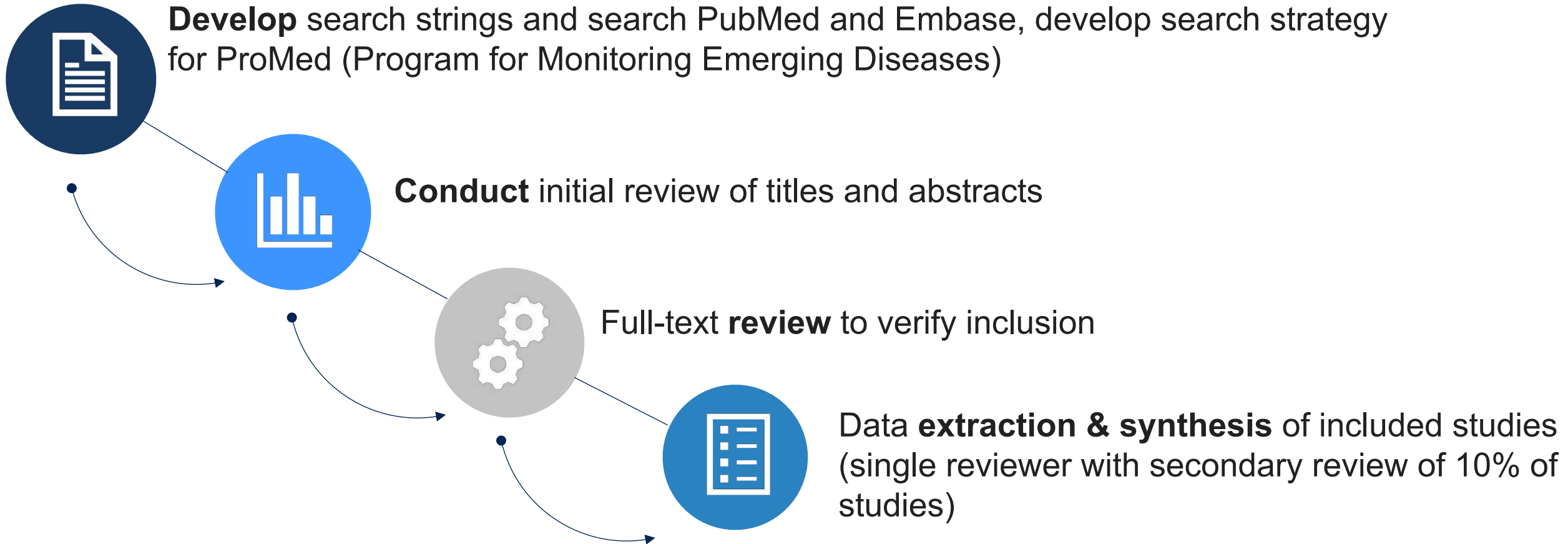


Dr. Brittany Kmush: Assistant Professor in the Department of Public Health working on a Hepatitis E Vaccine Progress Roadmap



Dr. Mae Dirac: Acting Assistant Professor of Health Metrics Sciences and of Family Medicine

LITERATURE SEARCH



SEARCH STRINGS

PubMed

("Hepatitis E"[Mesh] OR "Hepatitis E virus"[Mesh] OR "hepatitis e" or "water-borne hepatitis") AND (("Disease Outbreaks"[Mesh]) or "disease outbreak" or "Epidemics"[Mesh] or epidemic or prevalence) NOT (comment(PT) or editorial(PT) or letter (PT)) AND (2011:2021[pdat]) AND (humans[Filter]) AND (English[Language])

Embase

('hepatitis e' OR 'hepatitis e virus' OR 'hepatitis e vaccine')
AND (outbreak OR epidemic) AND English AND human

ProMED

“Hepatitis E” “Hepatitis E Virus” “HEV” “HEV outbreaks”

SCREENING CRITERIA



INCLUSION CRITERIA

- Outbreaks reporting on five or more cases
- Studies reporting on 1.5 times baseline (usually in a HEV endemic setting)
- All records reporting suspected and confirmed outbreaks



EXCLUSION CRITERIA

- Full text not available
- Publication prior to 2011
- Fewer than 5 cases reported
- HEV was tested but not detected
- Reports only evaluating the outbreak response (i.e., not reporting on the outbreak itself)

DATA EXTRACTION

Basic publication information (e.g., authors, year)

Year the outbreak was detected

Study setting/population (e.g., IDP camps, village)

Subpopulation (e.g., pregnant women)

Age of participants

Country

Population Size

Number of suspected versus confirmed cases

Number of case fatalities

Duration of the outbreak

HEV detection method (e.g., culture, PCR)

HEV genotype

Point source of the outbreak

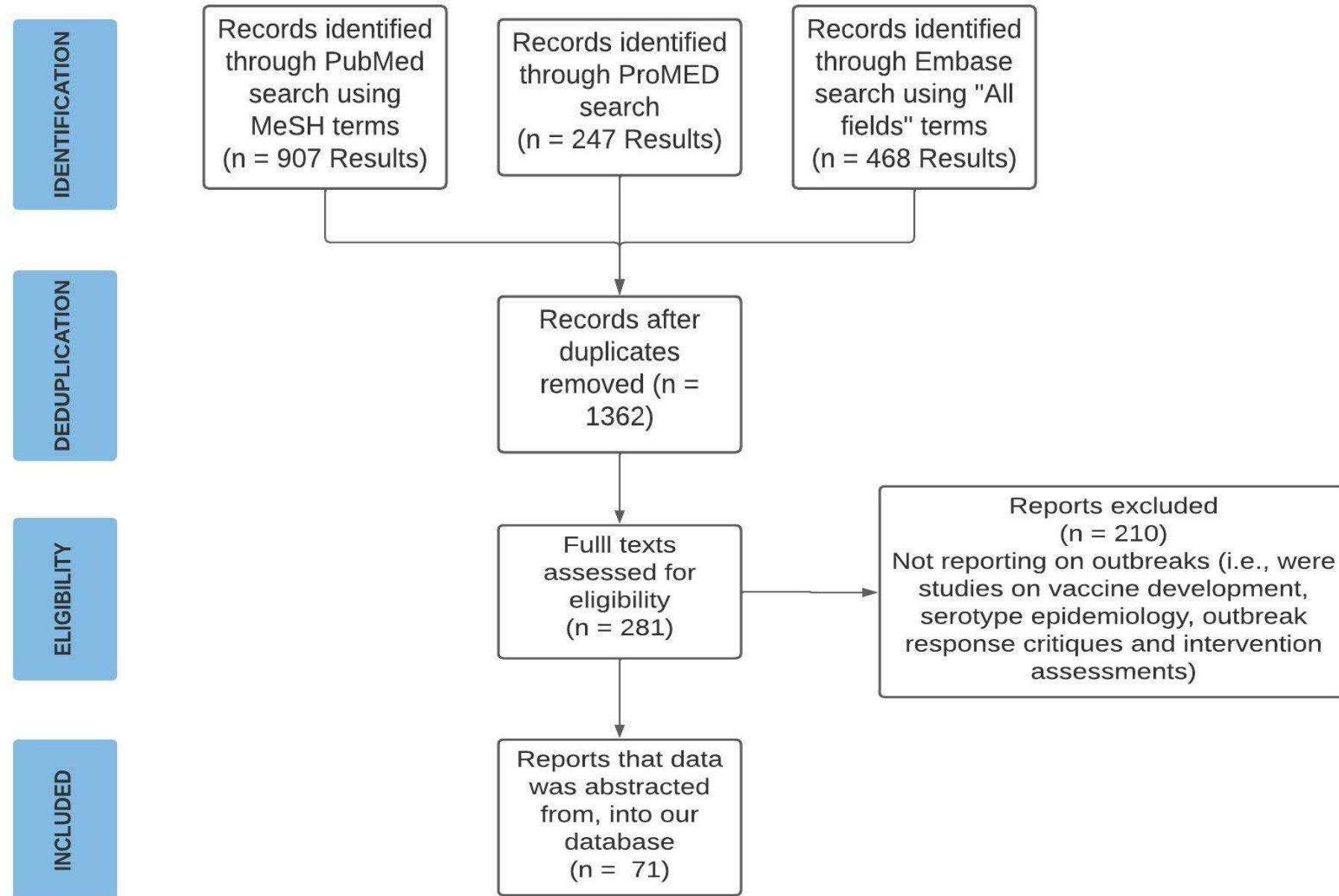
Any outbreak interventions

Entity reporting the outbreak

Reasons behind a lack of vaccine use

RESULTS

SCREENING RESULTS



PROMED REPORTS: **SOURCES OF INFORMATION**

HUMANITARIAN ORGANIZATIONS

- Médecins Sans Frontières

GOVERNMENT

- Republic of South Sudan Ministry of Health
- Epidemiology and Surveillance Division at the Uganda Ministry of Health

UNIVERSITIES

- Department of Microbiology, Jaipur National University
- University of Khartoum

NEWSPAPERS & MEDIA

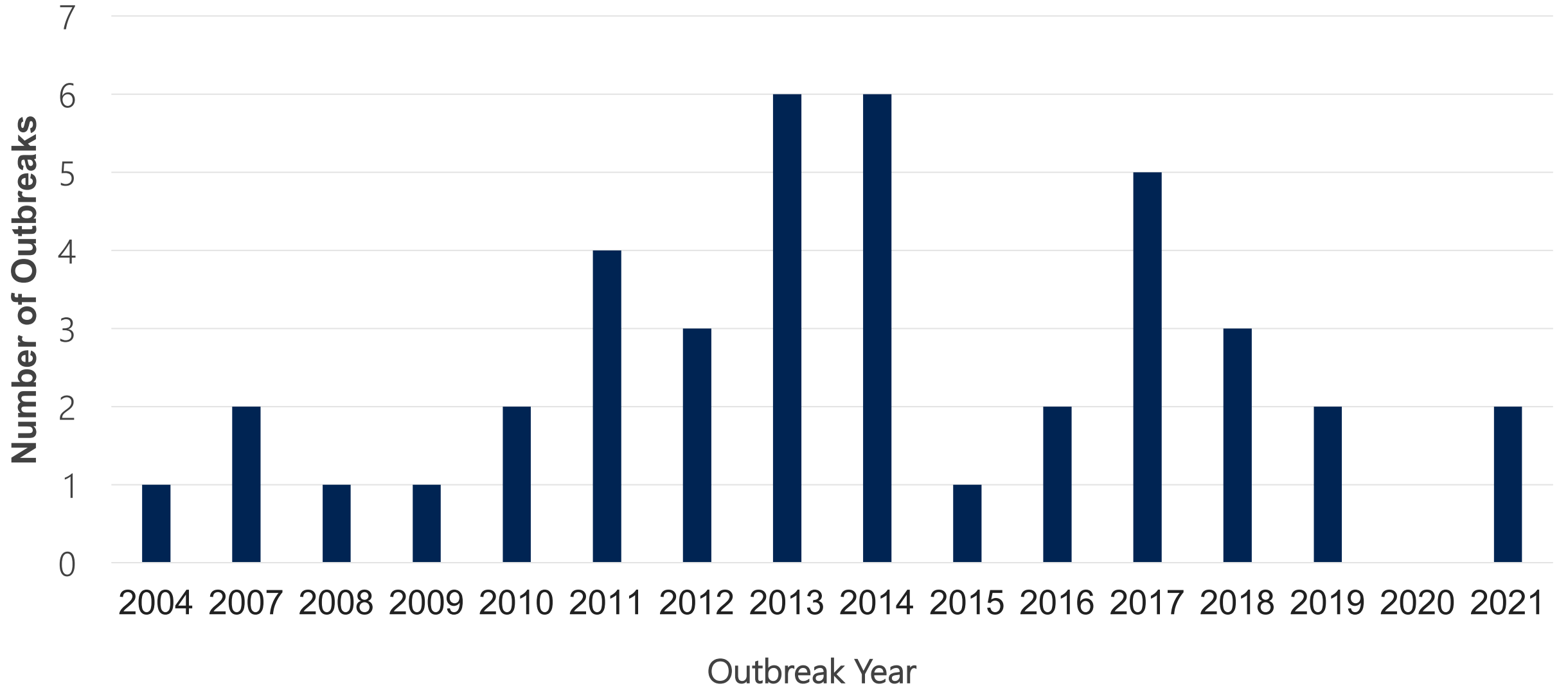
- The Daily Star
- The Times of India



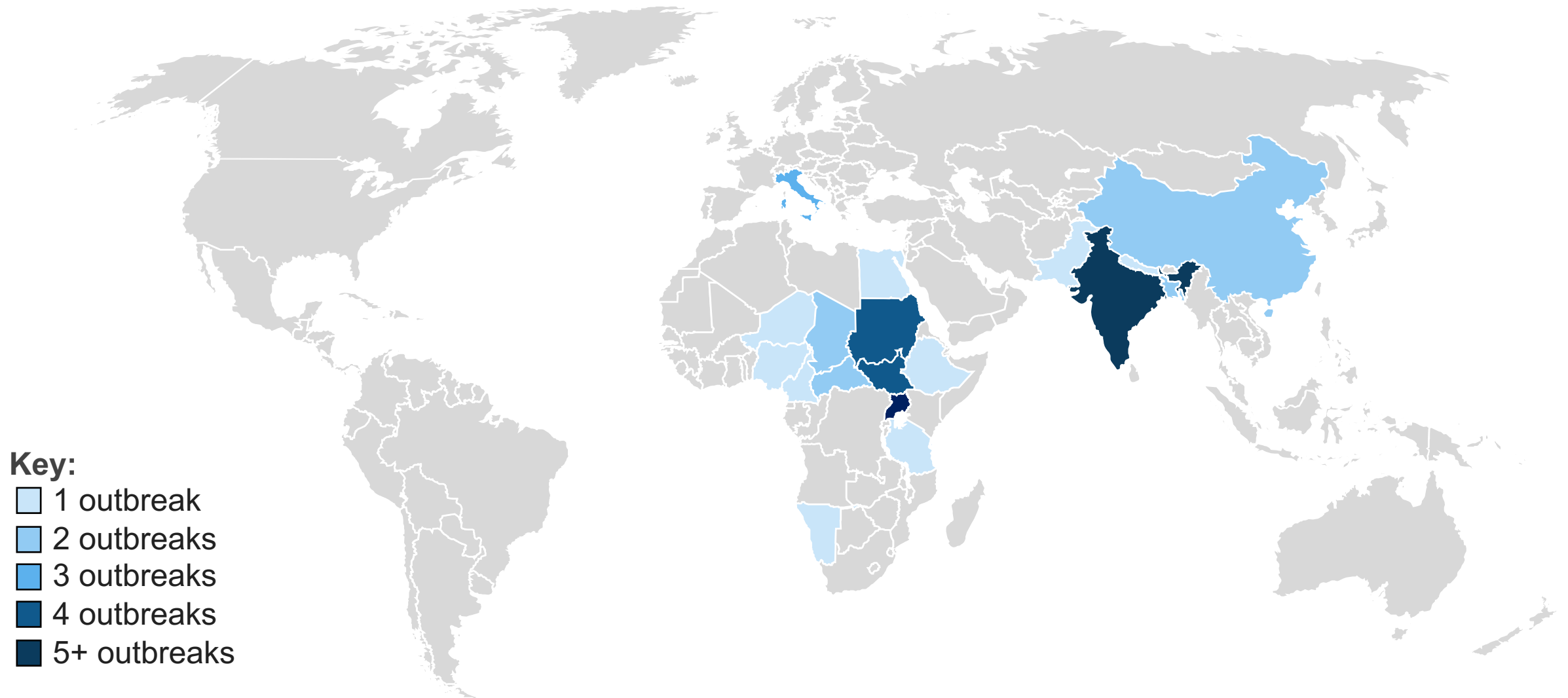
OUTBREAK SYNTHESIS

Characterizing the Global Burden of Hepatitis E Outbreaks												
Number of deaths (not including pregnant women)	What was the case fatality for pregnant women?	What was the HEV Genotype?	What was the specific sub-population?	What was the age range? (include cases by age group if reported)	What country/countries had this outbreak?	Population size	Setting (i.e., rural vs. urban)	Setting (e.g. camp, work site, military base, etc.)	Population at risk (e.g. IDP camp size)	Was the outbreak declared over?	How long did the outbreak last?	What was the point source?
9	3	1e	pregnant women, children <1 year of age and persons with AJS who were vomiting and/or had altered mental status	15–44 year olds	Chad	Not Reported	Am Timan (urban)	Not Reported	Not Reported	Not Reported	44 weeks	Having more than five people in the household were predictive of being a confirmed case
Not Reported	Not Reported	1	Patients with jaundice	8-65 year olds, with a mean of 31 and a median of 28 (HEV confirmed cases only)	Bangladesh	2162 suspected jaundice cases in 30 of the 35 administrative blocks or wards of Rajshahi City	Urban	Not Reported	Not Reported	Not Reported	4 months	This large HEV outbreak in a northern Bangladeshi city was caused by the contamination of municipal piped water.
0	1	1a	pregnant women and persons with AJS	2–65 year olds	India	9720	Rural	Not Reported	Not Reported	Yes	As per records, jaundice was reported in sporadic cases since September 2014 and suddenly the numbers increased in end November–early December 2014; the last jaundice case was seen on 7 February 2015 and the outbreak was declared over	The municipal water supply was contaminated and sanitary conditions and waste disposal were poor in the area.
Not Reported	Not Reported	3e and 3f	Not reported	28–85 yr. olds; median age was 63 yrs.	Italy	Not Reported	Abruzzo (urban) and Lazio (urban)	Not Reported	Not Reported	Not Reported	24 weeks	Pork products
8	0	41/89 cases were viremic (Genotypes 1,2,3, and 4)	Patients with immune-suppression, chronic liver disease, acute liver failure, and acute kidney injury	Mean age reported: 55.5 ± 16.7	Italy	Not Reported	Marche (Urban)	Not Reported	Not Reported	Not officially	Not Reported, but data was collected from 2011-2018	Pork products

INCLUDED OUTBREAKS (n=41)



GEOGRAPHIC DISTRIBUTION OF OUTBREAKS



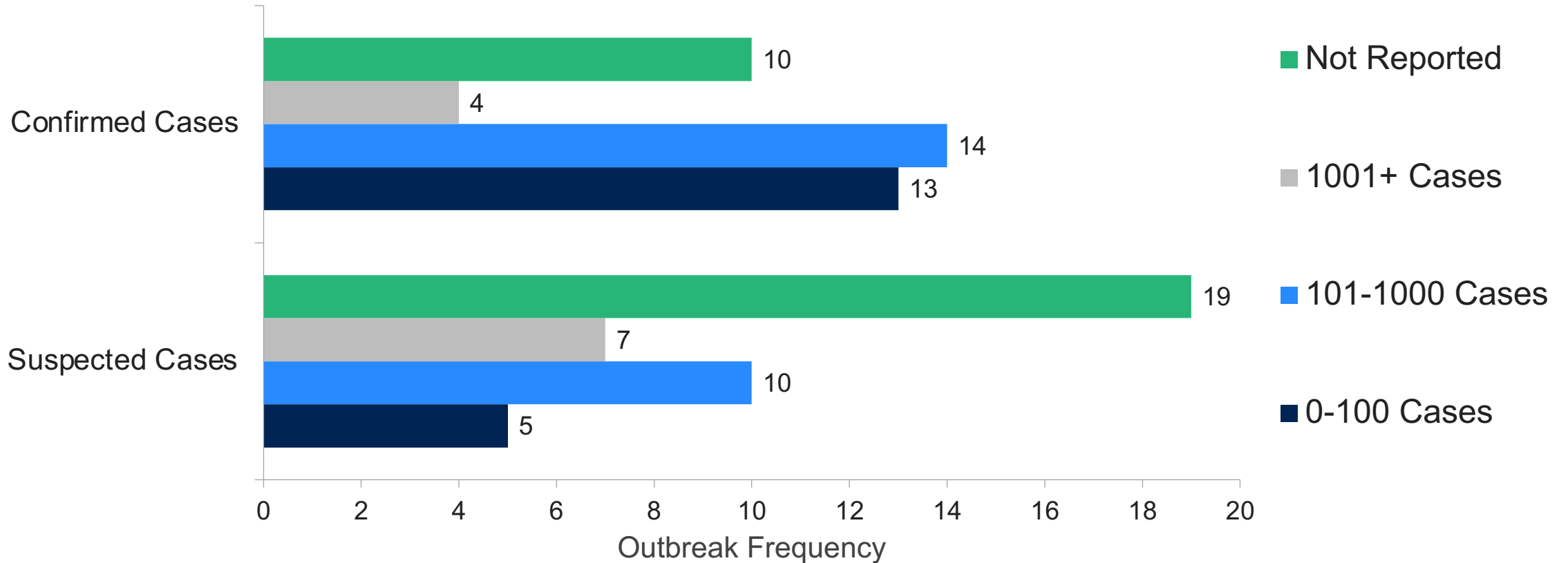
WHO REGIONAL DISTRIBUTION OF OUTBREAKS (n=41)

OUTBREAK CHARACTERISTICS	African Region (AFRO)	Region of the Americas (AMRO)	Eastern Mediterranean Region (EMRO)	European Region (EURO)	South-East Asian Region (SEARO)	Western Pacific Region (WPRO)
Reported Outbreaks	24	0	2	3	10	2
Countries with Outbreaks	11	0	2	1	3	1
Confirmed Cases*	14,846	0	95	133	5,830	435
Reported Fatalities*	580	0	Not Reported	8	38	Not Reported

*These values are subject to under-reporting

OUTBREAK SIZE DISTRIBUTION

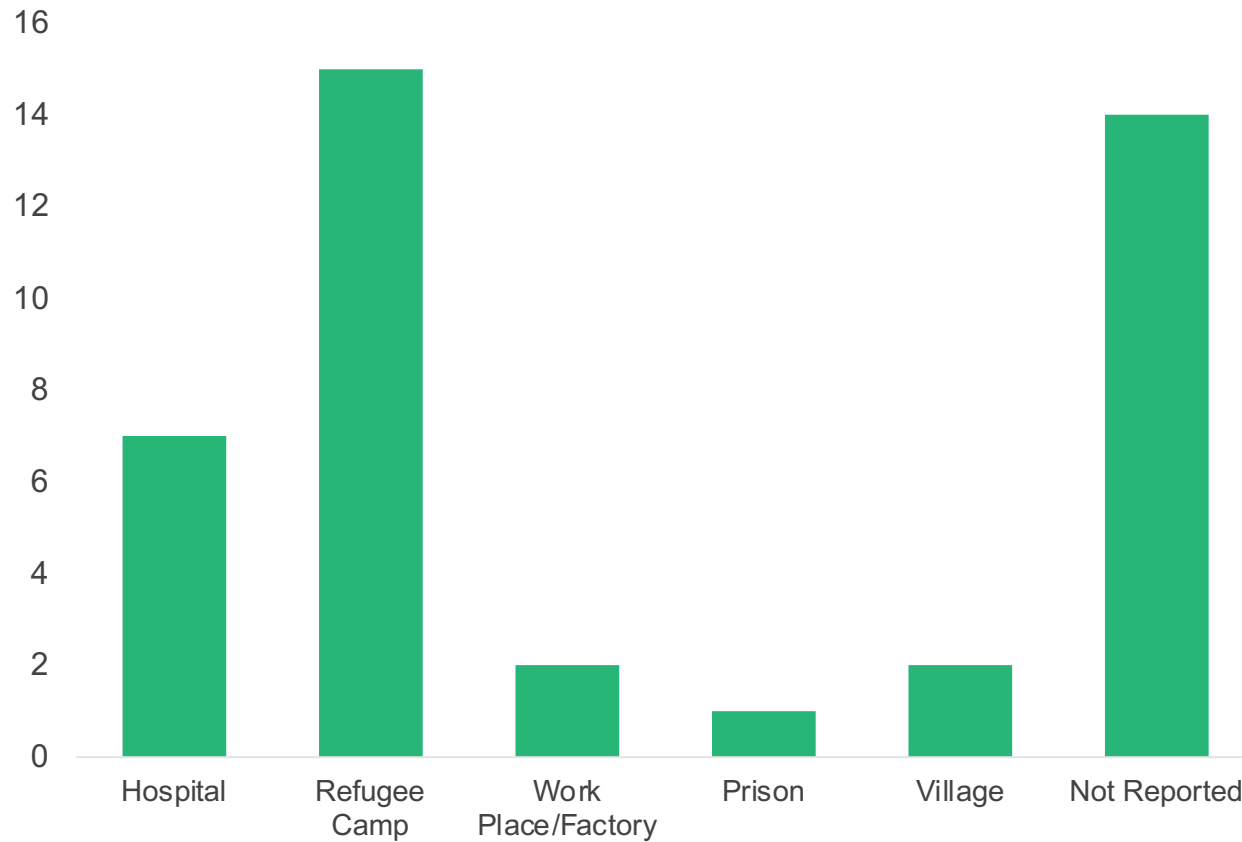
SUSPECTED & CONFIRMED CASES



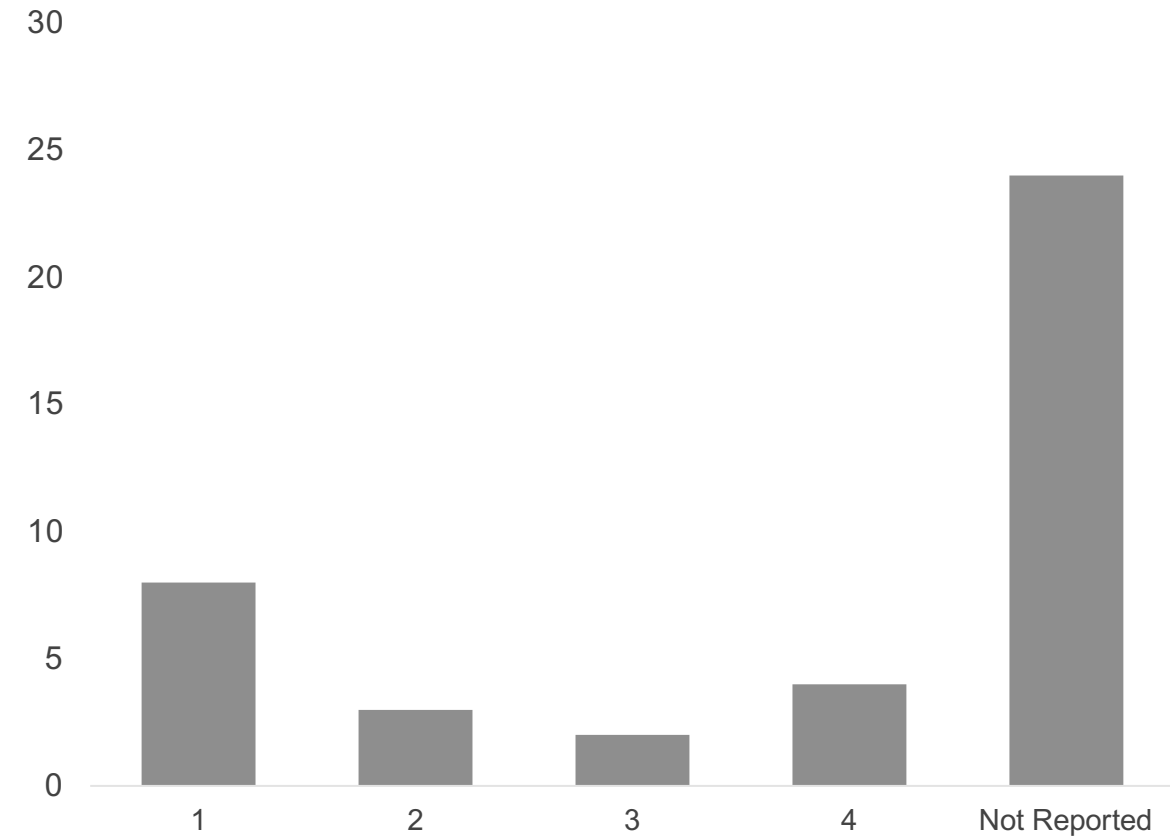
RESULTS

OUTBREAK CHARACTERISTICS (n=41)

Setting



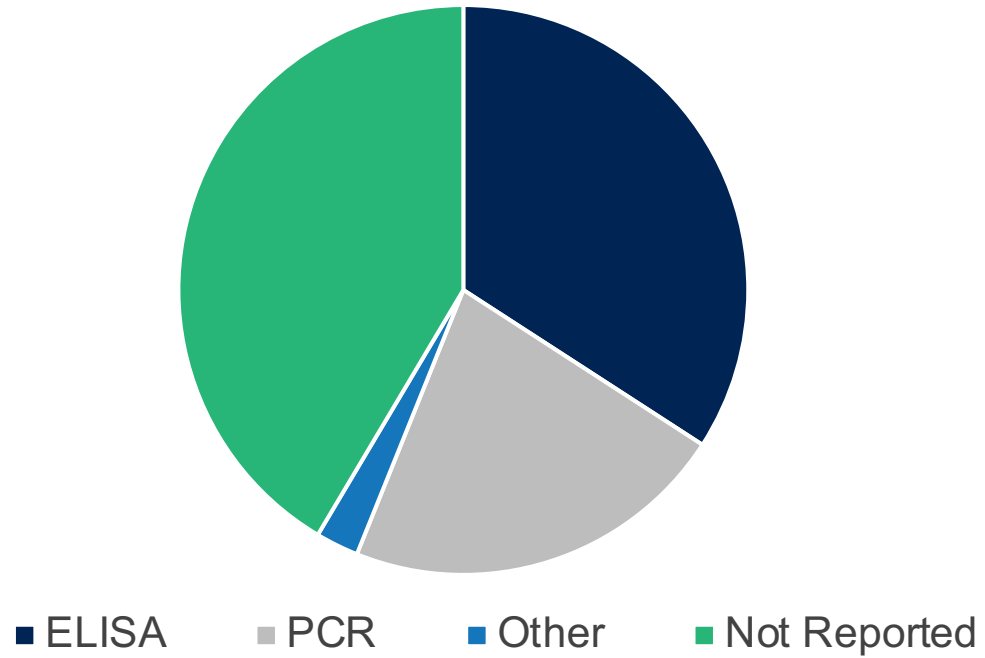
HEV Genotype*



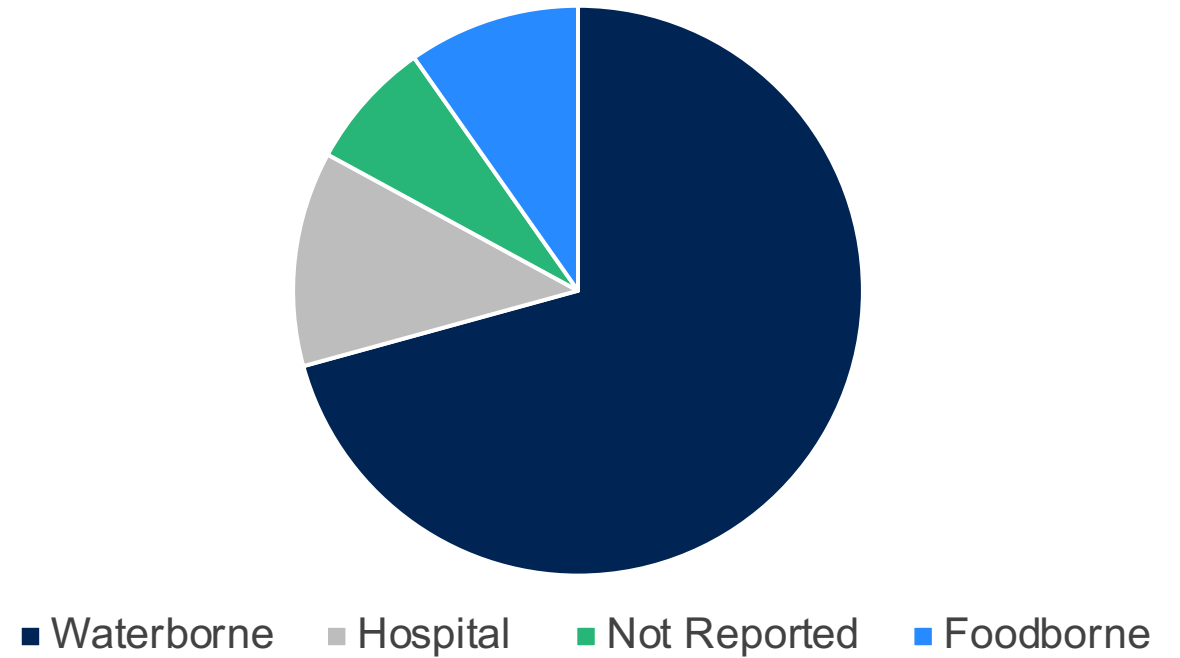
*Numbers do not add up to 41 due to multiple genotypes occasionally appearing in the same outbreaks

RESULTS

Laboratory Confirmation Method

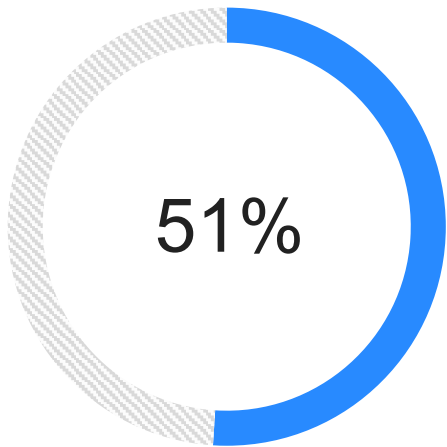


Mode Of Transmission

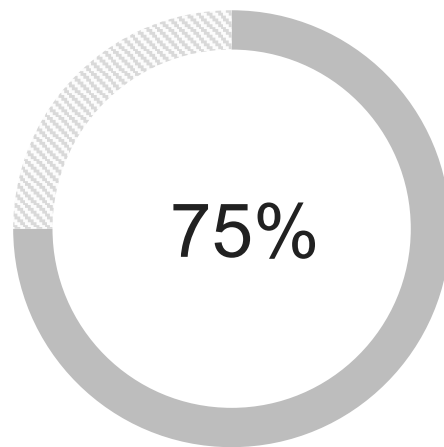


VARIABLES WITH COMMONLY MISSING DATA

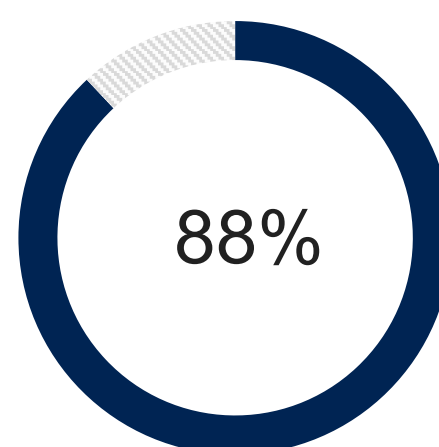
PERCENTAGE OF OUTBREAKS WITH MISSING DATA



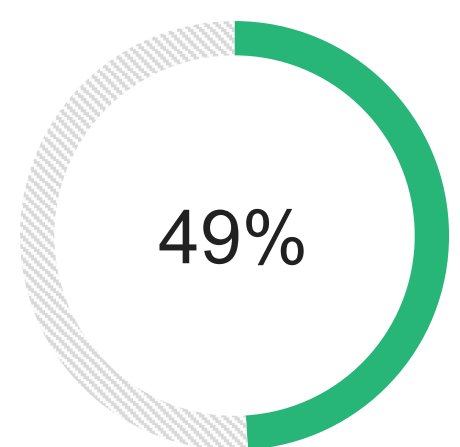
Testing
Strategy



HEV
Genotype



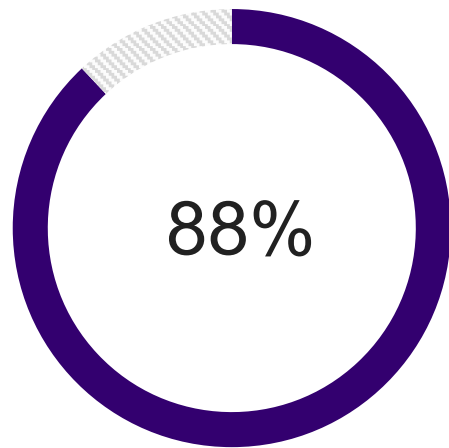
Vaccine
Use



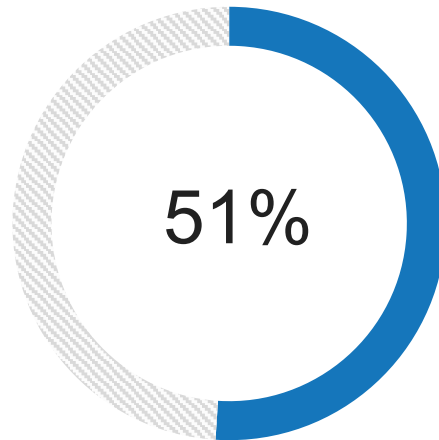
Outbreak
Fatalities

VARIABLES WITH COMMONLY MISSING DATA

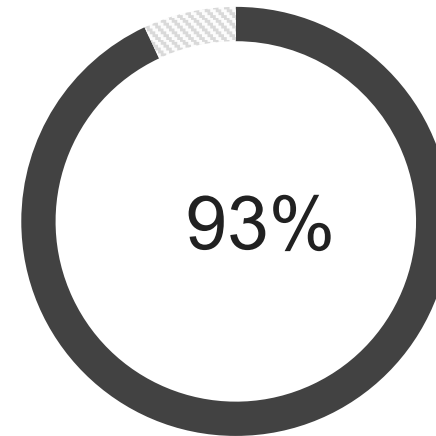
PERCENTAGE OF OUTBREAKS WITH MISSING DATA



Population
at Risk



Outbreak
Start Date



Outbreak
End Date

INTERVENTION STRATEGIES EMPLOYED



Case surveillance, a serosurvey investigation, and targeted prevention effort



Health education campaigns, film presentations, radio broadcasts, and printed messages in the local language to decrease consumption of untreated river water



WHO country office is also supporting passive and active surveillance strengthening, developing a case definition, surveillance tools, simple case management protocols and testing algorithm



The Health Department asked the authorities to super chlorinate the water sources immediately before it spreads further

EXAMPLES OF REPORTED REASONS FOR LACK OF VACCINE USE



“A recombinant, 3-dose series HEV vaccine is available but has **not yet been prequalified by the World Health Organization.**”



“While a marketed vaccine is available, the World Health Organization (WHO) does not recommend its routine use **because of insufficient safety and efficacy data.** These data also highlight the urgency of generating additional data to support the use of recently marketed HEV vaccine to mitigate or prevent outbreaks of Hepatitis E and its consequences in high-risk groups. “



“The vaccine has been shown to prevent symptomatic HEV infection and proven to be safe and effective in persons aged 16-64 years. Limited vaccine safety data in 37 pregnant women receiving 57 doses has been reported; however, **further research is needed, and safety for children is unknown.**”

SYNTHESIS & RECOMMENDATIONS

SYNTHESIS OF FINDINGS

LITERATURE REVIEW

71 Reports
Peer Reviewed Literature: 21
Gray Literature: 50

41 Outbreaks
18 Countries

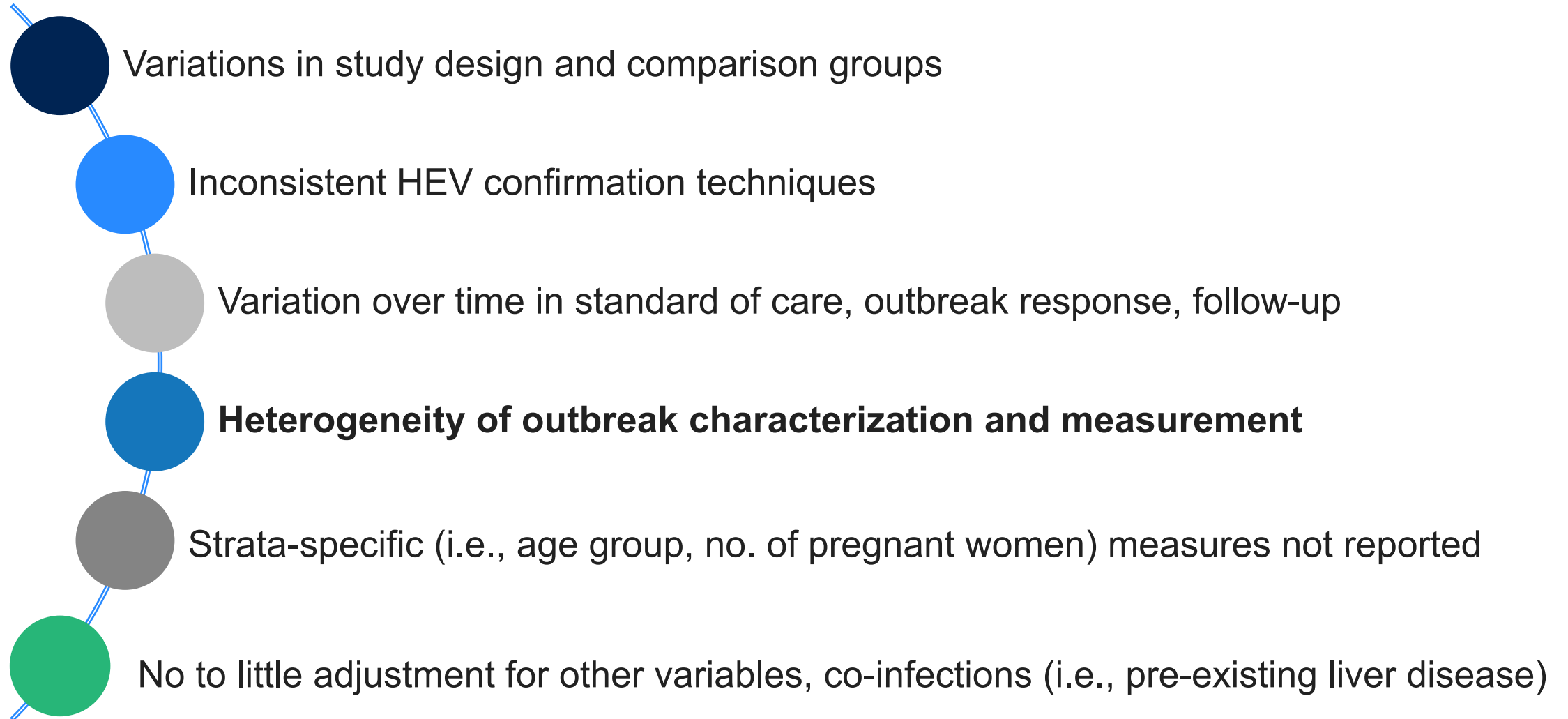
OUTBREAK CHARACTERISTIC TRENDS

Location: Camp Setting
Transmission: Waterborne
Testing: ELISA & PCR
Employed Interventions: Targeted
Preventions Efforts, Enhanced
Surveillance, Supportive Case
Management

KEY DATA GAPS

Vaccine Acceptance and Use
Case Definitions
Genotype
Testing & Surveillance Mechanisms
Final Outbreak Size (Case Counts
and Deaths)

CHALLENGES



STUDY REFLECTIONS

STRENGTHS

- Systematic literature review
 - WHO rapid review approach
- Specific range covered (2011- 2021)
- Cast a wide net in terms of characteristics captured
- Large number of reports screened
- Captured peer-reviewed and gray literature data

LIMITATIONS

- Many gaps in how outbreaks are reported (i.e., suspected vs. confirmed, confirmed by ELISA vs. other technique, etc.)
- Potentially missing valuable data by excluding studies that don't report studies as outbreaks/epidemics
- ProMed 2011 vs. PubMed 2011 (PubMed citing outbreaks before 2011)

RECOMMENDATIONS

- 1 Creation of a uniformed data platform to consolidate all known information about HEV outbreaks, as well as a universal protocol for reporting, detecting, and intervening in HEV outbreak settings
- 2 Agreement among key stakeholders to rely upon an accountability framework and standardized data reporting platform
- 3 Development of a toolkit for the diagnosis, triage, and management of HEV cases during an outbreak
- 4 Implementation of both active and passive coordinated surveillance systems

DISCUSSION QUESTIONS



What are some strategies to ensure that outbreak data is captured when Ministries of Health in other countries do not wish to report it?



Should we expect different standards of data collected from outbreaks in refugee settings versus hospital hospitals or workplaces?



With the gaps in outbreak data, what other data can be leveraged to support the value proposition of a Hepatitis E vaccine?



What parallels do we see between other outbreaks and Hepatitis E outbreaks in terms of accessible data sources and the availability of the data? What lessons can be learned from those outbreaks?

THANK YOU

Questions?

Please contact the START Center: start@uw.edu



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