GLOBAL TASK FORCE ON
CHOLERA CONTROL

SURVEILLANCE AND MONITORING SUB-GROUP
SURVEILLANCE WG WEBINAR UPDATE

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PRESENTATION OUTLINE

- Overview of subgroup work plan
- Update
  - Case definitions
  - Transmission settings
  - Minimum core data
- Next steps

WORKPLAN, SURVEILLANCE AND MONITORING SUBGROUP

- Three themes
  - Minimum indicator-based surveillance standards
  - GTFCC global cholera database
  - Cholera "elimination"

- Review (and revise as needed) current GTFCC cholera case definitions
- Develop classifications for different epidemiologic settings for *Vibrio cholerae* transmission and for each, develop recommendations for testing strategies in order to monitor trends in transmission and identify outbreaks.
- Recommend minimum standards for cholera routine indicator-based surveillance and enhanced cholera indicator-based surveillance (by settings) including:
  - recommendations on case-based vs aggregate data collection,
  - minimum core dataset (including standards for AMR reporting, sample (genomic/diagnostic) metadata, serotype/genotype reporting, and reporting of clinical cases and deaths),
  - reporting requirements, templates for sitreps and linelists

REVIEW OF CHOLERA CASE DEFINITIONS

- Context - cholera surveillance goals
- Approach to review
- Where we are
- Pending items

CHOLERA SURVEILLANCE GOALS

- Early warning function (outbreak detection)
- Outbreak monitoring
- Targeting prevention and control interventions
- Routine monitoring of trends (disease frequency)

→All rely on correct and systematic application of case definitions

→Required if aiming for sustained disease control and/ or elimination

APPROACH

- Identify components of different case definitions
- Gather evidence (publications, guidance documents, book chapters, expert opinions → limited by those available electronically)
- Review and document* rationale for different components of case definitions, their impact on sensitivity and specificity
  - Duration of illness
  - Age
  - Severity
- Discuss potential adjustments and additions, with aim to keep definitions simple (through meetings, survey, written feedback)
- Identify knowledge and research gaps

* Final write up to be completed by mid April

ACUTE WATERY DIARRHOEA

DEFINITION OF ACUTE WATERY DIARRHOEA

CURRENT

Acute watery diarrhoea (AWD) is an illness characterized by 3 or more loose or watery (non-bloody) stools within a 24-hour period.

→Missing definition of acute (duration); useful to exclude persistent diarrhoeas likely due to other aetiologies; useful for retrospective case finding

→Watery may benefit from more detailed description

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PROPOSED

Acute watery diarrhoea (AWD) is an illness, where

- *Acute* is defined as lasting seven days or less

Summary		Reference
Duration of illness	The clinical course of a cholera infection usually lasts <8 days (**3-8 days**)	Poulos 2012, Adagbada 2012
	97% of cholera cases had diarrhoea for **<6 days** (62% for <3 days)	Lucien 2015
Onset to presentation	**85%** of cholera cases sought health care do so **within 2 days** of illness onset (Nigeria)	Elimian 2019
	Almost **50%** of cholera cases sought health care **within 24h** of illness onset, >95% sought care within <7 days (Bangladesh)	Colombara 2013

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PROPOSED

Acute watery diarrhoea (AWD) is an illness, where

- *Acute* is defined as lasting seven days or less
- *Watery* is defined as non-bloody liquid stools that may contain mucous (*note: rice water stool discussed, but seen as too specific*)
- *Diarrhoea* is defined as three or more loose stools within a 24-hour period

Ideally, the surveillance guidance document will include recommendations on differential diagnoses

SUSPECTED CASE DEFINITION

APPLICATION OF SUSPECTED CASE DEFINITIONS

- **Entry point for case detection**
- **Routine surveillance** (i.e. no outbreak) for trends monitoring and **early warning** (i.e. early outbreak detection)
  - Low prevalence and poor specificity of the suspected case definition will result in low PPV → most suspected cases are likely not true cholera
  - Primary aim to have high **sensitivity** to avoid missing cases
  - Secondary aim to have as high **specificity** as possible without much compromise on sensitivity
- **Outbreak monitoring** to **target interventions** (i.e. outbreak detected)
  - Increase in prevalence will increase PPV; to some degree can compensate for drop in sensitivity of case definition
  - Aim to monitor changes in transmission including whether control interventions are effective

→ Suspected cases will be target population for testing

SUSPECTED CASE DEFINITION

CURRENT

In areas where a cholera outbreak has not been declared: Any patient aged 2 years and older presenting with acute watery diarrhoea and severe dehydration or dying from acute watery diarrhoea.

In areas where a cholera outbreak is declared: any person presenting with or dying from acute watery diarrhoea.

Discussion points:

- Outbreak "**declared**" → can be a political decision, different word?
- **Patient** → person?
- Definition of severe dehydration → refer to GTFCC outbreak fied manual
- Evidence for 2-year age cut-off → review of literature
- More general review of published literature on sensitivity and specificity of case definition (not a systematic review)
- Need for community definition? → agreement that this could be a simplified suspected case definition, adapated to context

SUSPECTED CASE DEFINITION

CURRENT

In areas where a cholera outbreak has not been declared: Any patient aged 2 years and older presenting with **AWD** and severe dehydration or dying from **AWD**.

In areas where a cholera outbreak is declared: any person presenting with or dying from **AWD**.

PROPOSED

In areas where there is **currently no known cholera outbreak,** a suspected cholera case is defined as:

- Any person aged **two years** and older presenting with **AWD**

  AND
  - **Severe dehydration***

  OR
  - **Dying** from AWD

In areas where a **cholera outbreak has currently been detected,** a suspected cholera case is defined as:

- Any person presenting with or dying from **AWD**

* Reference to GTFCC outbreak response field manual 2019, p.60

PROBABLE CASE DEFINITION

STILL UNDER DISCUSSION

PROBABLE CASE DEFINITION – IS IT NEEDED?

Pros	Cons
• Prioritise interventions where resources are limited • Increase visibility of RDT and giving it a "space" in cholera surveillance • Better than suspected case definition (poor PPV) to improve outbreak detection, monitoring of outbreaks • Continuity from case reporting to outbreak detection	• Interpretation difficult and prone to misuse unless denominator (e.g., number tested) are systematically provided. • A focus on reporting testing results systematically could achieve same goals. • In low prevalence settings probable cases defined as RDT positive will not be probable.
Reporting: diverging views that it may simplify or complicate	
Documentation: diverging views that it may lead to more systematic documentation of RDT results or no reporting of RDT results	

UNCERTAINTIES

- Survey result on probable case definition
  - All subgroup members indicated they can live with a probable case definition if the right wording is found (from survey)
  - Not all subgroup members think that a probable case definition is needed
- No RDT prequalified by WHO yet
- RDT PPV and NPV differs between scenarios
  - At risk countries with rare cases/ situations with low prevalence → RDT for outbreak detection? Guidance required to countries how to interpret and respond to positives, as there will be false positives; screening tool to identify suspected cases for confirmatory testing
  - Countries with persistent transmission → monitoring prevalence/ positivity rate?
  - Effective for outbreak monitoring (high prevalence, high PPV)
  - NPV generally expected to be high → how can this best be leveraged to be of practical use for countries?

STILL UNDER DISCUSSION

PROBABLE CASE DEFINITION – IS IT NEEDED?

UNDER DEVELOPMENT

A suspected cholera case

AND (options discussed)

- a reactive (positive) rapid diagnostic test (RDT), where the reported RDT performance is at least equivalent to the WHO prequalification target product profile (sensitivity = XX% ; specificity = XX%)
- a reactive (positive) rapid diagnostic test (RDT), where the reported RDT performance has a sensitivity ≥ XX% and specificity ≥ XX%
- a reactive (positive) rapid diagnostic test (RDT) in the process of prequalification by the WHO
- a reactive (positive) rapid diagnostic test (RDT) that is prequalified by the WHO

COMPONENTS TO CONSIDER

- Identify sensitivity and specificity to ensure acceptable PPV/ NPV (link with work on settings (prevalence), link to testing strategy)
- The group considered deaths and epi links to be included in the definition; discarded
  - RDT, deaths and epi-links not very comparable (e.g. in PPV and NPV), would be reporting on a wide "range of probability"
  - deaths should be counted separately

CONFIRMED CASE DEFINITION

Proposal for discussion

CONFIRMED CASE DEFINTION

CURRENT

A suspected case with *Vibrio cholerae* O1 or O139 confirmed by culture or PCR and, in countries where cholera is not present or has been eliminated, the *Vibrio cholerae* O1or O139 strain is demonstrated to be toxigenic.

PROPOSED

A suspected case infected with *Vibrio cholerae* identified by

- Culture followed by serogroup testing for O1 or O139 by agglutination tests with specific antisera

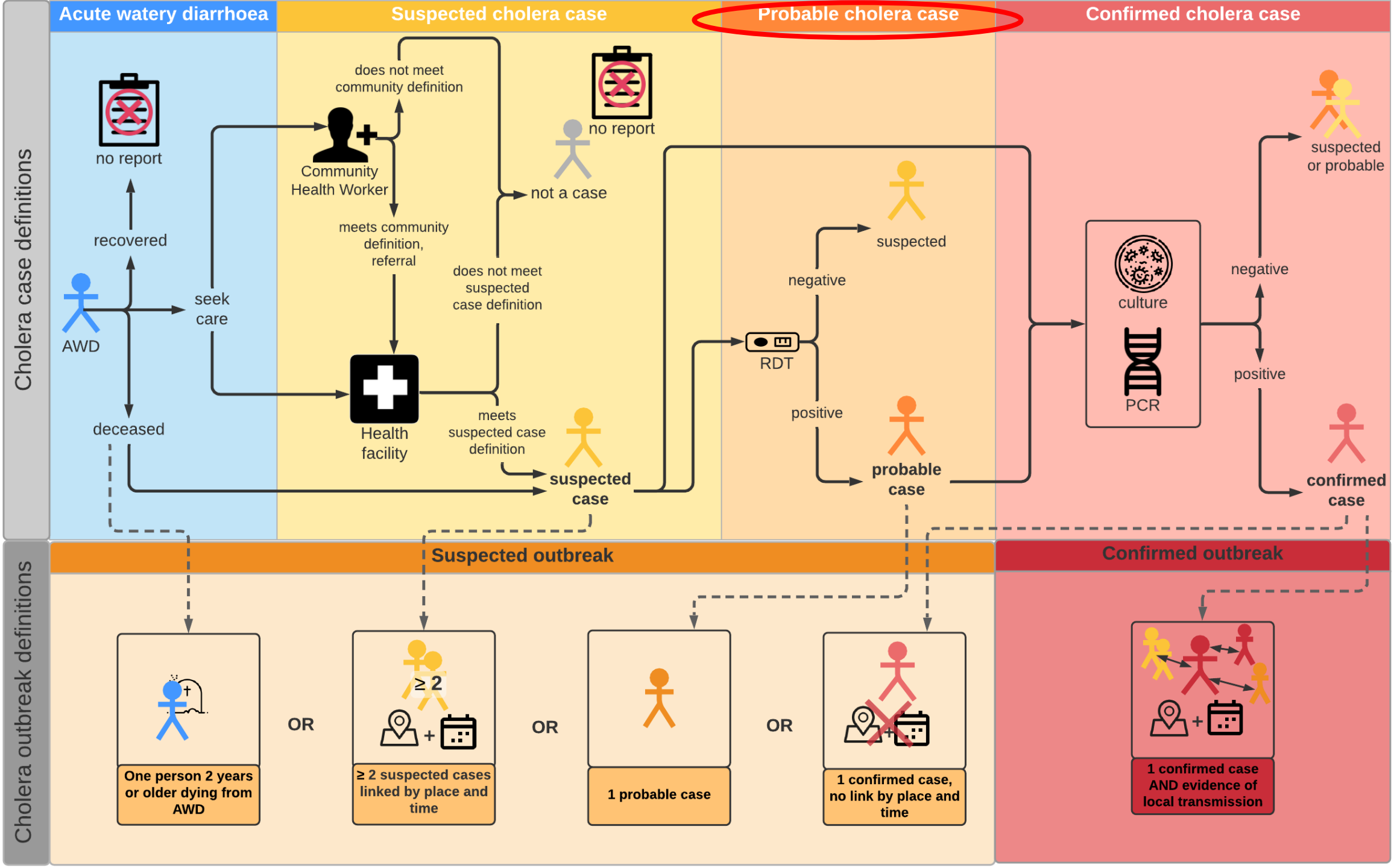
OR

- PCR targeting genes specific for *V. cholerae* species **AND** O1 or O139 antigens

AND in countries where cholera has not been detected for 3 years* or more, PCR targeting gene(s) specific for cholera toxin

* 3 years relates to current definition of elimination, this may be reviewed/ updated

SUMMARY


Cholera case definitions
Acute watery diarrhoea
Suspected cholera case
Probable cholera case
Confirmed cholera case
no report
recovered
AWD
seek care
deceased
Community Health Worker
does not meet community definition
meets community definition, referral
Health facility
does not meet suspected case definition
meets suspected case definition
no report
not a case
suspected case
RDT
negative
positive
suspected
probable case
culture
PCR
negative
positive
suspected or probable
confirmed case
Cholera outbreak definitions
Suspected outbreak
Confirmed outbreak
One person 2 years or older dying from AWD
OR
≥ 2
≥ 2 suspected cases linked by place and time
OR
1 probable case
OR
1 confirmed case, no link by place and time
1 confirmed case AND evidence of local transmission

NEXT STEPS

- Anchor case definitions within a testing strategy → When and how many suspected cases to test, by which test, and in which setting (joint work with lab working group)
- Practical application of case definitions to trigger public health action → Review and update existing guidance (investigation/ action thresholds, which actions to take, adjust recommendations to settings; joint work with outbreak subgroup)
- Prepare job aides that can be printed and displayed at health facilities, including recommended public health actions
- Define different transmission settings and recommend surveillance approaches per setting (initiated)
- Develop and agree on minimum core dataset that will allow to meet surveillance goals and support Roadmap 2030 goals
- Challenge beyond definition: accurate implementation, clear guidance, continuous training → important investments to move towards sustained control/ elimination

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THANK YOU