



GLOBAL TASK FORCE ON
CHOLERA CONTROL

RDT PERFORMANCE REVIEW

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OBJECTIVES

- ❖ Literature Reviewer RDT Performance
- ❖ Role of enrichment
 - ❖ Must, maybe or special situations only
- ❖ Use of RDT in different prevalence contexts
 - ❖ Confirmation?
- ❖ Field RDT Performance Evaluation Protocol

AIM 1: RDT PERFORMANCE METRICS: LITERATURE REVIEW

❖ Of >100; 32 Articles reviewed fully → 20 included in analysis

*Note: many of us use RDTs in our field work and do not publish data in this format

❖ Inclusion

❖ Direct Testing

❖ Crystal VC, SD Bioline, Cholkit

❖ Raw Data

❖ E.g. if presented only Latent Class Modeling analysis

❖ Exclusion

❖ Frozen specimens/not field collected

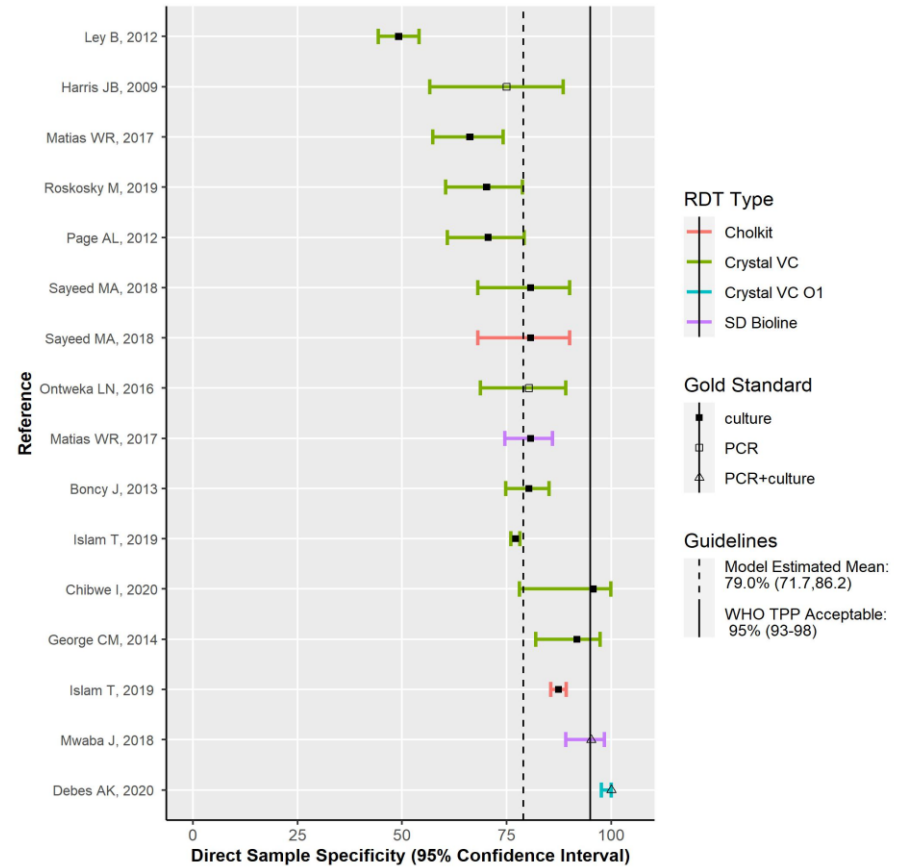
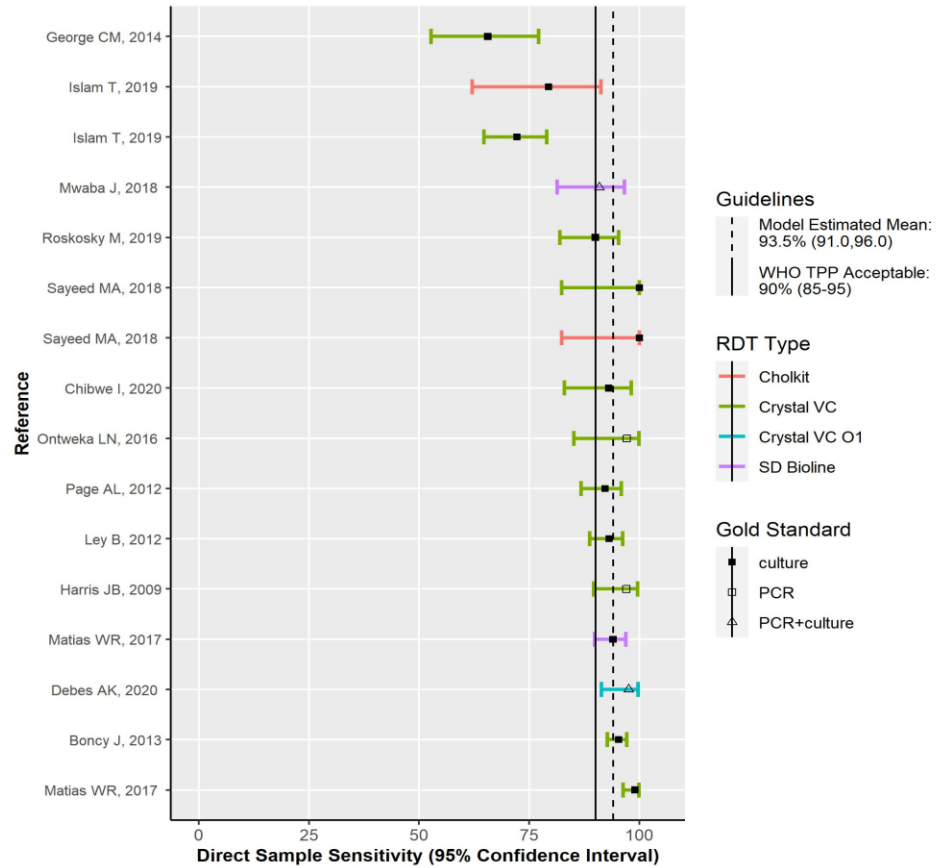
❖ Manufacturer's instructions not followed

❖ Lack of precision (e.g. low N/small sample size resulting in wide CI)

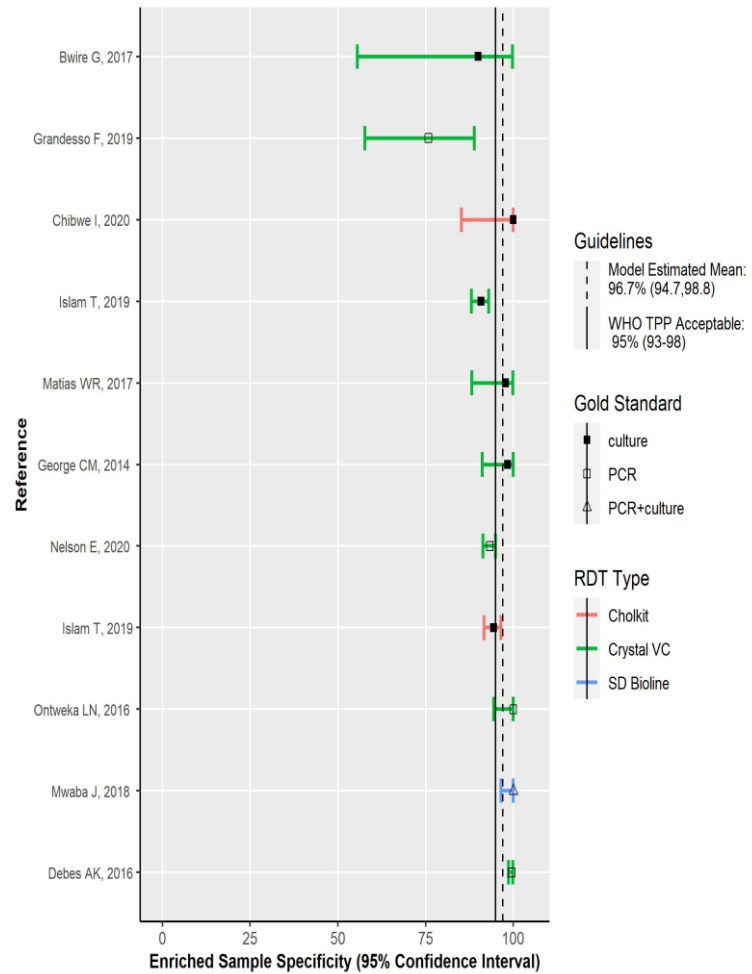
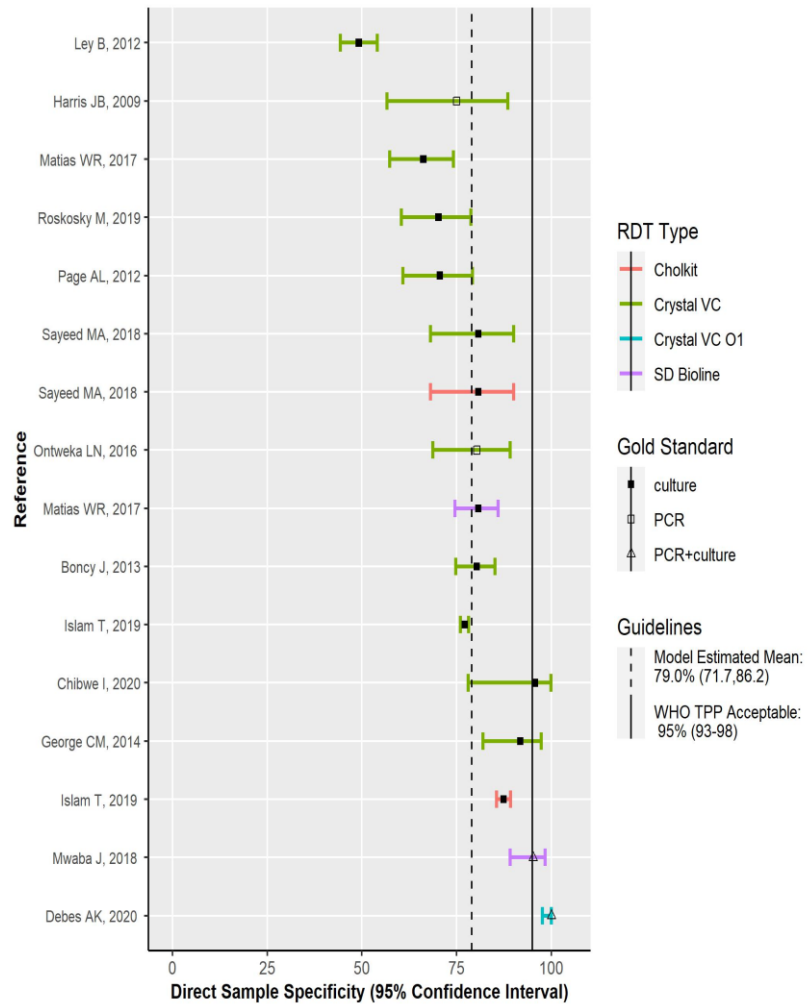
VARIABLES OF INTEREST

- ❖ Type RDT
- ❖ Country/Region where tested
- ❖ Field or lab evaluation
 - ❖ If Field, where testing conducted
 - ❖ Training/level person performing test
- ❖ Situation type:
 - ❖ early/mid/late outbreak
 - ❖ Surveillance
- ❖ Direct or Enriched
- ❖ Type of Confirmatory tests
- ❖ Antibiotic use
- ❖ Faint line considerations

Direct Sensitivity. V. Direct Specificity



Direct Specificity versus Enriched Specificity



TPP CRITERIA

Reference	RDT Type	Sample Type	Gold Standard	Sensitivity	Specificity	Both Criteria	Ref
Chibwe I, 2020	Cholkit	enriched	culture	98.3	100.0	✓	7
Mwaba J, 2018	SD Bioline	enriched	PCR+culture	95.5	100.0	✓	8
Ontweka LN, 2016	Crystal VC	enriched	PCR	86.1	100.0		9
Debes AK, 2016	Crystal VC	enriched	PCR	78.1	99.5		10
George CM, 2014	Crystal VC	enriched	culture	75.0	98.4		8
Matias WR, 2017	Crystal VC	enriched	culture	90.3	97.8	✓	11
Islam T, 2019	Cholkit	enriched	culture	66.7	94.4		12
Islam T, 2019	Crystal VC	enriched	culture	68.3	90.8		12
Nelson E, 2020	Crystal VC	enriched	PCR	95.8	93.3		13
Bwire G, 2017	Crystal VC	enriched	culture	98.9	90.0		14
Grandesso F, 2019	Crystal VC	enriched	PCR	82.1	75.8		15
Debes AK, 2020	Crystal VC O1	direct	PCR+culture	97.5	100.0	✓	(accepted w revision)
Chibwe I, 2020	Crystal VC	direct	culture	93.0	95.7	✓	7
Mwaba J, 2018	SD Bioline	direct	PCR+culture	90.9	95.2	✓	8
George CM, 2014	Crystal VC	direct	culture	65.6	91.8		8
Islam T, 2019	Cholkit	direct	culture	79.4	87.4		12
Islam T, 2019	Crystal VC	direct	culture	72.2	77.1		12
Sayeed MA, 2018	Cholkit	direct	culture	100.0	80.7		16
Sayeed MA, 2018	Crystal VC	direct	culture	100.0	80.7		16
Matias WR, 2017	SD Bioline	direct	culture	94.0	80.7		11
Matias WR, 2017	Crystal VC	direct	culture	99.0	66.2		11
Ontweka LN, 2016	Crystal VC	direct	PCR	97.1	80.3		9
Boncy J, 2013	Crystal VC	direct	culture	95.3	80.3		16
Harris JB, 2009	Crystal VC	direct	PCR	97.0	75.0		17

CLINICAL CASE DEF + RDT \geq CULTURE?

- ❖ What is a sufficient probability to have clinical case def + RDT sufficient to declare outbreak?
- ❖ Likelihood of RDT availability?
- ❖ Situation specific?

PREVALENCE

Population: persons presenting to health facility with clinically suspected cholera, different true prevalence scenarios

Events = Cases which receive RDT positive and are actually Cholera positive

Trials = Cases which receive RDT positive

Probability of Success: The probability of a case testing RDT+ and being Cholera+ (This is our PPV)

USE OF RDT IN DIFFERENT SITUATIONS

<u>Situation/use</u>	<u>1. Detect / Confirm</u>	<u>2. End of outbreak</u>	<u>3. Outbreak Monitoring</u>	<u>4. Burden of Disease Surveillance</u>
Evaluation	Field	Field	Lab	Lab
Locale	Health Facility	Health Facility/Lab	Lab	Lab
CATI	Yes	Yes	No	No
Title	Outbreak	Outbreak	Surveillance	Surveillance
Time of Outbreak	Beginning	Beginning or end	During?	any
Tech Level	Lab or HF staff	HF staff	Lab	Lab
Trained or untrained	Trained or untrained	Trained	Trained	Trained
Endemic v. Non endemic	Endemic (Uganda)/ Non-Endemic (S. America? Chad?)	Endemic (Haiti)	DRC (2011-2012)/Kenya (2016-2020)	endemic (Bangladesh)/non-endemic (Haiti 2010)
Specimen	Fresh/swab (swab needs APW)	Fresh	Fresh/Swab	swab/frozen/(any)
Processing	Direct/confirmed w enriched	Enriched	Direct	Enriched
Desired	High PPV (high NPV also)	High NPV	High NPV	High NPV

THE PROBABILITY OF AT LEAST ONE TRUE CHOLERA POSITIVE AMONG 10 PATIENTS TESTED VIA RDT BY PREVALENCE.

Prevalence	Probability of cholera positive based on case definition/among 10 people	Number of positive test out of ten tests										
		0	1	2	3	4	5	6	7	8	9	10
0.1	0.65132156	0.0870	0.3836	0.5838	0.7190	0.8103	0.8719	0.9135	0.9416	0.9606	0.9734	0.9820
0.2	0.892625818	0.1842	0.6060	0.8097	0.9081	0.9556	0.9786	0.9896	0.9950	0.9976	0.9988	0.9994
0.3	0.971752475	0.2929	0.7483	0.9104	0.9681	0.9886	0.9960	0.9986	0.9995	0.9998	0.9999	1.0000
0.4	0.993953382	0.4137	0.8442	0.9586	0.9890	0.9971	0.9992	0.9998	0.9999	1.0000	1.0000	1.0000
0.5	0.999023438	0.5465	0.9100	0.9821	0.9965	0.9993	0.9999	1.0000	1.0000	1.0000	1.0000	1.0000

THE PROBABILITY OF AT LEAST ONE TRUE CHOLERA AMONG X PATIENTS TESTED VIA RDT

The probability of at least one true		Number of tests									
		1	2	3	4	5	6	7	8	9	10
Number of positive tests	0	0.034061	0.066962	0.098742	0.12944	0.159093	0.187735	0.215401	0.242126	0.26794	0.292875
	1	0.65614	0.667853	0.679166	0.690094	0.70065	0.710846	0.720695	0.730208	0.739398	0.748274
	2	NA	0.881761	0.885788	0.889678	0.893436	0.897065	0.900572	0.903958	0.907229	0.910389
	3	NA	NA	0.959342	0.960727	0.962065	0.963357	0.964605	0.965811	0.966975	0.9681
	4	NA	NA	NA	0.986019	0.986496	0.986956	0.9874	0.987829	0.988244	0.988644
	5	NA	NA	NA	NA	0.995193	0.995356	0.995515	0.995667	0.995815	0.995957
	6	NA	NA	NA	NA	NA	0.998347	0.998403	0.998458	0.99851	0.998561
	7	NA	NA	NA	NA	NA	NA	0.999432	0.999451	0.99947	0.999488
	8	NA	NA	NA	NA	NA	NA	NA	0.999805	0.999811	0.999818
	9	NA	NA	NA	NA	NA	NA	NA	NA	0.999933	0.999935
	10	NA	NA	NA	NA	NA	NA	NA	NA	NA	0.999977

*cholera case situation where prevalence defined as true positives among cholera suspect cases presenting to the health facility is 40%.

RDT FIELD EVALUATION PROTOCOL

- ❖ Situation Specific Protocol
 - ❖ Outbreak monitoring?
- ❖ Defined Sample size?
- ❖ Given lack of Specificity in Direct RDT use – do we recommend enrichment?
- ❖ Options for confirmation
 - ❖ culture/PCR
 - ❖ PCR from specimen type? Where must be PCR be performed?
- ❖ Different person for field application of RDT and lab confirmation?
 - ❖ Blinding to results?
- ❖ Who will be supporting this effort?
 - ❖ Country? Collaborator? Manufacturer?