

# 1 Appendix S4: Summary of Findings for individual studies

## 2 Immunologically-based tests: Crystal VC

3 *Table 1. Sensitivity and specificity results for individual studies reporting on Crystal VC*

<b>Test: Crystal VC (Institut Pasteur/Spain Diagnostics)</b>				
<b>Intended Location: Field</b>				
<b>Target: lipopolysaccharide antigen of V. cholerae O1 and O139</b>				
<b>Reference test: Bacterial Culture</b>				
<b>Sample type: Stool</b>				
<b>Study ID</b>	<b>n</b>	<b>Enrichment details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>				
George 2014	125		65.6 (52.7-77.1)	91.8 (81.9-97.3)
Page 2012 (lab technicians)	256		93.0 (88.3-96.6)	85.2 (69.8-99.2)
Page 2012 (clinicians)	255		93.8 (89.2-97.2) <sup>1,4</sup>	78.4 (59.6-98.7) <sup>1,4</sup>
Ley 2012	622		93.1 (88.7-96.2) <sup>4</sup>	49.2 (44.3-54.1) <sup>4</sup>
Mukherjee 2010	212		91.70	72.90
Islam 2019	5865		72.2 (64.6-78.9)	77.1 (75.9-78.2)
Sayeed 2018	76		97.5 (87.5-99.9) <sup>4</sup>	98.4 (92.0-99.9) <sup>4</sup>
Matias 2017	511		98.6 (96.5-99.6)	71.1 (64.6-76.9)
<i>Enriched samples</i>				
George 2014	125	6h enrichment in APW	75 (62.6-85)	98.4 (91.2-100)
Bwire 2017	102	6h enrichment in APW	98.9 (94.09-99.97)	90 (55.5-99.75)
Islam 2019	614	Overnight enrichment in APW	68.3 (51.9-81.9)	90.8 (88.1-92.9)
<b>Sample type: Water</b>				
<i>Enriched samples</i>				
Rashid 2017 <sup>2</sup>	1648	18h enrichment in APW	65.6 (55.2-75)	99.6 (99.2-99.9)
Chakraborty 2013	550	24h incubation in APW	87 (74.9-94.3) <sup>1</sup>	100 (99-100) <sup>1</sup>

<b>Reference test: PCR</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Ontweka 2016	100		94.4 (81.3-99.3)	79.7 (67.8-88.7)
Harris 2009	99		97 (88.7-99.5)	75 (56.2-87.9) <sup>3</sup>
<i>Enriched Samples</i>				
Ontweka 2016	100	4-6h enrichment in APW	86.1 (70.5-95.3)	100 (94.4-100)
Debes 2016	673	24h enrichment in APW	89.3 (71.8-97.7) <sup>3</sup>	98.9 (97.8-99.6) <sup>3</sup>
<b>Reference test: Culture or PCR</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Page 2012 (lab technicians)	256		88.2 (82.6-92.4)	88.6 (78.7-94.9)
Page 2012 (clinicians)	255		91.9 (87-95.4)	82.6 (71.6-90.7)

<sup>1</sup>Confidence Intervals not provided; calculated from raw numbers

<sup>2</sup>Combined supply and stored water

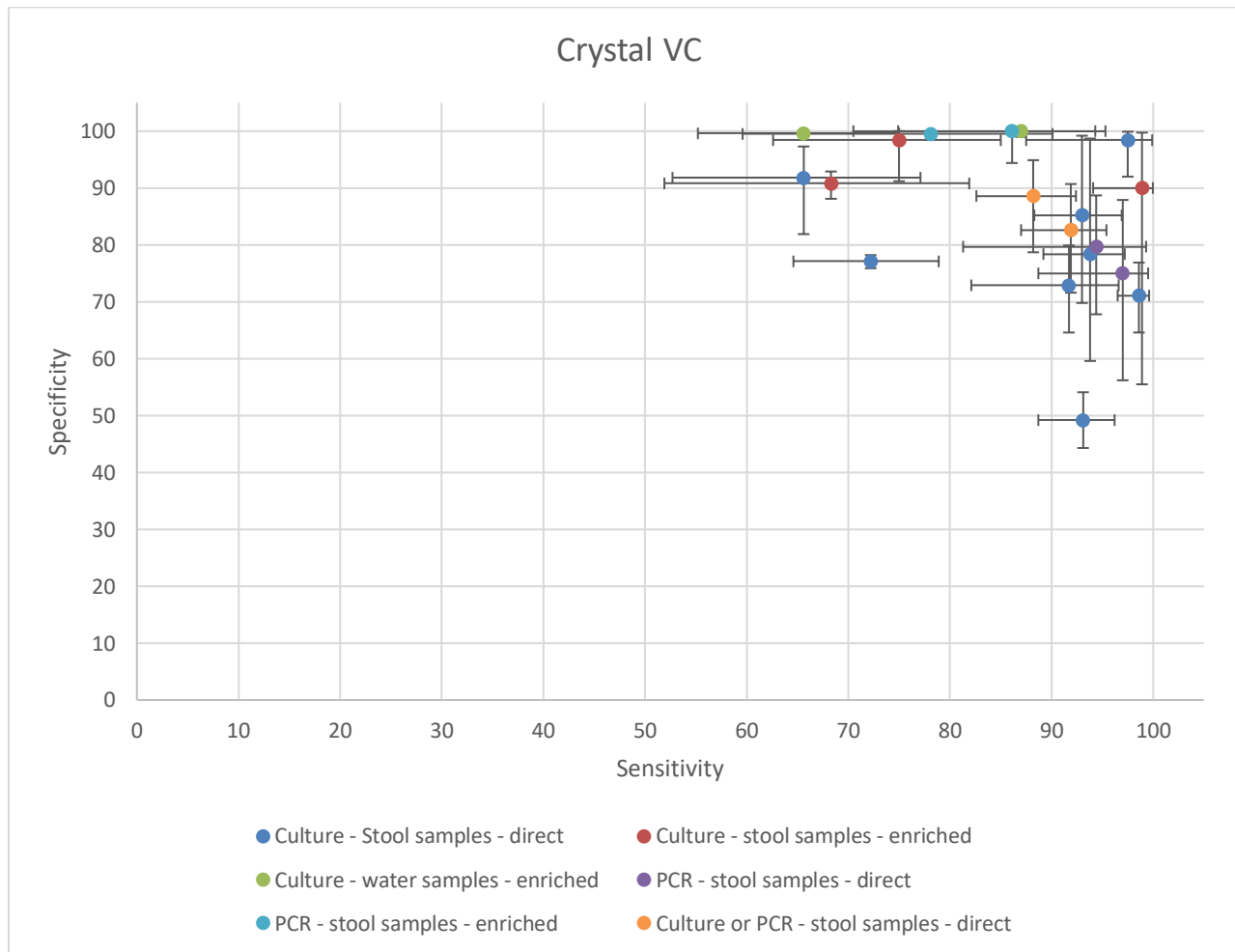
<sup>3</sup>Sensitivity and specificity re-calculated using raw numbers due to errors in paper

<sup>4</sup> Estimated by Bayesian Latent Modelling

4

5

6 Figure 1. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to 'reference test – sample type – enrichment  
7 status' as per the legend below. Error bars show 95% Confidence Intervals.



8

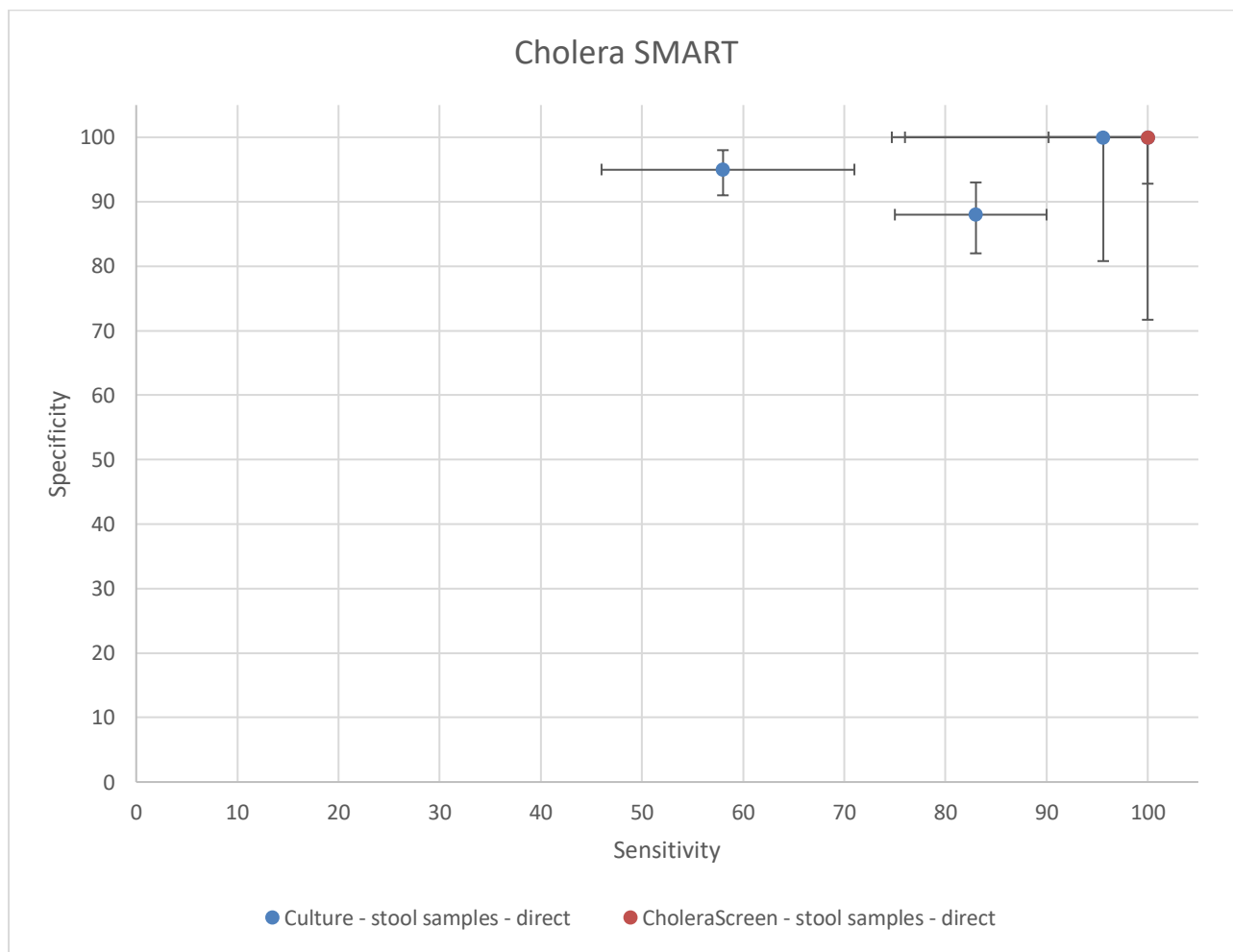
9 **Immunologically-based tests: CholeraSMART**

10 *Table 2. Sensitivity and specificity results for individual studies reporting on Cholera SMART*

<b>Test: Cholera SMART (New Horizons Diagnostics)</b>				
<b>Intended Location: Field</b>				
<b>Target: Antigen A of V. cholerae O1 lipopolysaccharide</b>				
<b>Reference test: Bacterial Culture</b>				
<b>Sample type: Stool</b>				
<b>Study ID</b>	<b>n</b>	<b>Enrichment details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>				
Bolaños 2004	28		100 (74.7-100) <sup>1</sup>	100 (71.7-100) <sup>1</sup>
Hasan 1994b (Bangladesh)	44		95.6 (76-99.8) <sup>1</sup>	100 (80.8-100) <sup>1</sup>
Kalluri 2006 (lab technicians)	254		83 (75-90)	88 (82-93)
Kalluri 2006 (field technicians)	212		58 (46-71)	95 (91-98)
<b>Reference test: Cholera Screen</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Hasan 1994b (Mexico)	108		100 (90.2-100) <sup>1</sup>	100 (92.8-100) <sup>1</sup>

11 <sup>1</sup>Confidence Intervals not provided; calculated from raw numbers

12 Figure 2. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to 'reference test – sample type – enrichment  
13 status' as per the legend below. Error bars show 95% Confidence Intervals



14

15

16 **Immunologically-based tests: IP Dipstick**

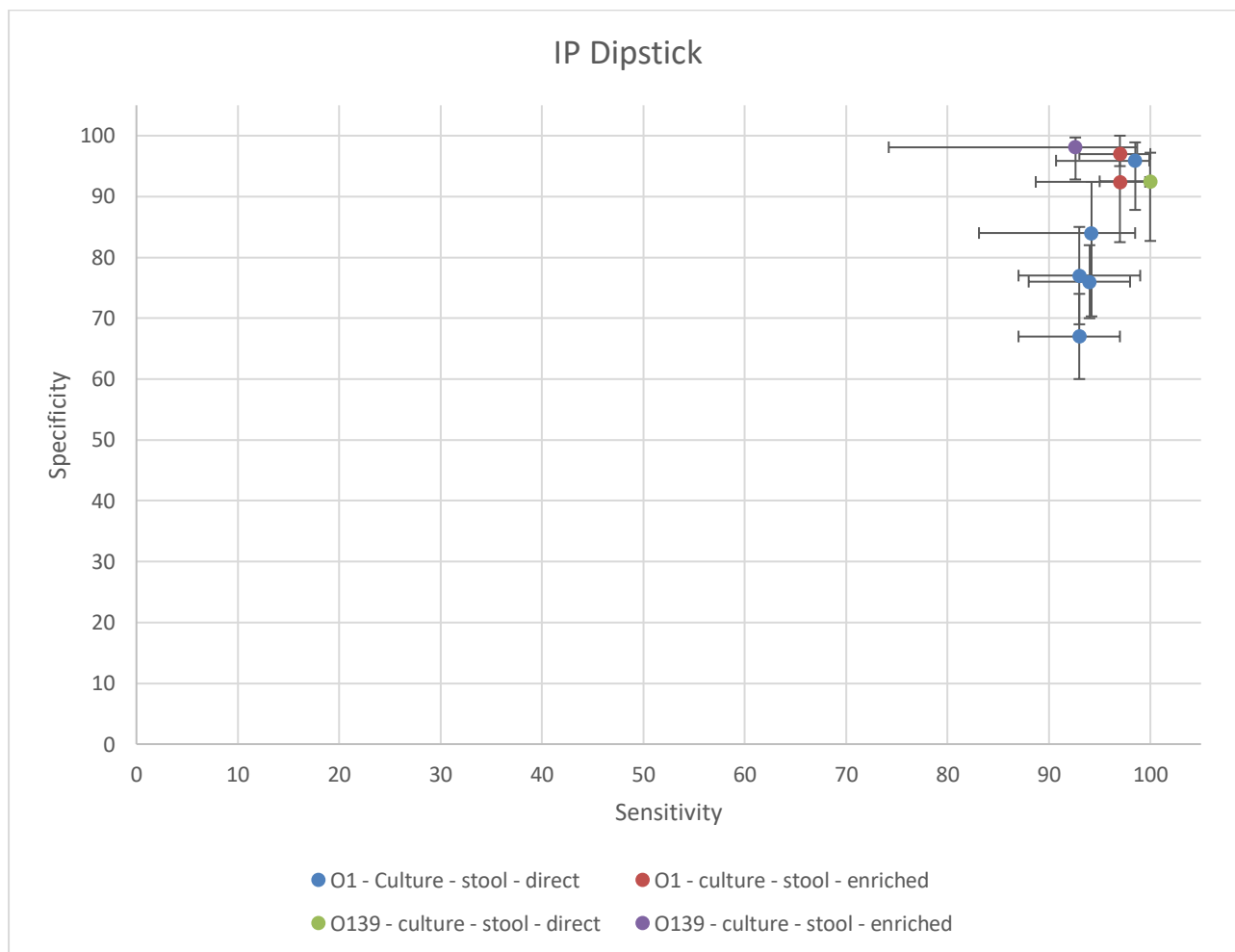
17 *Table 3. Sensitivity and specificity results for individual studies reporting on IP Dipstick*

<b>Test: IP Dipstick (Institut Pasteur)</b>				
<b>Intended Location: Field</b>				
<b>Target: V. cholerae O1 lipopolysaccharide</b>				
<b>Reference test: Bacterial Culture</b>				
<b>Sample type: Stool</b>				
<b>Study ID</b>	<b>n</b>	<b>Enrichment details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>				
Wang 2006	172		93 (87-99)	77 (69-85)
Kalluri 2006 (field technicians)	NR		93 (87-97)	67 (60-74)
Kalluri 2006 (lab technicians)	NR		94 (88-98)	76 (70-82)
Nato 2003 (Madagascar)	140		98.5 (90.7-99.9) <sup>1</sup>	95.9 (87.8-98.9) <sup>1</sup>
Nato 2003 (Bangladesh)	102		94.2 (83.1-98.5) <sup>1</sup>	84 (70.3-92.4) <sup>1</sup>
<i>Enriched Samples</i>				
Wang 2006	219	6h in APW	97 (93-100)	97 (95-100)
Bhuiyan 2003	133	4h in APW	97 (88.7-99.5) <sup>1</sup>	92.4 (82.5-97.2) <sup>1</sup>
<b>Target: V. cholerae O139 lipopolysaccharides</b>				
<b>Reference test: Bacterial Culture</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Nato 2003 (Bangladesh)	158		100 (95-100) <sup>1</sup>	92.5 (82.7-97.2) <sup>1</sup>
<i>Enriched Samples</i>				
Bhuiyan 2003	134	4h in APW	92.6 (74.2-98.7) <sup>1</sup>	98.1 (92.8-99.7) <sup>1</sup>

<sup>1</sup> Confidence Intervals not provided; calculated from raw numbers

18

19 Figure 3. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to 'serotype - reference test – sample type –  
20 enrichment status' as per the legend below. Error bars show 95% Confidence Intervals



21

22

23 **Immunologically-based tests: Cholera Screen**

24 *Table 4. Sensitivity and specificity results for individual studies reporting on Cholera Screen*

<b>Test: Cholera Screen</b>				
<b>Intended Location: Field</b>				
<b>Target: 'A' factor of V. cholerae lipopolysaccharide O1</b>				
<b>Reference test: Bacterial Culture</b>				
<b>Sample type: Stool</b>				
<b>Study ID</b>	<b>n</b>	<b>Enrichment details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>				
Colwell 1992 (Guatemala)	17		100 (65.5-100) <sup>1</sup>	42.9 (11.8-79.8) <sup>1</sup>
Colwell 1992 (Bangladesh)	77		98 (88-99.9) <sup>1</sup>	77.8 (57.3-90.6) <sup>1</sup>
Carillo 1994	99		98.8 (92.4-99.9) <sup>1</sup>	22.2 (7.4-48.1) <sup>1</sup>
Islam 1994	57		100 (39.58-100) <sup>1</sup>	100 (91.58-100) <sup>1</sup>

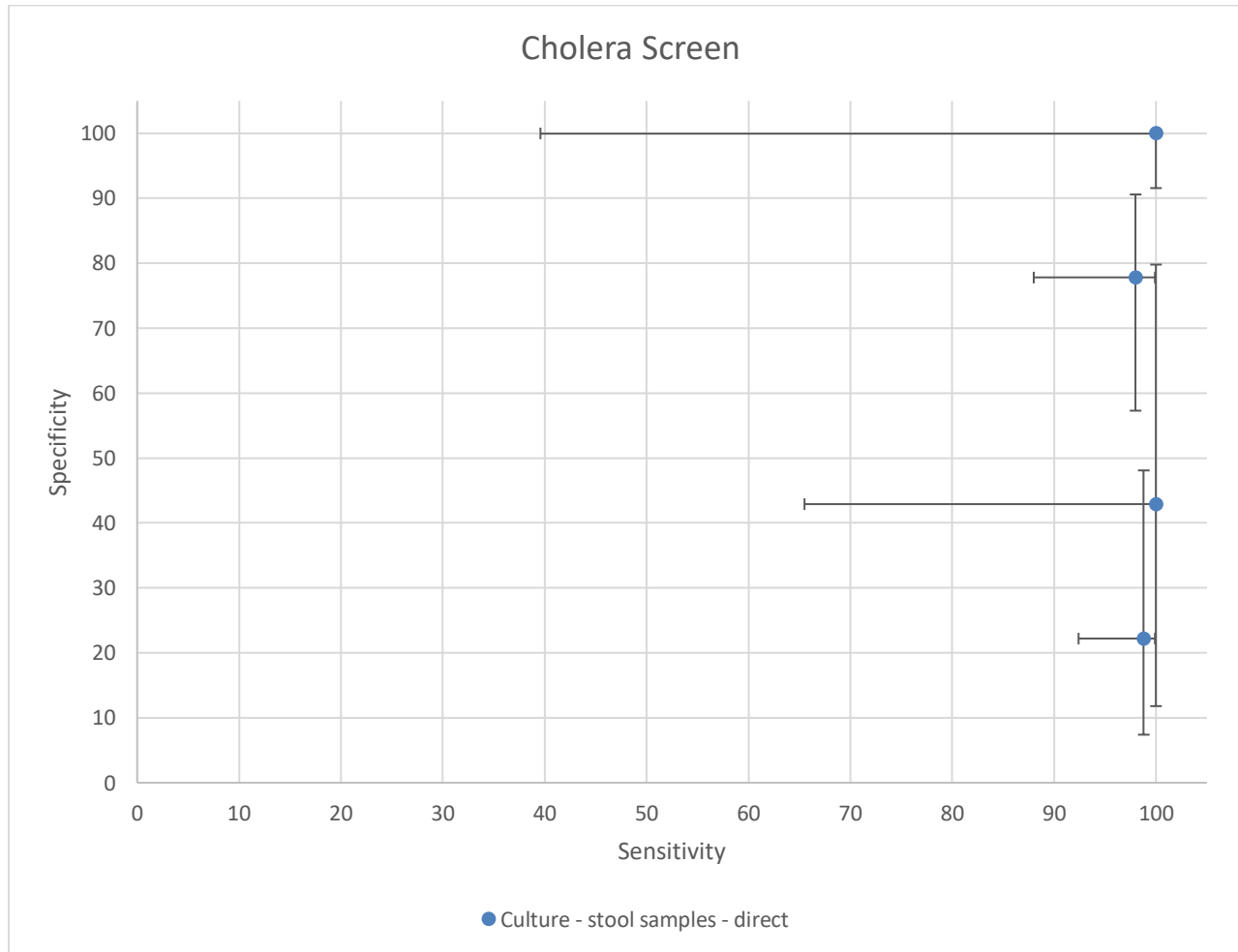
<sup>1</sup> Confidence Intervals not provided; calculated from raw numbers

25



26 Figure 4. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to 'reference test – sample type – enrichment  
27 status' as per the legend below. Error bars show 95% Confidence Intervals

28



29

30

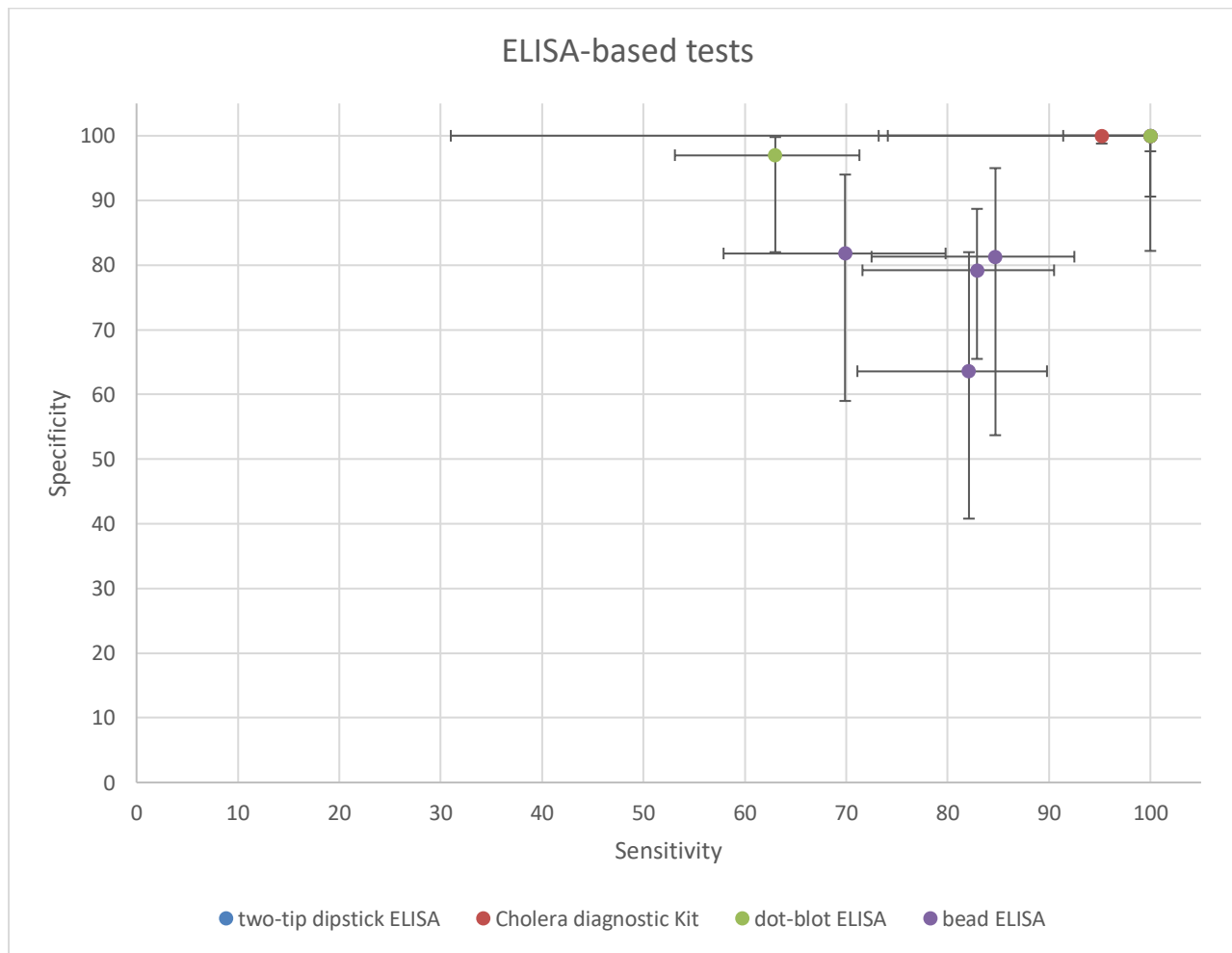
31 **Immunologically-based tests: ELISA-based tests**32 *Table 5. Sensitivity and specificity results for individual studies reporting on ELISA-based tests*

<b>Test: ELISA-based tests - two-tip dipstick sandwich ELISA</b>				
<b>Intended Location: field</b>				
<b>Target: V. cholerae O1 and O139 (Stool); Ctx b and ompw of O1 and O139 (water)</b>				
<b>Reference test: Culture</b>				
<b>Sample type: Stool or water</b>				
<b>Study ID</b>	<b>n</b>	<b>Enrichment and sub-group details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Enriched Samples</i>				
Tuteja 2007 (Stool samples)	75	4h in APW	100 (91.4-100) <sup>1</sup>	100 (82.2-100) <sup>1</sup>
Tuteja 2007 (Water samples)	50	4h in APW	100 (31-100) <sup>1</sup>	100 (90.6-100) <sup>1</sup>
<b>Test: ELISA-based tests - Cholera diagnostic kit (Mab-based dot-blot ELISA)</b>				
<b>Intended Location: field</b>				
<b>Target: V cholerae O1 antigen A</b>				
<b>Reference test: Culture</b>				
<b>Sample type: Stool</b>				
<i>Enriched Samples</i>				
Supawat 1994 (Diarrhoeic patients)	211	4h in APW	100 (73.2-100) <sup>1</sup>	100 (97.6-100) <sup>1</sup>
Supawat 1994 (Household contacts)	415	4h in APW	95.2 (74.1-99.8) <sup>1</sup>	100 (98.8-100) <sup>1</sup>
<b>Test: ELISA-based tests - dot-blot ELISA</b>				
<b>Intended Location: laboratory</b>				
<b>Target: V. cholerae O1 antigen or V. cholerae O139 antigen</b>				
<b>Reference test: Culture</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Chaicumpa 1995	147	O1 antigen	63 (53.1-71.3) <sup>1</sup>	97 (82-99.8) <sup>1</sup>

<i>Enriched Samples</i>				
Chaicumpa 1998	6497	O139 antigen	100 (89.6-100) <sup>1</sup>	99.95 (99.8-99.9) <sup>1</sup>
<b>Test: ELISA-based tests - bead ELISA</b>				
<b>Intended Location: laboratory</b>				
<b>Target: Cholera toxin</b>				
<b>Reference test: Culture</b>				
<b>Sample type: Stool</b>				
<i>Direct Samples</i>				
Ramamurthy 1996 (PAb-based)	95		82.1 (71.1-89.8) <sup>1</sup>	63.6 (40.8-82) <sup>1</sup>
Ramamurthy 1996 (MAb-based)	95		69.9 (57.9-79.8) <sup>1</sup>	81.8 (59-94) <sup>1</sup>
Ramamurthy 1993	123		82.9 (71.6-90.5) <sup>1</sup>	79.2 (65.5-88.7) <sup>1</sup>
Ramamurthy 1992	75		84.7 (72.5-92.5) <sup>1</sup>	81.3 (53.7-95) <sup>1</sup>

<sup>1</sup> Confidence Intervals not provided; calculated from raw numbers

34 Figure 5. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to type of ELISA test, as per the legend below.  
35 Error bars show 95% Confidence Intervals



36

37

38 **Other tests**39 *Table 6. Sensitivity and specificity results for individual studies reporting on other tests not mentioned above*

<b>Test: Other tests</b>						
<b>Intended Location: Field</b>						
<b>Reference test: Culture</b>						
<b>Sample type: Stool</b>						
<b>Study</b>	<b>Test name</b>	<b>Target</b>	<b>n</b>	<b>Enrichment and sub-group details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>						
Kalluri 2006	Medicos Cholera Dip Stick	Unknown	304	Field technicians	84 (77-91)	79 (73-85)
Kalluri 2006	Medicos Cholera Dip Stick	Unknown	303	Lab technicians	88 (81-94)	80 (73-95)
Bolaños 2004	PDK (Pathogen Detection Kit)	Antigen A of <i>V. cholerae</i> O1 lipopolysaccharide	27	High probability specimens	100 (71.7-100) <sup>1</sup>	86 (56.2-97.5) <sup>1</sup>
Qadri 1995	Bengal SMART	A' factor of <i>V. cholerae</i> O139	189		97 (89.5-99.1) <sup>1</sup>	100 (95.5-100) <sup>1</sup>
Hasan 1995	BengalScreen	lipopolysaccharide antigen of <i>V. cholerae</i> O139	35		95 (71.9-99.7) <sup>1</sup>	100 (75.9-100) <sup>1</sup>
Hasan 1995	Bengal DFA	lipopolysaccharide antigen of <i>V. cholerae</i> O139	35		100 (79.1-100) <sup>1</sup>	100 (75.9-100) <sup>1</sup>
Qadri 1994	co-agglutination test (COAT)	lipopolysaccharide antigens of <i>V. cholerae</i> O139	230		92 (84.1-96.5) <sup>1</sup>	100 (96.7-100) <sup>1</sup>
Carillo 1994	latex agglutination test	A' factor of <i>V. cholerae</i> lipopolysaccharide O1	100		100 (94.4-100) <sup>1</sup>	33 (14.4-58.8) <sup>1</sup>
Islam 2019	Cholkit	lipopolysaccharide antigen of <i>V. cholerae</i> O1	1355		79.4 (62.1-91.3)	87.4 (85.5-89.1)
Sayeed 2018	Cholkit	lipopolysaccharide antigen of <i>V. cholerae</i> O1	76		97.7 (88.4-99.9) <sup>2</sup>	96.5 (88.6-99.6) <sup>2</sup>
Matias 2017	Artron RDT	<i>Vibrio cholerae</i> O1 and O139	129		98.6 (92.7-100)	69.1 (55.2-80.9)
Matias 2017	SD Bioline	<i>V. cholerae</i> O1 and O139 antigens	451		81.1 (75.6-85.8)	92.8 (88.4-95.9)

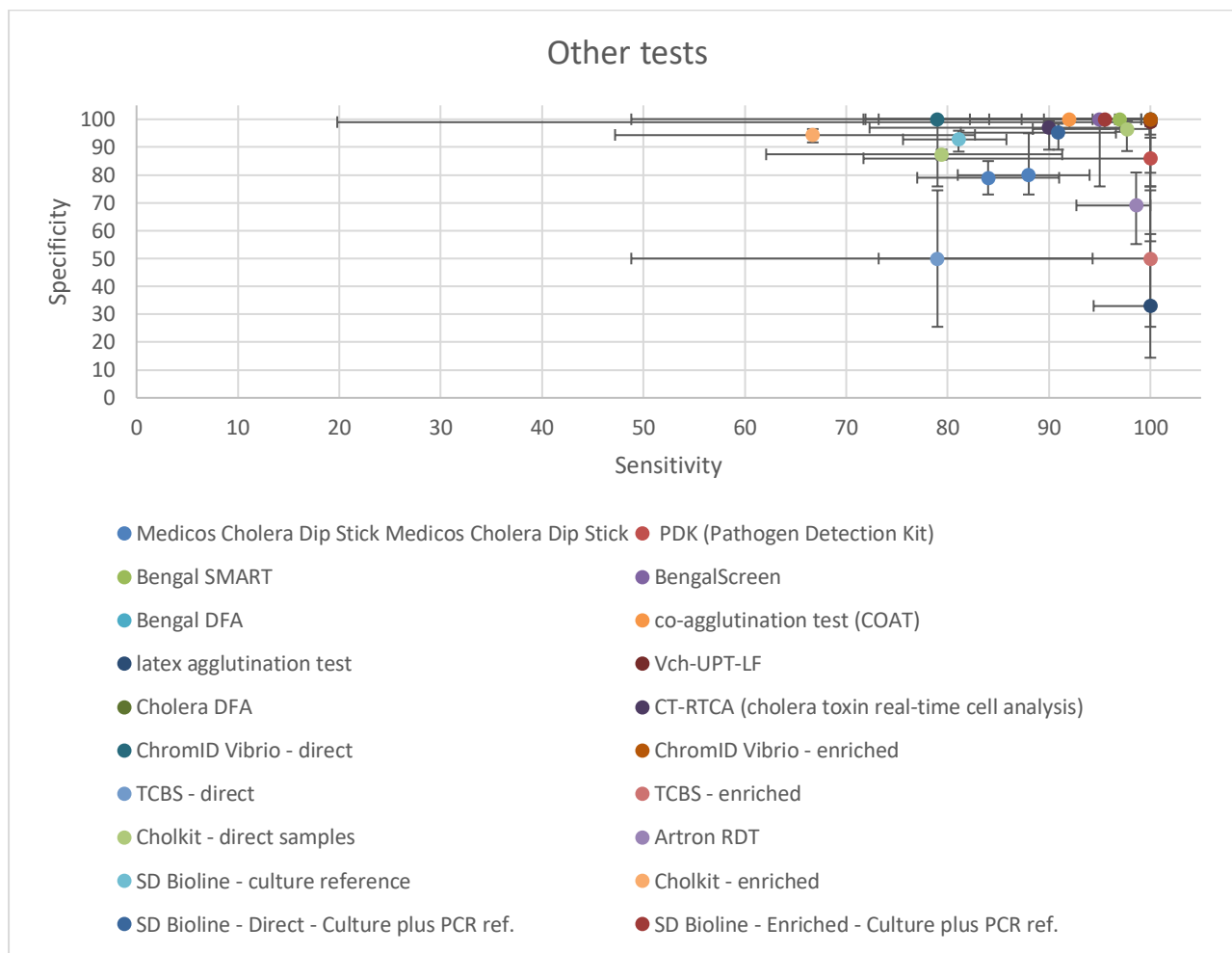
<i>Enriched Samples</i>						
Islam 2019	Cholkit	lipopolysaccharide antigen of V. cholerae O1	424		66.7 (47.2-82.7)	94.4 (91.7-96.5)
<b>Reference test: Culture plus PCR</b>						
<b>Sample type: Stool</b>						
<i>Direct Samples</i>						
Mwaba 2018	SD Bioline	V. cholerae O1 and O139 antigens	170		90.9 (81.3-96.6)	95.2 (89.1-98.4)
<i>Enriched Samples</i>						
Mwaba 2018	SD Bioline	V. cholerae O1 and O139 antigens	170		95.5 (87.3-99.1)	100 (96.5-100)
<b>Reference test: Combination</b>						
<b>Sample type: Water</b>						
<i>Direct Samples</i>						
Hao 2017	Vch-UPT-LF	V. cholerae O1 or O139	96	O1	100 (71.7-100) <sup>1</sup>	100 (94.5-100) <sup>1</sup>
Hao 2017	Vch-UPT-LF	V. cholerae O1 or O139	96	O139	100 (19.8-100) <sup>1</sup>	99 (93.4-99.9) <sup>1</sup>
<b>Test: Other tests</b>						
<b>Intended Location: Laboratory</b>						
<b>Reference test: Culture</b>						
<b>Sample type: Stool</b>						
<i>Direct Samples</i>						
Hasan 1994a	Cholera DFA	A' factor of V. cholerae lipopolysaccharide O1	44		100 (82.2-100) <sup>1</sup>	100 (80.8-100) <sup>1</sup>
<b>Reference test: Combination</b>						
<b>Sample type: Stool</b>						
<i>Direct Samples</i>						
Jin 2013	CT-RTCA (cholera toxin real-time cell analysis)	Cholera toxin	100		90 (72.3-97.4) <sup>1</sup>	97 (89.1-99.5) <sup>1</sup>
Eddabra 2011	ChromID Vibrio	V. cholerae bacterial strains	30		79 (48.8-94.3) <sup>1</sup>	100 (75.9-100) <sup>1</sup>

Eddabra 2011	TCBS	V. cholerae bacterial strains	30		79 (48.8-94.3) <sup>1</sup>	50 (25.5-74.5) <sup>1</sup>
<i>Enriched Samples</i>						
Eddabra 2011	ChromID Vibrio	V. cholerae bacterial strains	30	Yes - 5-8h in APW	100 (73.2-100) <sup>1</sup>	100 (75.9-100) <sup>1</sup>
Eddabra 2011	TCBS	V. cholerae bacterial strains	30	Yes - 5-8h in APW	100 (73.2-100) <sup>1</sup>	50 (25.5-74.5) <sup>1</sup>

<sup>1</sup> Confidence Intervals not provided; calculated from raw numbers

<sup>2</sup> Result estimated using Bayesian Latent Modelling

41 Figure 6. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to type test, as per the legend below. Error bars  
 42 show 95% Confidence Intervals



43  
 44  
 45



46 **PCR-based tests**47 *Table 7. Sensitivity and specificity results for individual studies reporting on PCR-based tests*

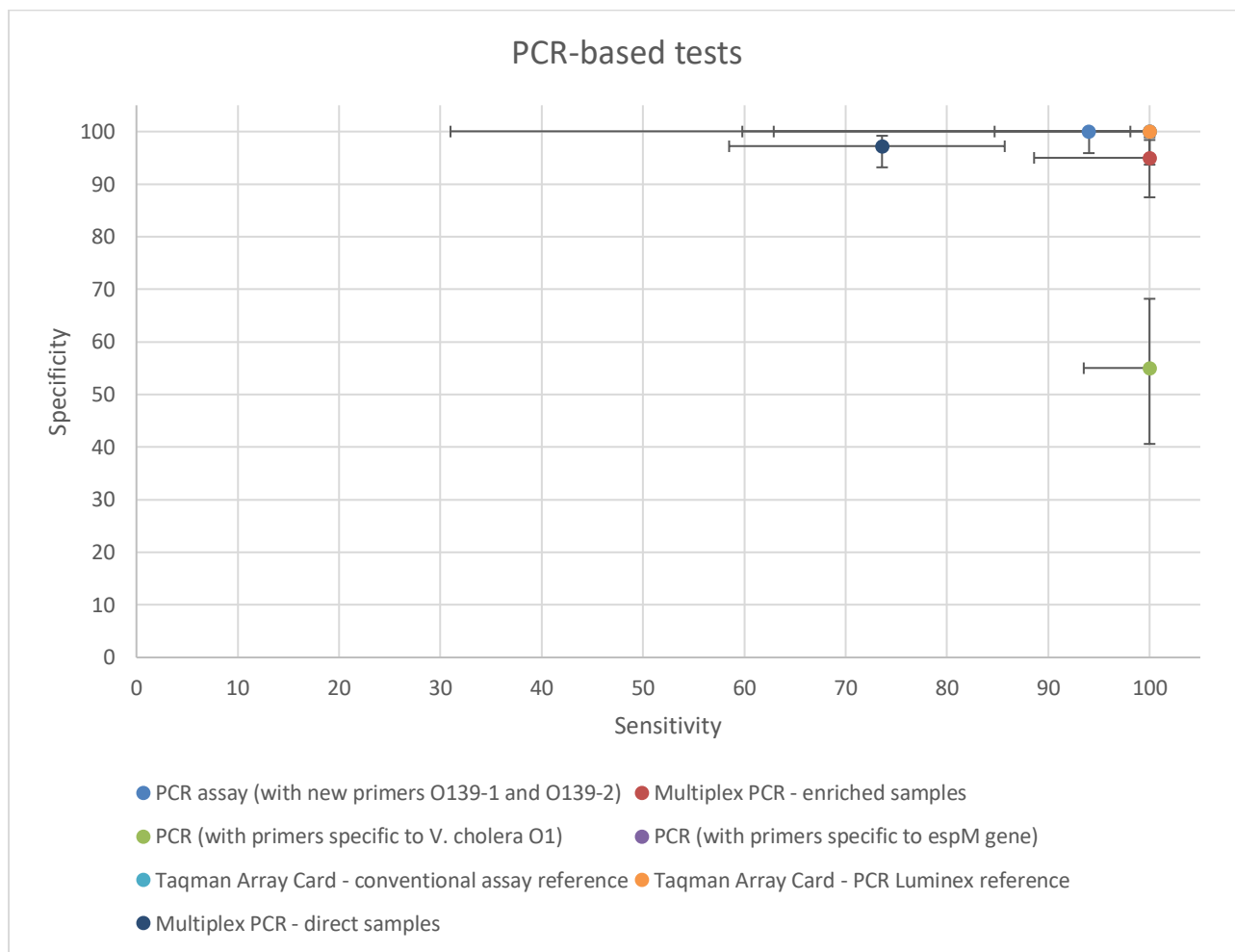
<b>Test: PCR-based tests</b>						
<b>Intended Location: laboratory</b>						
<b>Reference test: Culture</b>						
<b>Sample type: Stool</b>						
<b>Study</b>	<b>Test name</b>	<b>Target</b>	<b>n</b>	<b>Enrichment and sub-group details (if relevant)</b>	<b>Sensitivity</b>	<b>Specificity</b>
<i>Direct Samples</i>						
Albert 1997	PCR assay (with new primers O139-1 and O139-2)	V. cholerae O139	180	Undiluted sample	94 (84.7-98.1) <sup>1</sup>	100 (95.9-100) <sup>1</sup>
Sayed 2018	Multiplex PCR	V. cholerae O1 and O139 specific rfb genes and cholera toxin gene ctxA	76		73.6 (58.5-85.7) <sup>2</sup>	97.2 (93.2-99.2) <sup>2</sup>
<i>Enriched Samples</i>						
Hoshino 1998	Multiplex PCR (with: O139-rfb primers - O139F-2, O139R-2; O1-rfb primers - O1F-2, O1R-2; cholera toxin primers - VCT1, VCT2)	V. cholerae O1 and O139 rfb-specific genes and the ctxA gene.	121	18h in APW	100 (88.6-100) <sup>1</sup>	95 (87.5-98.4) <sup>1</sup>
Ramamurthy 1993	PCR (with primers specific to V. cholera O1)	Cholera Toxin gene of V. cholerae O1.	123	18h in APW	100 (93.5-100) <sup>1</sup>	55 (40.6-68.2) <sup>1</sup>
<b>Reference test: Culture</b>						
<b>Sample type: Water</b>						
<i>Enriched Samples</i>						
Momtaz 2013	PCR (with primers specific to espM gene)	espM gene of V. cholerae	448	6-8h in APW	100 (31-100) <sup>1</sup>	100 (98.9-100) <sup>1</sup>
<b>Reference test: Conventional assay</b>						
<b>Sample type: Stool</b>						
<i>Direct Samples</i>						

Liu 2013	Taqman array Card	toxR gene	80		100 (59.8-100) <sup>1</sup>	100 (93.7-100) <sup>1</sup>
<b>Reference test: PCR Luminex</b>						
<b>Sample type: Stool</b>						
<i>Direct Samples</i>						
Liu 2013	Taqman array Card	toxR gene	109		100 (62.9-100) <sup>1</sup>	100 (95.4-100) <sup>1</sup>

<sup>1</sup> Confidence Intervals not provided; calculated from raw numbers

<sup>2</sup> Result estimated using Bayesian Latent Modelling

49 Figure 7. Plot of sensitivities and specificities for individual studies. Each dot represents a single study result, sub-grouped by colour according to type PCR test and reference or enrichment  
50 status, as per the legend below. Error bars show 95% Confidence Intervals.



51

52