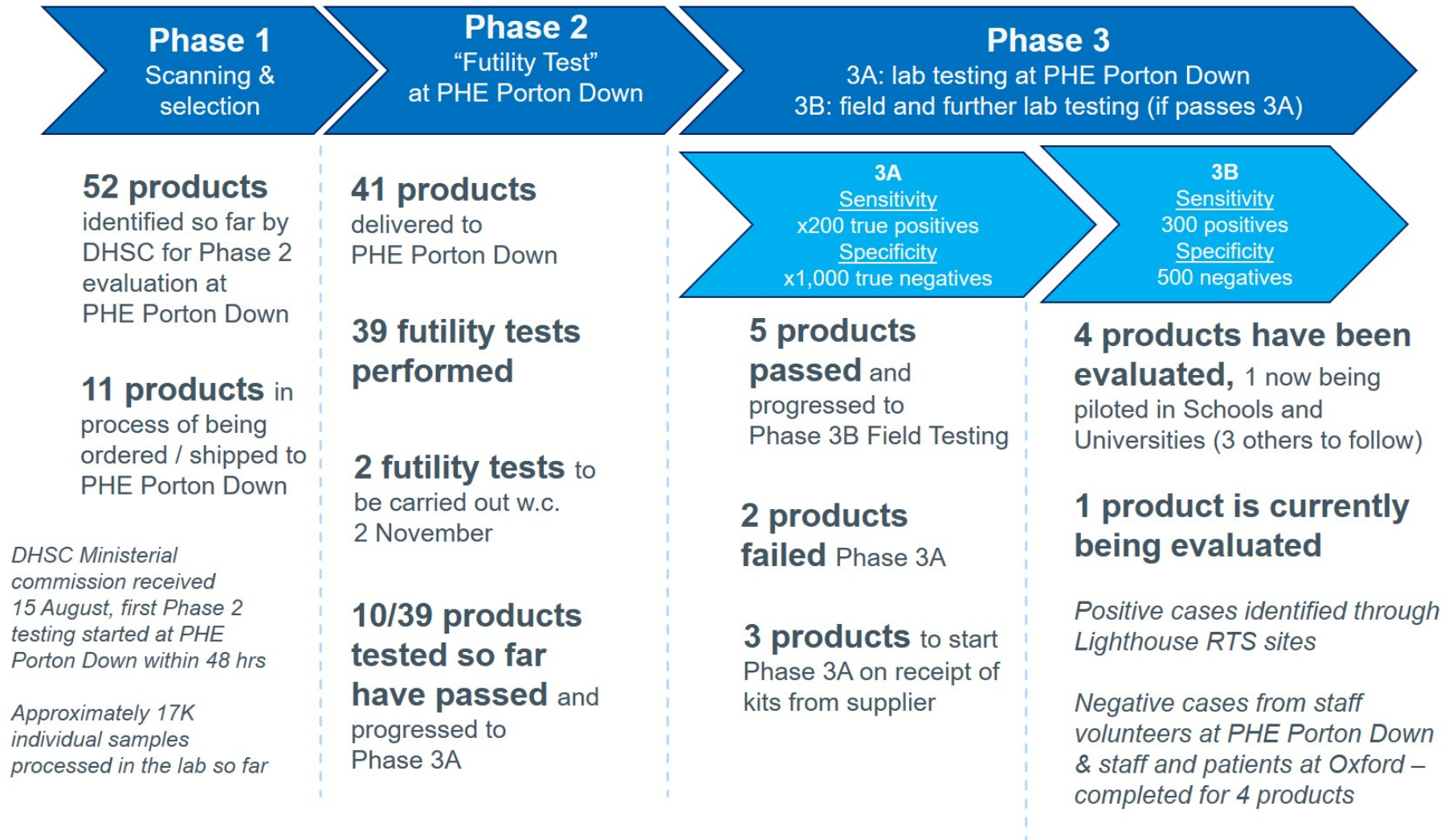


Innova Results - Preview

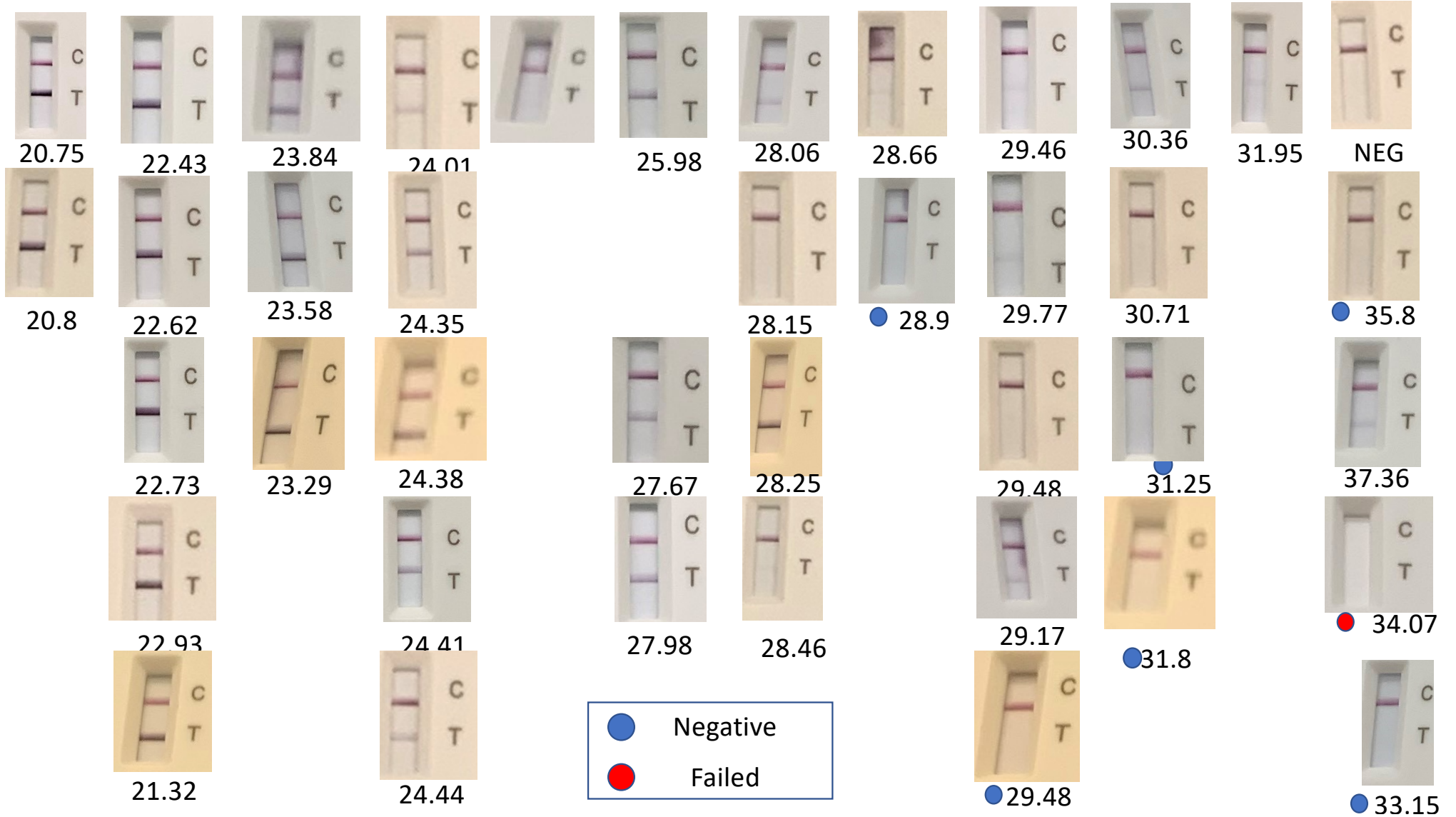
November 10th 2020

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Lateral flow antigen test evaluation: PHE Porton Down & Oxford collaboration - status @ 31.10.20



Examples of Innova Results: Numbers Refer to Viral Load CT values



Number of evaluations performed. Kit failure rate and PCR results

Innova LFD evaluation phase	LFD failures		LFD successes				
	fail//total	%	PCR+	PCR-	PCR-void	PCR-not done	TOTAL
Phase 2 negatives	0/72	0	0	72	0	0	72
Phase 2 positive dilution series	0/215	0	215	0	0	0	215
Phase 3a positives	12/212	6	199	0	1	0	200
Phase 3a negatives	50/1040	5.1	0	990	0	0	990
Phase 3b FALCON (Dry swabs- field)	28/296	10.4	252	15	1	0	268
Phase 3b FALCON (Dry swabs- lab)	9/221	4.2	204	8	0	0	212
Phase 3b FALCON (VTM swabs)	9/166	5.7	142	14	1	0	157
Phase 4 hospital staff	17/375	4.7	2	346	10	0	358
Phase 4 armed forces	6/163	3.8	46	111	0	0	157
Phase 4 PHE staff	19/231	8.9	0	212	0	0	212
Phase 4 school 1	311/2166	16.8	0	0	0	1855	1855
Phase 4 school 2 + 3 + 4	14/2146	0.65	0	0	0	2132	2132
Phase 4 COVID-19 testing centre	27/1973	1.4	139	1789	18	0	1946
TOTAL	502/9276	5.4	1199	3557	31	3987	8774

Kit failure rates ranged from 0.65% to 16.8% ($P < 0.00001$; $\chi^2(2) = 530$)

This suggests that there might be differences between batches.

Specificity (against conventional PCR)

Evaluation Phase	Test Center	False positives/total	False positives 95% CI
Phase 2 evaluation	Porton	0/72	0.00% (0.00-5.07)
Phase 3a evaluation- negative samples	Porton	0/940	0.00% (0.00-0.41)
Phase 4 evaluation- armed forces	Porton	0/105	0.00% (0.00-3.53)
Phase 4 evaluation- PHE staff	Porton	0/209	0.00% (0.00-1.80)
Phase 4 evaluation- hospital staff	Oxford	1/329*	0.30% (0.05-1.70)
<i>Subtotal (Experienced laboratory workers)</i>		<i>1/1655</i>	<i>0.06% (0.02-0.3)</i>
Phase 4 evaluation- school 1	Local	9/1855**	0.49% (0.26-0.92)
Phase 4 evaluation- school 2 + 3 + 4	Local	7/2130**	0.33% (0.16-0.68)
Phase 4 evaluation- COVID-19 testing centre	Local	5/1327***	0.38% (0.16-0.88)
<i>Subtotal (Locally trained)</i>		<i>21/5312</i>	<i>0.39% (0.24-0.60)</i>
TOTAL		22/6967	0.32% (0.21-0.47)

Laboratory-based testing testing (0.06%) compared to Field Testing 0.39% P=0.041.
 Many false positives had 'weak' bands and were negative with retesting with LFD.

Limit of Detection
saliva spiked with virions (plaque forming units*)

PFU/ml	Ct equivalent	Positive LFD /total LFD tests	% positive
100000	16	20/20	100.0
10000	19	25/25	100.0
1000	23.7	65/65	100.0
390	25.2	5/5	100.0
100	25.5	63/65	95.5
40	28.5	3/5	60.0
20	29.3	0/5	0.0
10	30.2	0/5	0.0
5	31	0/5	0.0
2.5	31.7	0/5	0.0
1.2	32.5	0/5	0.0

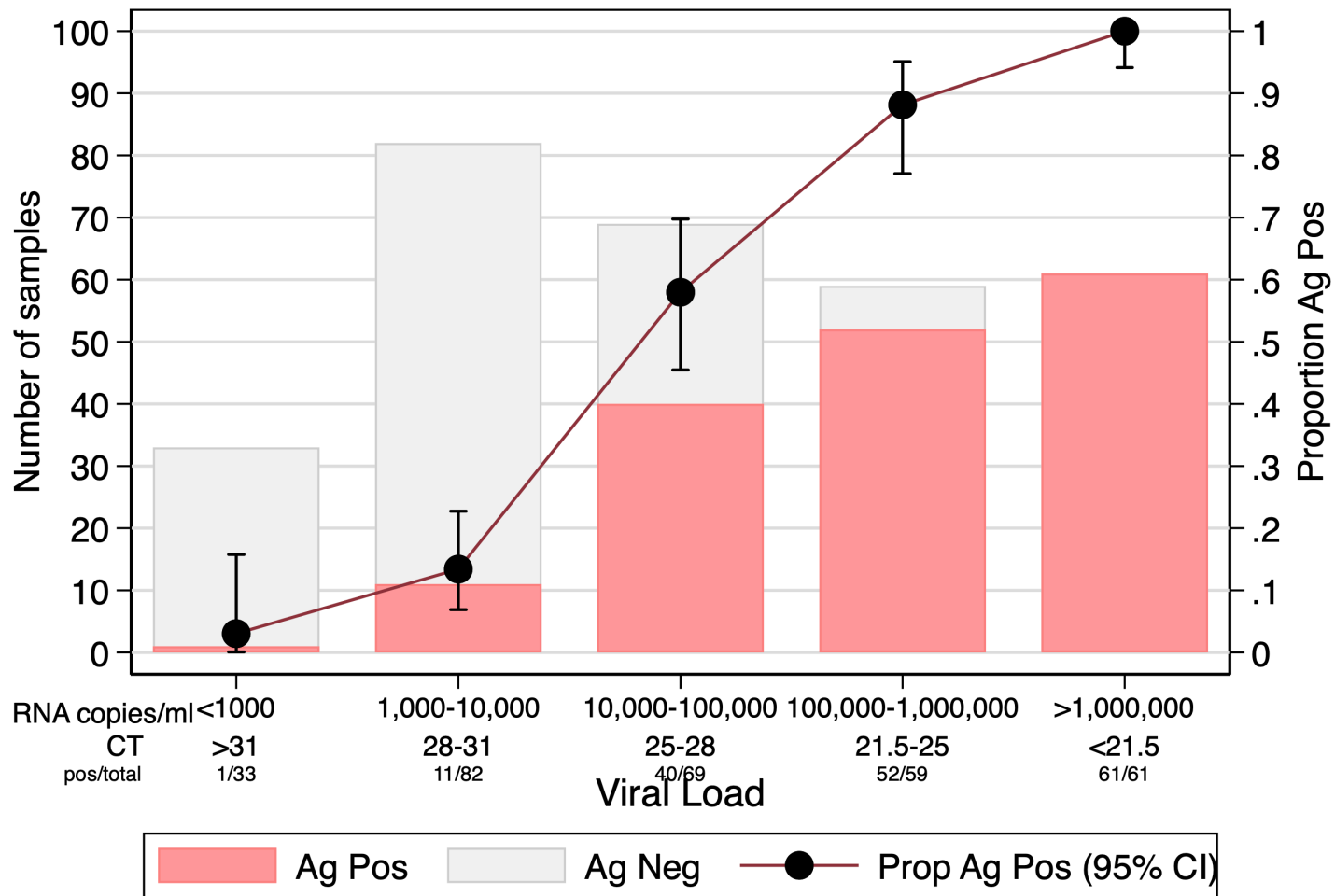
*1 plaque forming unit is approximately 1000 RNA copies.

Viral Antigen Detection in VTM from virus obtained from clinical Samples

- Patients with Covid19 had swabs taken and placed in viral transport medium and transported to Porton for PCR and LFD testing
- 200 samples from freezer in Oxford collected from March/April 2020
- Samples collected from individuals tested positive in RTS and recalled for (2-4 days later).
 - 1 swab taken and transported in viral transport medium for qPCR and LFD testing in Porton
 - Second swab with no viral transport medium ('dry' swab)

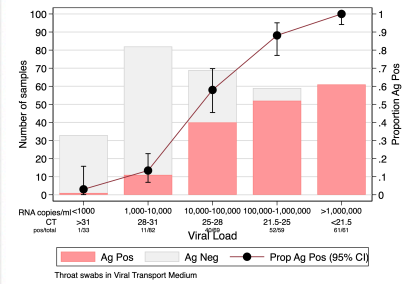
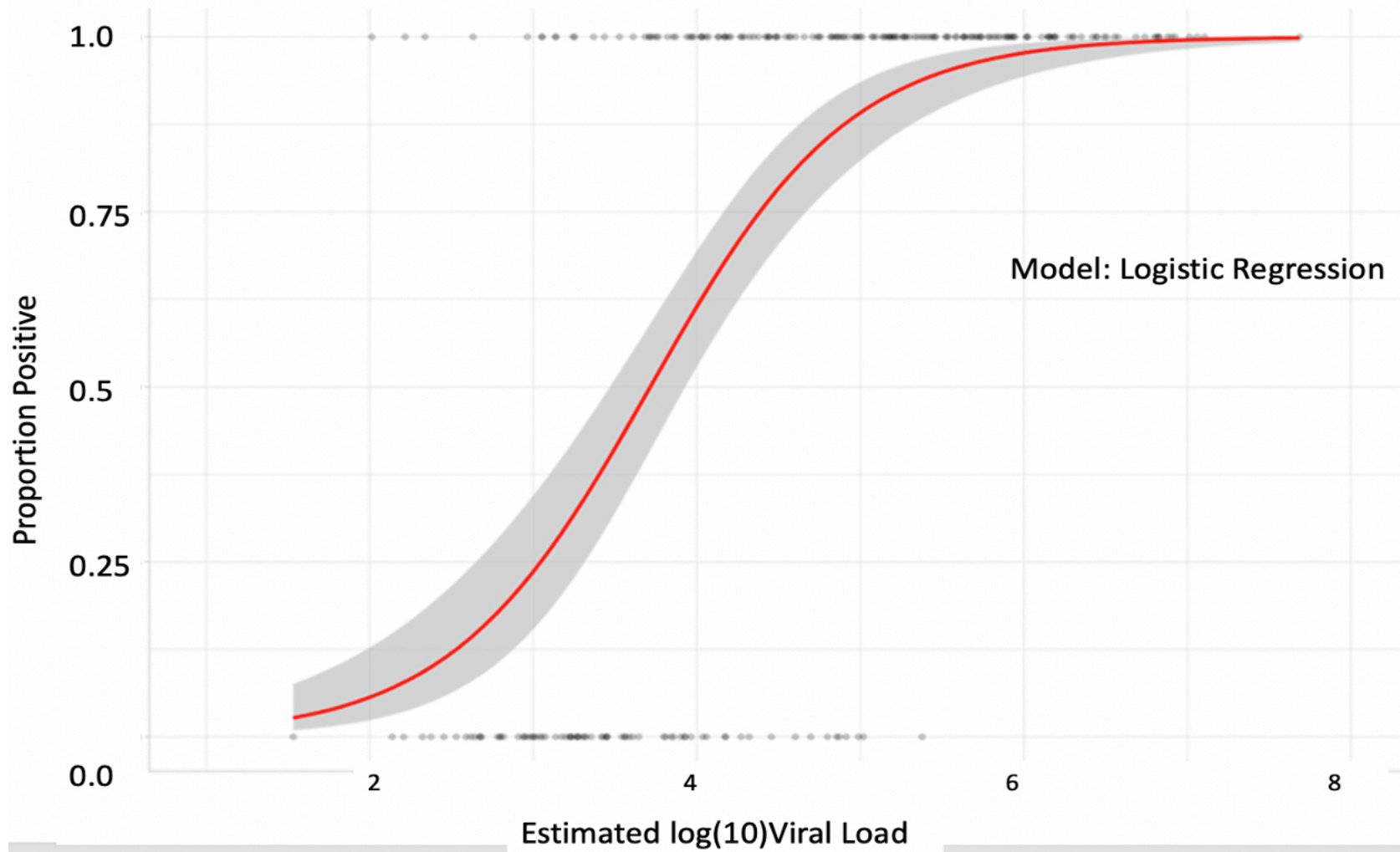
Antigen Detection by Viral Load

(Sample placed in Viral Transport Medium)



Throat swabs in Viral Transport Medium

Relationship between Antigen Detection with Viral Load

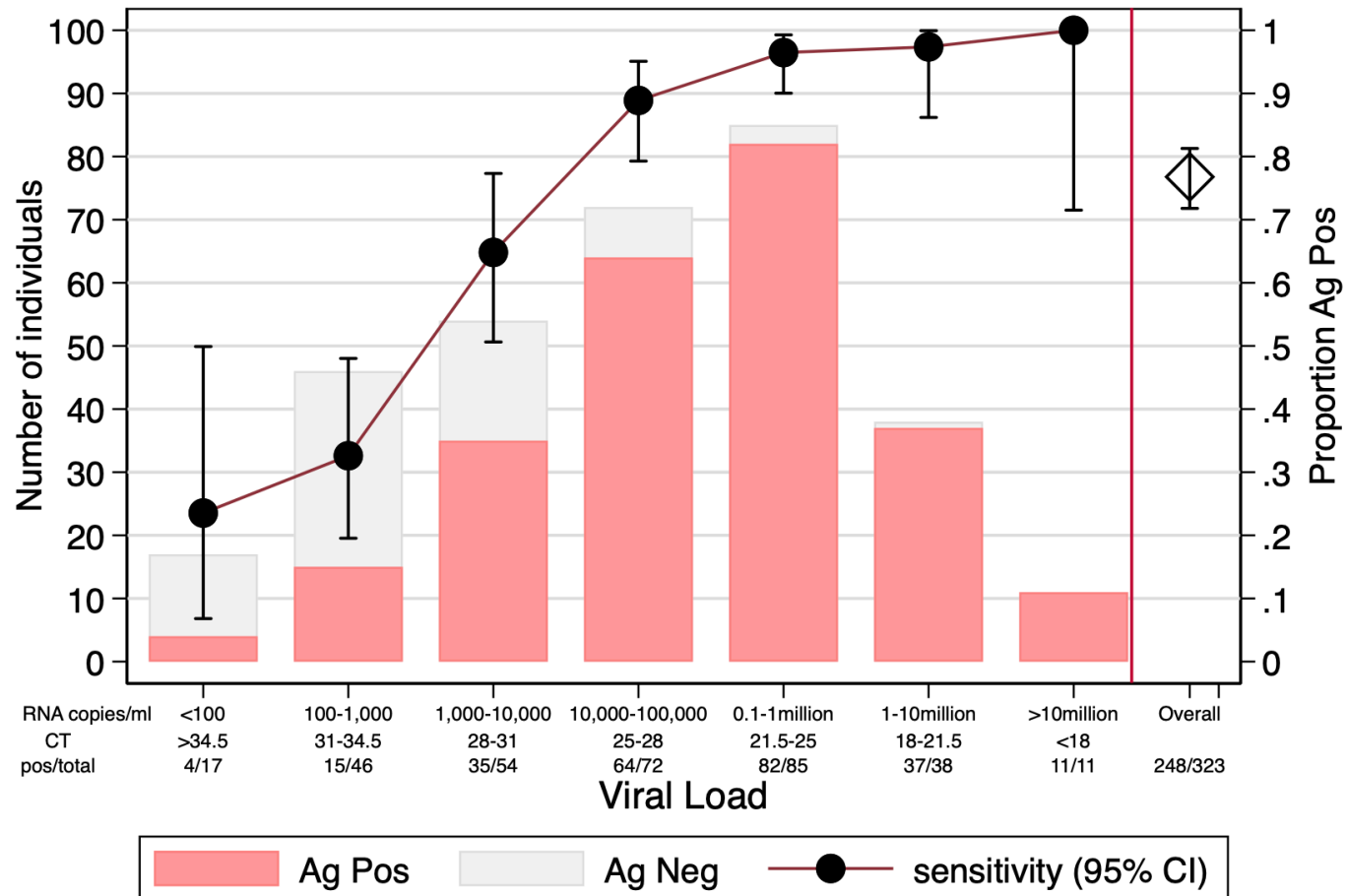


Dry Swab Results

- Swabs are used according to manufacture's instructions. PCR could not be reliably measured from these swabs
- Trained Health Care Professionals
 - 197 swabs were transported to Porton at 4degC for LFD testing
 - PHE Porton Laboratory Scientists
 - 126 swabs were tested local at RTS with LFD
 - Fully Trained Health Care Professionals (Clinical Trial Researchers)

Combined Results are shown.

Proportion Individuals Ag Positive by their Viral Load



Individuals swabbed 2-4 days after first positive test: LFD used by trained health-care professional

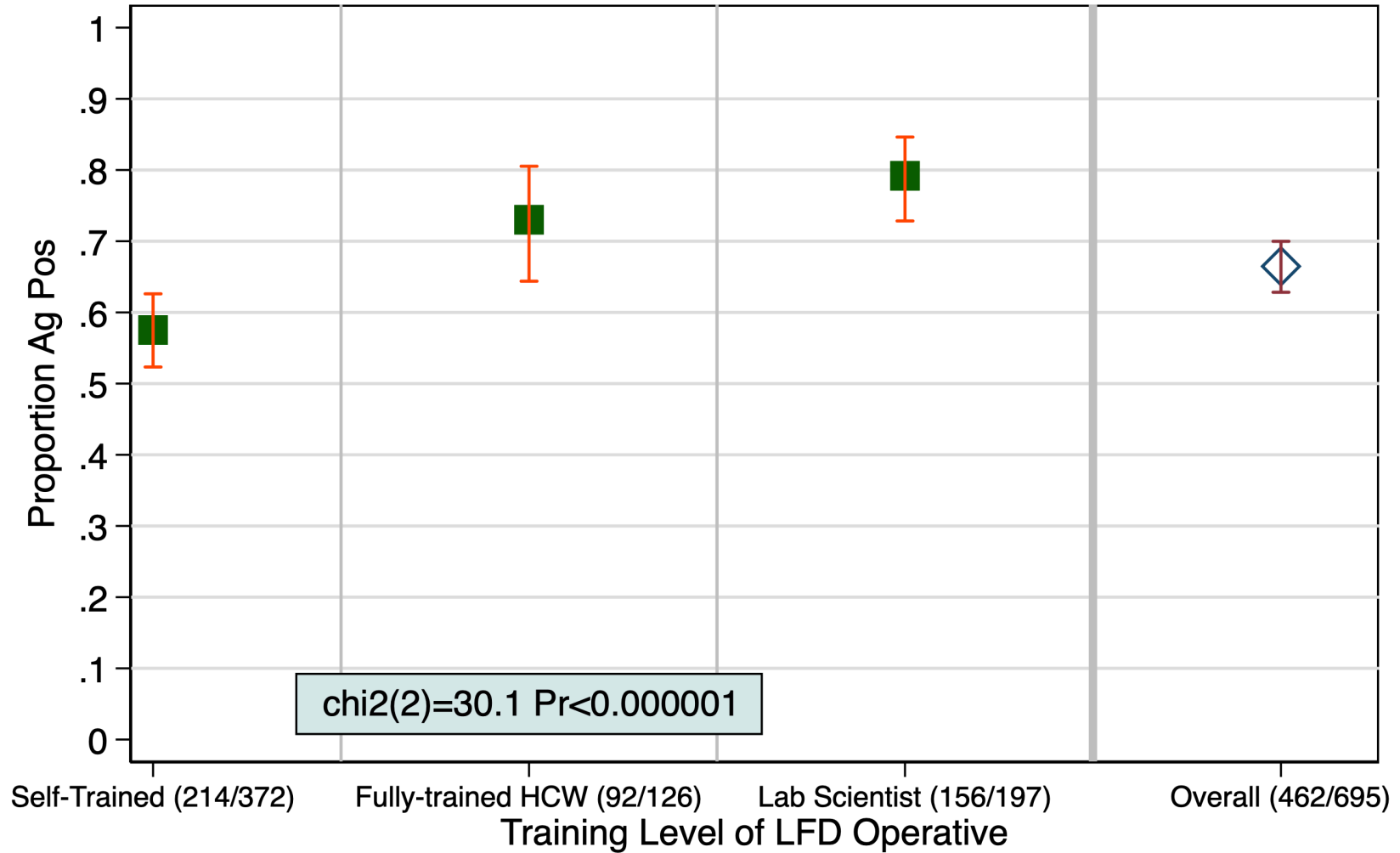
Conclusions on Relationship between LFD

- 'Dry Swabs' perform better than swabs placed in viral transport medium
- LFD detects >95% of individuals with viral loads > median viral load (CT=26 (Porton Cobas result)).
- LFD Detects, overall, 76.7% of all PCR+ cases

Field Trial Repeated

- Consecutive Individuals arriving at RTS with high Covid19 prevalence were invited to participate
 - Overall Prevalence of Ag positivity 14%
- LFD performed locally by self-trained non-health care professionals.
- Parallel swab sent to Lighthouse for PCR.
- 1365 complete results available (372 PCR Positive)
- Proportion of PCR+ Positive individuals with detectable antigen compared to the previous study.

Effect of Training on Proportion Ag Detected All PCR positive individuals



Antigen detection in Asymptomatic Individuals

- Symptoms are available from 170 individuals swabbed at the RTS,
 - tested by a fully-trained HCW
 - Asymptomatic: 77% Ag positive (33/43)
 - Symptomatics: 79% Ag positive (100/127)
- [Odd Ratio 1.12 (0.44 – 2.71) P=0.78]

Summary

- Overall results:
 - Kit Failures – 5%
 - Specificity – 99.65-99.9%%
 - Early results suggest that false positives are often ‘faint bands’ and test negative with a repeat LFD.
 - Sensitivity (against PCR) is 77% when used by competent individuals
 - >95% sensitivity against high viral loads (CT<26) (representing about half the individuals)
- There is good evidence that performance varies according to center.
- There is no evidence that the presence or absence of symptoms affects the ability to detect antigen
- Simple modelling suggests that it is possible that quarantining individuals with positive LFD will reduce the force of transmission by c90%

Current control methods for Covid19

- Decrease rate of transmission from all infectious individuals (background)
 - Universal social distancing
 - Use Face masks / hand washing
 - Avoidance of skin-to-skin contact (outside households)
- Quarantine of individuals at 'high risk' of being infectious ('guilty by association' – unpopular and expensive)

	quarantine-days/tx
• Lock down of regions with high disease incidence	1000
• Quarantine of contacts of known positives	70
- Individual assessments

• Quarantine of individuals with symptoms suggestive of covid19	70
• Quarantine of known PCR+ individuals (regardless of viral load)	20
• Quarantine PCR+ at the time of onset of covid symptom	5
- *Positive Lateral flow antigen* <5

Challenges for Lateral Flow Antigen Tests

- Direct data on infectiousness with different viral loads
- Many different kits and swabs may cause confusion
- Need for resilience to minor divergences from the protocol
- Reliable training modules and assurance of competence of users
- Reliable recording of results (? aided by photoimaging software)
- Early feedback suggests that uptake will depend on
 - Lifting of some restrictions following negative tests.
 - Self (or at least very local) testing
- Generous supply of testing kits.