Kevin Corbett questions 05 May 2020

Q1) ***Why is isolation of the COVID-19 virus [SARS-CoV-2] not the gold standard in the PCR test for the virus?***

WHO have advised that laboratories do not routinely attempt virus isolation. WHO interim guidance published on 2 March 2020:

https://apps.who.int/iris/bitstream/handle/10665/331329/WHO-COVID-19-laboratory-2020.4-eng.pdf

Q2) ***What gold standard does PHE use to evaluate the RT-PCR test for SARS-Cov-2 infection?***

This publication describes how the multi-country collaborative assay (including PHE as a partner) was evaluated.

https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.3.2000045

Q3) ***Which specificity? Analytical or clinical? As per the MIQE guidelines [1].***

See the publication at Q2)

Q4) ***"Analytical sensitivity refers to the minimum number of copies in a sample that can be measured accurately with an assay, whereas clinical sensitivity is the percentage of individuals with a given disorder whom the assay identifies as positive for that condition".***

Do you agree that in the case of the test under discussion, the "assay" is RT-PCR and the "given disorder" is SARS-CoV-2 infection?

Yes

Q5) ***What gold standard does PHE use to calculate clinical specificity?***

Please see the publication referred to in Q2), link here again
https://www.eurosurveillance.org/content/10.2807/1560-7917.ES.2020.25.3.2000045

Q6) ***The UK population is approximately 67 million and the prevalence of SARS-Cov-2 infection unknown. Estimates based on ELISA have been published but the specificity of ELISA is based on a PCR gold standard (as per Professor Crook's paper you supplied). The gold standard for the ELISA cannot be any better than the gold standard for the RT-PCR. However, PHE has yet to say what this is.***

It is elementary that the amount by which "the specificity exceeds 95%" is critical for calculating the probability that a positive test (positive predictive value, PPV), is proof of infection. Applying a 95.1% specific test to a 1/1000 prevalence population for example, results in a PPV of 2% with 98% false positives. The PPV for a prevalence of 1/100 is better but still far short of desirable: 17% with 83% false-positives.

Please see below for up to date surveillance data from UK

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/883784/COVID19_Epidemiological_Summary_w19_FINAL.pdf

Q7) ***Are RT-PCR tests reported PCR positive/negative or SARS-CoV-2 positive/negative?***

Samples tested in the PHE Colindale laboratory are reported as 'SARS-CoV-2 detected/not detected in this sample'. This will vary between different labs.

Q8) ***Is the caveat of PPVs reflected in reports PHE and other laboratories issue to physicians?***

No.

Q9) ***In the table below I contend that whatever gold standard PHE employs, that GS is, by definition, what the RT-PCR procedure tests for. Do you agree?***

Test result	PHE GS +	PHE GS -	Totals
RT- PCR test +	A	B	A+B
RT-PRC test -	C	D	C+D

Please see how assays are evaluated in the publications at Q2)

Q10) ***In my previous e-mail, I requested data proving the sensitivity and specificity of the RT-PCR test for SARS-CoV-2 infection.***

Test result	?? pos	?? neg	Totals
RT- PCR test +	A	B	A+B
RT-PRC test -	C	D	C+D

Would you please send me these data and indicate PHE's column titles?

Please see the response to Q2)

Q11) ***Are gold standards other than RT-PCR used to evaluate antibody tests for infection with SARS-CoV-2?***
Q12) ***If so, what is this gold standard?***

Please see below. There are several players in this arena (both serology and PCR) – it is a collaborative effort and data is still emerging and will be published when completed.

https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/878121/coronavirus-covid-19-testing-strategy.pdf