Relationship of Viral Load and Infectivity to the Limit of Detection of SARS-CoV-2 Antigen Tests

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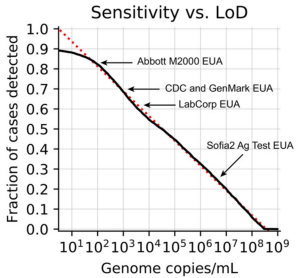
QUESTION:
When/how should we use SARS-CoV-2 antigen versus PCR tests?

ANTIGEN TESTS
RAPID
INEXPENSIVE
POINT-OF-CARE
INSENSITIVE?

PCR
SLOW
EXPENSIVE
SENSITIVE

INFECTION VERSUS INFECTIVITY
INFECTIVITY SURROGATE =
VIRAL CULTURE



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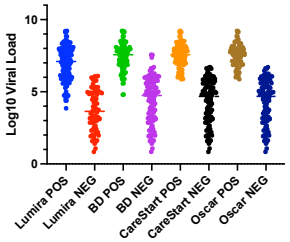

Figure 1. Antigen Testing Results Compared with Log10 Viral Load. Viral load in genome copies/mL POS = positive antigen test result. NEG = negative antigen testing reslt. Lumira = LumiraDx Ag test; BD = BD Veritor Ag test.

Sensitivity/Specificity versus Viral Culture
LumiraDx 90% (83-94% C.I.) / 70% (59-79%)
Other Ag 74% (65-82% C.I.) / 92% (84-96%)

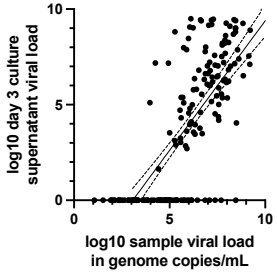

Figure 2. Quantitative Relationship Between Culturable Virus and Sample Viral Load. Day 3 viral culture supernatant for each sample was analyzed by RT-qPCR. The viral load in log10 genome copies/mL of culture supernatant is plotted against the log10 viral load in genome copies/mL of the original patient sample. Linear regression (solid line) with 95% confidence intervals (dashed lines) shown. $R^2 = 0.55$

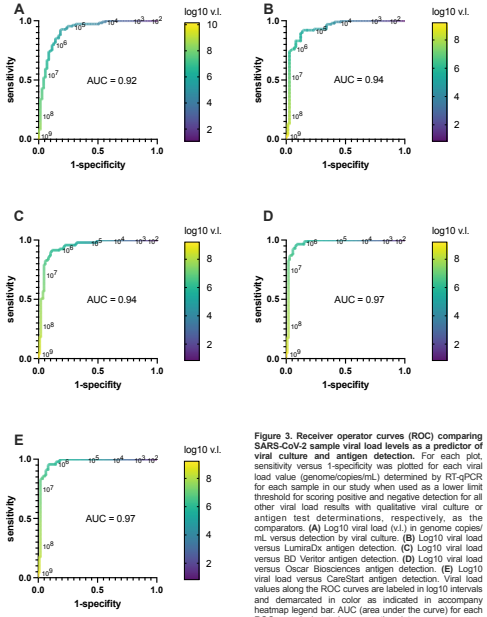

Figure 3. Receiver operator curves (ROC) comparing SARS-CoV-2 sample viral load levels as a predictor of viral culture and antigen detection. For each plot, sensitivity versus 1-specificity was plotted for each viral load value (genome/copies/mL) determined by RT-qPCR for each sample in our study when used as a lower limit threshold for scoring positive and negative detection for all other viral load results with qualitative viral culture or antigen test determinations, respectively, as the comparators. **(A)** Log10 viral load (v.l.) in genome copies/mL versus detection by viral culture. **(B)** Log10 viral load versus LumiraDx antigen detection. **(C)** Log10 viral load versus BD Veritor antigen detection. **(D)** Log10 viral load versus Oscar Biosciences antigen detection. **(E)** Log10 viral load versus CareStart antigen detection. Viral load values along the ROC curves are labeled in log10 intervals and demarcated in color as indicated in accompany heatmap legend bar. AUC (area under the curve) for each ROC curve is denoted on respective plots.

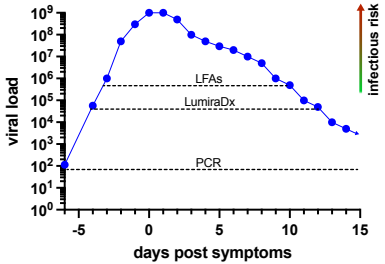

Figure 4. Model of Infectious Risk versus SARS-CoV-2 Detection by RT-qPCR and Antigen Tests. Both Lumira and lateral flow-based antigen tests (e.g., BD Veritor, CareStart, and Oscar Biosciences) are able to detect individuals with viable, culturable virus and who therefore pose an immediate infectious risk to others. Dotted lines indicate reliable detection threshold predicted for each method. Presumptively, infectious risk is proportional to the amount of culturable virus which is roughly proportional to the viral load in samples. Antigen tests are excellent in detecting patients with the highest viral loads which may be four to five log10-fold greater than viral loads detected at the lowest levels where virus can be consistently cultured. PCR and to a lesser extent, the LumiraDx test, can detect individuals before and after the expected infectious period and therefore may be more appropriate for screening programs where testing is performed at longer intervals. The viral load curve shown is for representational purposes and may not reflect viral load kinetics in any specific individual.

Conclusions:

1. Use Ag tests to identify *infectious* individuals at time of testing. Will allow isolation of significantly infectious individuals from communal events, same-day healthcare procedures, communal travel arrangements, and other functions with significant person-to-person contact in settings where universal masking is neither feasible nor desired.
2. PCR tests for no-margin-for-error situations (hospital admission), vulnerable populations; sample pooling strategies; and screening of cohorted populations (e.g., school) at decreased intervals.

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