Diagnostic sensitivity and specificity of a rapid antigen test for SARS-CoV-2

Concept Note

# Background

To stop the ongoing COVID-19 pandemic, a readily available, reliable and fast diagnostic test is needed to quickly identify and isolate patients and quarantine their close contacts to stop further transmission. Currently, the gold standard for a confirmed diagnosis of COVID-19 is a positive RT-PCR of a respiratory swab for SARS-CoV-2, a test that requires specialized training and equipment to conduct. An inability to meet testing demand has hampered efforts to contain the pandemic in many countries. An accurate and sensitive COVID-19 antigen test that is conducted at the home of mildly-affected suspect cases would allow the test to be conducted by an individual with limited training and decrease the time and expense associated with identifying cases.

In Bangladesh, community support teams (CST) have been deployed in selected areas of Dhaka and Khulna districts. These teams conduct passive surveillance for COVID-19 by responding to notifications from community members who are experiencing symptoms. CST then visit the household and use a standard case definition (a fever of 100°F or more and at least one respiratory symptom, either coughing or shortness of breath) to identify suspect COVID-19 patients and make a recommendation about self-isolation, quarantine of close contacts and provide advice on how to seek care if symptoms become severe. Patients must go to a designated site to be tested for COVID-19 by RT-PCR before they are identified as a confirmed case. This additional step for confirming diagnosis could result in significantly lower case detection rate due to confirmation of only the more severely affected cases who seek medical care outside of the home.

Based on experience with surveillance for highly pathogenic avian influenza (HPAI) H5N1 in backyard poultry flocks, Robyn, et al, demonstrated that a combination of applying a standard case definition followed by one or more rapid antigen tests can increase the sensitivity of case detection to closer to that of the gold standard, RT-PCR, while maintaining specificity. A similar approach could be taken at the household level for the detection and confirmation of COVID-19 patients. To determine the benefit and feasibility of adding a COVID-19 antigen test to the passive surveillance being conducted by CST for confirmation of diagnosis at the household, the sensitivity and specificity of the antigen test, with or without the application of the case definition, needs to be assessed.

# Objective

To determine diagnostic accuracy for COVID-19 diagnosis at the household level of using: (1) the standard case definition of COVID-19 currently being used by CST, (2) the COVID-19 antigen test alone, and (3) a combination of the case definition and COVID-19 antigen test, compared to the gold-standard RT-PCR. In addition, we will investigate whether there is any impact on the sensitivity and specificity of household-level screening for COVID-19 if the antigen test is used to test asymptomatic household members when the suspect COVID-19 patient result is negative but meets the case definition.

# Methods

This is a field-based, prospective evaluation of three methods for diagnosing COVID-19 (case definition alone, antigen test alone, and case definition plus antigen test) compared to a gold standard test (RT-PCR). CST will be trained on study methods and will collect data and samples from potential COVID-19 patients. When a CST receives a call from a member of the community with symptoms of COVID-19, the CST will visit the household and determine if the case definition has been met. Regardless, the CST will then explain the purpose of the study to the patient and obtain consent for participation. If the patient agrees to participate, the CST will collect one respiratory swab for submission to the laboratory for testing by RT-PCR and one respiratory swab to run the COVID-19 antigen test. If the test is negative but the case definition is meet, the CST will request permission to run the antigen test on one or more asymptomatic household members. Once all sampling and testing has been completed, or if the patient does not agree to participate in the evaluation, the CST will proceed with their normal activities of advising suspect patients to self-isolate, recommending quarantine of close contacts, and providing information on where to receive further treatment.

Our sample size estimate is based on determining the difference between two proportions (<https://epitools.ausvet.com.au/twoproportions>). To calculate a decrease of 10% or more in sensitivity or specificity with power of 0.8 and 95% confidence using any of the three diagnostic methods versus the gold standard, at least 93 samples are required for each test. Therefore, CST will enroll the first 100 households visited who give consent to participate.

# References

Robyn M, Priyono WB, Kim LM, Brum E. Diagnostic sensitivity and specificity of a participatory disease surveillance method for highly pathogenic avian influenza in household chicken flocks in Indonesia. *Avian Dis*. 2012;56(2):377‐380. doi:10.1637/9936-091511-Reg.1