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Testing Frequency Matters: An Evaluation of the Diagnostic Performance of a Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Rapid Antigen Test in US Correctional Facilities

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Background. The Centers for Disease Control and Prevention recommends serial rapid antigen assay collection within congregate facilities. Although modeling and observational studies from communities and long-term care facilities have shown serial collection provides adequate sensitivity and specificity, the accuracy within correctional facilities remains unknown.

Methods. Using Connecticut Department of Correction data from 21 November 2020 to 15 June 2021, we estimated the accuracy of a rapid assay, BinaxNOW (Abbott), under 3 collection strategies: single test collection and serial collection of 2 and 3 tests separated by 1–4 days. The sensitivity and specificity of the first (including single), second, and third serially collected BinaxNOW tests were estimated relative to RT-PCRs collected ≤1 day of the BinaxNOW test. The accuracy metrics of the testing strategies were then estimated as the sum (sensitivity) and product (specificity) of tests in each strategy.

Results. Of the 13 112 residents who contributed ≥1 BinaxNOW test during the study period, 3825 contributed ≥1 RT-PCR paired BinaxNOW test. In relation to RT-PCR, the 3-rapid-antigen-test strategy had a sensitivity of 95.9% (95% CI: 93.6–97.5%) and specificity of 98.3% (95% CI: 96.7–99.1%). The sensitivities of the 2- and 1-rapid-antigen-test strategies were 88.8% and 66.8%, and the specificities were 98.5% and 99.4%, respectively. The sensitivity was higher among symptomatic residents and when RT-PCRs were collected before BinaxNOW tests.

Conclusions. We found serial antigen test collection resulted in high diagnostic accuracy. These findings support serial collection for outbreak investigation, screening, and when rapid detection is required (such as intakes or transfers).

Keywords. diagnostic accuracy; COVID-19; rapid antigen test; correctional facility.

Within the United States, state- and federal-run correctional facilities have experienced high transmission rates of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and remain high-risk settings for coronavirus disease 2019 (COVID-19) [1, 2]. In fact, data from September through November 2020 show that residents of Federal Bureau of Prisons were 4.7 times more likely to become infected with SARS-CoV-2 and 2.6 times more likely to die from COVID-19 than general US residents [2]. Despite the development of COVID-19 vaccines and vaccination programs for incarcerated populations, vaccine coverage remains below that needed for population-level protection [3–9]. Rapid and accurate SAR-CoV-2 testing will therefore remain a key component of infection prevention within correctional facilities.

In August 2020, the Food and Drug Administration (FDA) issued an Emergency Use Authorization of Abbott's BinaxNOW, a COVID-19 rapid antigen test [10, 11]. Compared with reverse transcription–polymerase chain reaction (RT-PCR), the rapid turnaround time and low cost of rapid antigen tests makes them a cost-effective strategy for congregate settings, where transmission risk is high and implementation of serial mass screening is feasible [12]. Unfortunately, prior studies from community, educational, and long-term care facility settings found the sensitivity of rapid antigen tests to be poor to moderate (53–77%) and to be lower among asymptomatic individuals and individuals early or late in their course of infection [13–18]. These findings thus call into question the use of rapid antigen tests as single point-of-care tests.

Single test collection is not, however, the intended testing strategy for rapid antigen tests outside of healthcare settings [11, 19, 20]. Instead, both the manufacturer and the FDA advise

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serial collection of at least 2 tests [11, 19]. In alignment with the intended use, the Centers for Disease Control and Prevention (CDC) recommends serial collection of rapid antigen testing within congregate settings for screening and during outbreaks regardless of symptom presentation [21]. This guidance is supported by modeled evidence that outbreak control depends largely on frequency and speed of testing and observational data showing that serial testing improves the sensitivity of rapid antigen tests in both nursing home and community settings [12, 14, 22, 23]. However, the value of serial testing within correctional facilities remains unknown.

Herein, we present findings of a study that evaluated the accuracy of serial BinaxNOW rapid antigen testing during a mass screening and testing program implemented by the Connecticut Department of Correction (DOC) during the COVID-19 pandemic wave in late 2020 and early 2021. We specifically compared the accuracy of the rapid antigen test relative to RT-PCR under 3 collection strategies: serial testing of up to 3 negative rapid antigen tests, serial testing of up to 2 negative rapid antigen tests, and rapid antigen collection in isolation.

METHODS

Setting and Specimen Collection

On 21 November 2020, the DOC initiated the implementation of the Abbott BinoxNOW rapid antigen test (headquarters: Chicago, IL) collection into their SARS-CoV-2 testing program for symptomatic testing, contact tracing, testing of residents undergoing admission to the correctional facilities, and inter-facility transfer and mass voluntary asymptomatic screening. For each instance of rapid antigen use, the DOC guidelines recommend the serial collection of up to 3 negative rapid antigen tests taken on day 1, 4, and 7 (where day 1 is the day of exposure, if exposed). Due to concerns around the sensitivity of the rapid antigen test, phased implementation of rapid antigen testing with confirmatory RT-PCR was performed. While undergoing serial test collection, residents of DOC facilities were placed in quarantine or isolation.

Trained medical staff collected anterior nasal and nasopharyngeal swab specimens for rapid antigen and RT-PCR testing. Quest Diagnostic facilities performed SARS-CoV-2 RT-PCR testing of nasopharyngeal swab specimens using the SARS-CoV-2 RNA (COVID-19), Qualitative nucleic acid amplification test (NAAT) assay and defined positive tests as a cycle threshold value of less than 40 [24]. At the time rapid antigen test collection was implemented, the DOC oversaw 17 facilities with a resident census of approximately 10 000 residents (9945 residents on 1 July 2020) [25, 26]. The Yale University Institutional Review Board classified this study as public health surveillance.

Data Collection and Cohort Development

Using resident and testing data queried from internally maintained DOC databases, we retrospectively identified all rapid antigen (BinaxNOW) and RT-PCR testing records from 21 November 2020 to 15 June 2021. We included tests collected among residents with prior documented SARS-CoV-2 infections but excluded duplicated records (same day, assay, and assay results) and reporting errors (negative recorded on the same day as a positive).

Following the DOC recommendations for serial rapid antigen test collection, we identified series of rapid antigen tests (rapid antigen tests collected within 1 and 4 days of each other or tests collected in the absence of any test in the prior or following 4 days) (Figure 1*A*). We then paired the first, second, and third rapid antigen tests of the identified series with RT-PCR tests collected between 1 day prior to or following the rapid antigen test (Figure 1*B*). In the event of multiple RT-PCR matches per rapid antigen test, ordered preference was given to positive RT-PCRs (Figure 1*B*; Option A), RT-PCRs collected on the same day as the rapid antigen test (Figure 1*B*; Option B), and RT-PCRs collected before the rapid antigen test (Figure 1*B*; Option C). We defined symptoms as the presence or absence of COVID-19–related symptoms reported at the time of rapid antigen testing [27].

Statistical Approach: Diagnostic Accuracy

The characteristics of residents with at least 1 RT-PCR paired rapid antigen test were summarized by presence of RT-PCR–positive SARS-CoV-2 events using counts and percentages for categorical factors and means and standard errors for continuous factors. We estimated the sensitivity and specificity for each testing strategy using the following equations [28]:

$$\text{One}-\text{Test Sensitivity Equation: Weighted Average}\ (\text{Test1}_{sen},\ \text{Test2}_{sen},\ \text{Test3}_{sen})$$

$$\text{Two}-\text{Test Sensitivity Equation: } \text{Test1}_{sen} + (1-\text{Test1}_{sen}) \times \text{Test2}_{sen}$$

$$\text{Three}-\text{Test Sensitivity Equation: } \text{Test1}_{sen} + (1-\text{Test1}_{sen}) \times \text{Test2}_{sen} + (1-(\text{Test1}_{sen}+\text{Test2}_{sen})) \times \text{Test3}_{sen}$$

$$\text{One}-\text{Test Specificity Equation: Weighted Average}\ (\text{Test1}_{spec}, \text{Test2}_{spec}, \text{Test3}_{spec})$$

$$\text{Two}-\text{Test Specificity Equation: } \text{Test1}_{spec} \times \text{Test2}_{spec}$$

$$\text{Three}-\text{Test Specificity Equation: } \text{Test1}_{spec} \times \text{Test2}_{spec} \times \text{Test3}_{spec}$$

where $\text{Test1}_{sen/spec}$ was the sensitivity or specificity of RT-PCR paired first rapid antigen tests, $\text{Test2}_{sen/spec}$ was the sensitivity or specificity of RT-PCR paired second rapid antigen tests, and so on (Supplementary Figure 1). The sensitivity and specificity of RT-PCR paired first, second, and third rapid antigen tests were estimated using Generalized Estimating Equations (GEEs) with robust standard errors and a logit link. We propagated the uncertainty through the serial testing equations using posterior simulation of 1000 random draws of the GEE

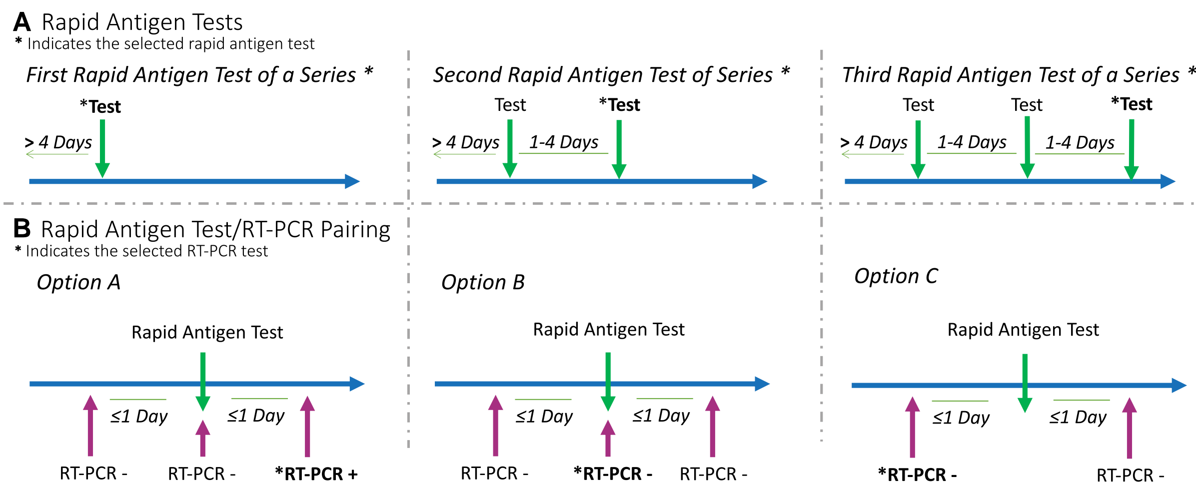

Figure 1. Depiction of the selected rapid antigen tests and the paired RT-PCRs. (*A*) The first 3 tests of rapid antigen test series (rapid antigen tests collected within 1 and 4 days of each other or tests collected in the absence of any test in the prior or following 4 days) were selected. (*B*) Rapid antigen tests were matched to RT-PCRs collected within 1 day prior to or following the rapid antigen test. If more than 1 RT-PCR was paired to the rapid antigen test, we preferentially selected positive RT-PCRs (Option A) followed by those collected on the same day as the rapid antigen test (Option B) and those collected prior to the rapid antigen test (Option C). Abbreviation: RT-PCR, reverse transcription–polymerase chain reaction.

estimates [29, 30]. Additionally, we estimated the diagnostic accuracy stratified by the following a priori selected factors: age, symptom presence, and test order. We tested for additive differences in the diagnostic accuracy of the stratified samples by subtracting the draws of each sample from a selected reference category and defined significance as confidence intervals above or below the null (zero).

For the positive predictive value (PPV) and negative predicted value (NPV), we simulated 1000 average daily prevalence estimates using a Poisson regression with an outcome of positive SARS-CoV-2 test (either rapid antigen or RT-PCR test). To reduce the risk of including multiple positive tests from the same testing event, we excluded positive events within 5 days of each other. With the estimated prevalence, sensitivity, and specificity, we estimated the PPV and NPV for each of the sensitivity, specificity, and prevalence drawn estimates (n = 1000) [31]. For each accuracy metric, we calculated 95% confidence interval (CI) as the 2.5 and 97.5 percentiles [30]. All analyses were conducted in R 4.1.0 using the geepack and multcomp packages (R Foundation for Statistical Computing) [32, 33].

Sensitivity Analyses

To test the robustness of our findings, we performed sensitivity analyses where we selected first, second, and third tests at random instead of the observed order, limited to rapid antigen test series where tests were collected exactly 3 days apart, and invoked different selection approaches in the event of multiple RT-PCRs linked to a rapid antigen test. Finally, in a post hoc analysis, we performed an age-stratified analysis among residents whose RT-PCR and rapid antigen tests were collected on the same day.

RESULTS

Between 21 November 2020 and 15 June 2021, 128 986 RT-PCR and 30 112 rapid antigen tests were collected among 17 669 DOC residents (Supplementary Figure 2). Of these residents, 3825 contributed at least 1 RT-PCR paired rapid antigen test. The majority of residents were male (76.5%), and the most frequently observed race was Black (40.9%). Residents who experienced a paired RT-PCR–positive SARS-CoV-2 event were demographically similar to residents who did not experience a paired RT-PCR–positive SARS-CoV-2 event (Table 1).

Among the 18 186 identified rapid antigen test series, 4919 consisted of 2 or more tests and 2911 consisted of 3 or more tests. A total of 3844 first, 677 second, and 314 third rapid antigen tests from identified series were collected within 1 day of an RT-PCR and considered RT-PCR paired (Figure 2). The test collection order and proportion of tests collected among symptomatic and asymptomatic residents were similar between RT-PCR paired first, second, and third rapid antigen tests (Supplementary Table 1).

Most RT-PCR paired rapid antigen tests were negative (first test: 91.5%; second test: 88.2%; third test: 89.8%). Of the negative rapid antigen tests, most were paired with negative RT-PCRs (first test: 91.5%; second test: 89.2%; third test: 89.8%) (Supplementary Table 2). Relative to RT-PCR, the sensitivities of the first, second, and third rapid antigen tests were 67.7% (95% CI: 62.9–72.0%), 65.4% (95% CI: 55.9–74.1%), and 62.7% (95% CI: 49.1–75.2%), respectively. This resulted in sensitivities of 66.8% (95% CI: 62.8–70.6%), 88.8% (95% CI: 85.1–91.9%), and 95.9% (95% CI: 93.6–97.5%) for the 1-, 2-, and 3-rapid-antigen-test collection strategies, respectively. The

specificity of the first, second, and third rapid antigen tests were above 99%. The specificity of 2 and 3 serially collected rapid antigen tests was 98.5% (95% CI: 97.3–99.1%) and 98.3% (95% CI: 96.7–99.1%), respectively (Table 2). The PPV, based on an observed prevalence of 57 (95% CI: 53–62) cases per 100 000 residents, was highest for the 1-rapid-antigen-test collection strategy (76.7%; 95% CI: 69.0–83.1%) and lowest for the 3-rapid-antigen-test collection strategy (62.9%; 95% CI: 46.6–75.5%). The NPV for each rapid antigen test collection strategy was high (1 rapid antigen test: 99.0%; 2 rapid antigen tests: 99.0%; 3 rapid antigen tests: 98.9%) (Supplementary Table 3).

Table 1. Demographic Characteristics of Residents of Connecticut State Correctional Facilities With Time-Matched Rapid Antigen and RT-PCR Tests by Occurrence of SARS-CoV-2 Infection

		RT-PCR–Positive SARS-CoV-2	
Characteristics	Full Population	Yes	No
Participants	(N = 3825)	(n = 522)	(n = 3425)
Sex, n (%)			
Female	897 (23.5%)	118 (22.6%)	832 (24.3%)
Male	2928 (76.5%)	404 (77.4%)	2593 (75.7%)
Age, mean (SD), years	37 (12)	38 (11)	37 (12)
Race, n (%)			
American Indian	15 (0.4%)	3 (0.6%)	13 (0.4%)
Asian	19 (0.5%)	2 (0.4%)	18 (0.5%)
Black	1564 (40.9%)	207 (39.7%)	1392 (40.6%)
White	1186 (31.0%)	186 (35.6%)	1053 (30.7%)
Unknown/missing	1041 (27.2%)	124 (23.8%)	949 (27.7%)
RT-PCR paired rapid antigen tests	(N = 4835)	(n = 557)	(n = 4278)
Sex, n (%)			
Female	1385 (28.6%)	141 (25.3%)	1244 (29.1%)
Male	3450 (71.4%)	416 (74.7%)	3034 (70.9%)
Age, mean (SD), years	37 (12)	38 (11)	37 (12)
Race, n (%)			
American Indian	21 (0.4%)	3 (0.5%)	18 (0.4%)
Asian	22 (0.5%)	2 (0.4%)	20 (0.5%)
Black	1903 (39.4%)	219 (39.3%)	1684 (39.4%)
White	1584 (32.8%)	202 (36.3%)	1382 (32.3%)
Unknown/missing	1305 (27.0%)	131 (23.5%)	1174 (27.4%)
Rapid antigen tests in series,[a] n (%)			
First	3844 (79.5%)	402 (72.2%)	3442 (80.5%)
Second	677 (14.0%)	104 (18.7%)	573 (13.4%)
Third	314 (6.5%)	51 (9.2%)	263 (6.1%)

Abbreviations: RT-PCR, reverse transcription–polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

[a]Rapid antigen test series defined as tests collected within 1–4 days of each other or in the absence of a test in the 4 days prior

The sensitivity of each collection strategy was significantly higher among symptomatic residents than among asymptomatic residents (difference for 1 rapid antigen test: 30.8% [95% CI: 23.5–37.4%]; 2 rapid antigen tests: 16.2% [95% CI: 11.0–22.0%]; 3 rapid antigen tests: 8.6% [95% CI: 5.2–13.0%]). The sensitivity was higher when rapid antigen tests were collected on the same day as RT-PCRs than when rapid antigen tests were collected on the day before RT-PCRs (difference for 1 rapid antigen test: 28.3% [95% CI: 18.3–38.0%]; 2 rapid antigen tests: 25.4% [95% CI: 12.1–38.2%]; 3 rapid antigen tests: 27.0% [95% CI: 11.0–41.2%]). The sensitivity of the 2-rapid-antigen-test collection strategy was significantly higher for residents younger than 37 years of age than for residents older than 37 years of age (difference: 6.8%; 95% CI: 0.2–13.9%) (Table 3).

The specificity for each rapid antigen test collection strategy was significantly higher among asymptomatic residents than among symptomatic residents (difference for 1 rapid antigen test: 4.2% (95% CI: .9–11.2%); 2 rapid antigen tests: 16.1% (95% CI: 3.5–42.9%); 3 rapid antigen tests: no sample). Interestingly, the specificity of RT-PCR paired second rapid antigen tests collected among symptomatic residents was low (85.8%; 95% CI: 58.4–96.4%) but the specificity of RT-PCR paired first rapid antigen tests was high (97.5; 95% CI: 90.5–99.3%). The specificities did not vary significantly by age or timing of tests (Table 3).

Sensitivity Analyses

We performed multiple sensitivity analyses to test the robustness of our findings to varying rapid antigen test collection orders,

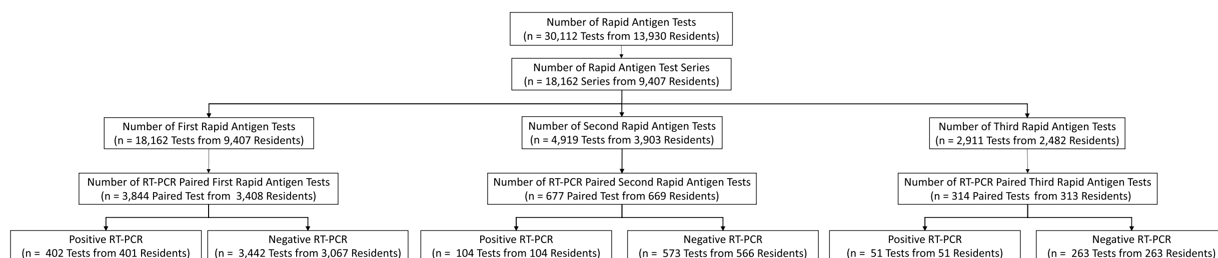

Figure 2. Flowchart of residents of Connecticut State–run correctional facilities between 21 November 2020 and 15 June 2021, and rapid antigen tests included in the analysis. The first 3 tests of rapid antigen test series (rapid antigen tests collected within 1 and 4 days of each other or tests collected in the absence of any test in the prior or following 4 days) were selected. RT-PCR paired rapid antigen tests were defined as rapid antigen tests with RT-PCR tests collected between 1 day prior to and 1 day after the rapid antigen test. Abbreviation: RT-PCR, reverse transcription–polymerase chain reaction.

Table 2. Rapid Antigen Test Accuracy Relative to RT-PCR Among Residents of Connecticut State Correctional Facilities Under Varying Collection Strategies

	No. of RT-PCR–Positive Pairs	Sensitivity (95% CI)		No. of RT-PCR–Negative Pairs	Specificity (95% CI)	
		Single Test[a]	Testing Strategy[b]		Single Test[a]	Testing Strategy[b]
First rapid antigen test	402	67.7 (62.9, 72.0%)	66.8 (62.8, 70.6%)	3442	99.4 (99.1, 99.6%)	99.4 (99.1, 99.6%)
Second rapid antigen test	104	65.4 (55.9, 74.1%)	88.8 (85.1, 91.9%)	573	99.1 (97.9, 99.6%)	98.5 (97.3, 99.1%)
Third rapid antigen test	51	62.7 (49.1, 75.2%)	95.9 (93.6, 97.5%)	263	100 (98.6, 100%)	98.3 (96.7, 99.1%)

Abbreviations: CI, confidence interval; RT-PCR, reverse transcription–polymerase chain reaction.

[a]95% CI estimated using Generalized Estimating Equations with robust standard errors when >1 test pair per person was present; alternatively, Wald CIs were estimated.

[b]Serial testing sensitivity was estimated as the additive probability (positive for any rapid antigen test); serial testing specificity was estimated as the multiplicative probability (negative for all rapid antigen test), posterior simulation of 1000 draws was used to propagate uncertainty through the equations

rapid antigen test collection windows, and RT-PCR pair selection. The sensitivity of the 1-, 2-, and 3-rapid-antigen-test collection strategies ranged from 57.2–74.6%, 84.7–97.6%, and 92.8–98.7%, respectively (Supplementary Tables 4–6; Supplementary Figure 3). The highest and lowest sensitivities were observed when we selected the first, second, and third tests at random (Supplementary Figure 3). As with the primary analysis, we observed high specificities for each testing strategy (1 rapid antigen test: 98.9–99.8%; 2 rapid antigen tests: 98.0–99.5%; 3 rapid antigen tests: 96.8–99.3%) (Supplementary Tables 4–6; Supplementary Figure 3). In a post hoc analysis, we found that the accuracy of the rapid antigen test did not differ significantly by age group among residents whose RT-PCR and rapid antigen tests were collected on the same day (Supplementary Table 7).

DISCUSSION

We evaluated the predictive accuracy of the rapid COVID-19 antigen test, BinaxNOW, in relation to RT-PCR under 3 different collection strategies (a single test in isolation and 2 and 3 serial tests separated by 1–4-day intervals) among residents of Connecticut state prisons and jails between 21 November 2020 and 15 June 2021. The 3-rapid-antigen-test collection strategy is currently recommended by Connecticut DOC [34]. In alignment with diagnostic accuracy estimates from other congregate settings, we found that rapid antigen tests had a moderate sensitivity when collected in isolation, but the sensitivity increased significantly when rapid antigen tests were collected in pairs and triplets [13, 14, 22].

In relation to RT-PCR, we found the current DOC rapid antigen test collection strategy, 3 rapid antigen tests, had a high sensitivity (96%) and specificity (98%). While the specificity of the 2- and 1-rapid-antigen-test collection strategies were higher (99% and 99%, respectively), the sensitivities for these less intensive collection strategies were significantly lower (89% and 67%, respectively). These findings suggest that, among 100 residents infected with SARS-CoV-2, 96 would be captured by the 3-rapid-antigen-test collection strategy. Compared with this strategy, the 2-rapid-antigen-test and the 1-rapid-antigen-test collection strategies would miss an additional 7 and 29 infected residents, respectively. Conversely, the 3-rapid-antigen-test collection strategy would only misdiagnose 2 out of 100 uninfected residents. Although this is one more than the 1-rapid-antigen-test collection strategy, the cost of false negatives (missed infections) far outweighs the cost of false positives (excess isolation) under scenarios of highly transmissible infectious diseases, such as SARS-CoV-2 [35].

In alignment with prior studies, we found the sensitivity of rapid antigen testing to be significantly higher later in the course of infection (rapid antigen tests collected on the same day or after RT-PCR) and among residents exhibiting COVID-19 symptoms [36, 37]. However, contrary to previous findings, we found the specificity was lower among symptomatic residents than among asymptomatic residents [37–39]. While surprising, prior studies found the specificity of the Access Bio CareState test was significantly and the BinaxNOW was nonsignificantly lower among residents who had experienced symptoms for a prolonged period of time (>7 days) [39, 40]. Although symptom duration data were unavailable, the observed difference was driven by the specificity of second, serially collected antigen tests. This suggests that, like other rapid antigen tests, the specificity of the BinaxNOW may decline with increased symptom duration. Despite the observed differences, the specificity among symptomatic residents remained high for each testing strategy with available data (1 rapid antigen test: 95.3%; 2 rapid antigen tests: 82.9%). Thus, this difference in specificity does not invalidate serial test collection among symptomatic residents of correctional facilities.

Taken collectively, our findings support the use of serial rapid antigen testing under scenarios when RT-PCR turnround time is long, rapid detection is required, or when isolating/quarantining all exposed residents is unfeasible. Such scenarios include times of unknown exposure (intake and transfers), contact tracing, asymptomatic and symptomatic screening, and during outbreak investigations. These recommendations stem

Table 3. Rapid Antigen Test Accuracy Relative to RT-PCR Among Residents of Connecticut State Correctional Facilities Under Varying Collection Strategies by Demographic and Clinical Characteristics

Characteristics	No. of RT-PCR– Positive Pairs	Sensitivity (95% CI)			No. of RT-PCR– Negative Pairs	Specificity (95% CI)		
		Single Test[a]	Serial Testing[b]	Difference in Serial Testing Accuracy[c]		Single Test[a,c]	Serial Testing[b,c]	Difference in Serial Testing Accuracy[b]
First rapid antigen test								
Sample collection sequence								
Rapid antigen test collected before RT-PCR	95	49.6% (39.8, 59.3%)	45.9% (37.3, 54.8%)	−28.3% (−38.0, −18.3%)	832	99.6% (98.9, 99.9%)	99.5% (98.7, 99.8%)	0.1% (−.8, .6%)
Rapid antigen test collected same day as RT-PCR	236	76.3% (70.4, 81.2%)	74.2% (69.4, 78.5%)	…	1702	99.5% (99.0, 99.7%)	99.4% (98.9, 99.7%)	…
Rapid antigen test collected after RT-PCR	71	63.4% (51.7, 73.7%)	65.0% (54.7, 74.1%)	−9.2% (−20.5, 1.0%)	908	99.1% (98.2, 99.6%)	99.0% (98.2, 99.5%)	−0.4% (−1.3, .3%)
Symptom presentation[d]								
Symptomatic	131	88.6% (81.9, 92.9%)	88.1% (82.4, 92.2%)	30.8% (23.5, 37.4%)	79	97.5% (90.5, 99.3%)	95.3% (88.5, 98.2%)	−4.2% (−11.2, −.9%)
Asymptomatic	269	58.0% (52.0, 63.7%)	57.2% (52.2, 62.0%)	…	3357	99.5% (99.1, 99.7%)	99.5% (99.2, 99.7%)	…
Age[e]								
≤37 years	199	67.3% (60.6, 73.6%)	68.5% (63.0, 73.6%)	3.7% (−3.8, 11.5%)	2020	99.6% (99.1, 99.8%)	99.4% (99.0, 99.6%)	0.1% (−.4, .7%)
>37 years	203	67.9% (61.5, 74.0%)	64.7% (59.2, 70.0%)	…	1422	99.2% (98.6, 99.6%)	99.3% (98.7, 99.6%)	…
Second rapid antigen test								
Sample collection sequence								
Rapid antigen test collected before RT-PCR	17	35.2% (16.9, 59.2%)	67.7% (55.1, 80.4%)	−25.4% (−38.2, −12.1%)	130	99.2% (94.8, 99.9%)	98.8% (94.3, 99.6%)	0.1% (−4.3, 2.3%)
Rapid antigen test collected same day as RT-PCR	69	70.9% (59.4, 80.7%)	93.2% (89.7, 95.6%)	…	267	99.2% (97.1, 99.8%)	98.7% (96.5, 99.4%)	…
Rapid antigen test collected after RT-PCR	18	72.4% (48.6, 88.0%)	90.1% (80.0, 95.8%)	−3.1% (−13.5, 3.7%)	176	98.9% (95.5, 99.7%)	97.9% (94.6, 99.0%)	−0.7% (−4.2, 1.6%)
Symptom presentation[d]								
Symptomatic	26	88.5% (69.5, 96.2%)	98.7% (96.1, 99.6%)	16.2% (11.0, 22.0%)	14	85.8% (58.2, 96.4%)	82.9% (56.4, 94.3%)	−16.0% (−42.9, −3.5%)
Asymptomatic	78	57.8% (46.6, 68.1%)	82.3% (76.7, 87.0%)	…	559	99.5% (98.3, 99.8%)	98.9% (97.8, 99.4%)	…
Age[e]								
≤37 years	57	75.3% (62.6, 84.8%)	92.0% (87.4, 95.3%)	6.8% (.2, 13.9%)	353	98.6% (96.6, 99.4%)	98.1% (96.2, 99.0%)	−0.8% (−2.9, .9%)
>37 years	47	53.0% (38.9, 66.8%)	85.1% (79.2, 89.9%)	…	220	100% (98.4, 100%)	99.0% (97.5, 99.5%)	…
Third rapid antigen test								
Sample collection sequence								
Rapid antigen test collected before RT-PCR	5	0.1% (.0, 51.6%)	70.9% (56.7, 86.8%)	−27.0% (−41.2, −11.0%)	73	100% (95.1, 100%)	98.0% (92.1, 99.6%)	−0.2% (−6.0, 3.2%)
Rapid antigen test collected same day as RT-PCR	46	69.7% (55.0, 81.1%)	97.9% (96.3, 98.9%)	…	132	100% (97.3, 100%)	98.2% (95.3, 99.3%)	…

Table 3. Continued

Characteristics	No. of RT-PCR–Positive Pairs	Sensitivity (95% CI)			No. of RT-PCR–Negative Pairs	Specificity (95% CI)		
		Single Test[a]	Serial Testing[b]	Difference in Serial Testing Accuracy[c]		Single Test[a,c]	Serial Testing[b,c]	Difference in Serial Testing Accuracy[b]
Rapid antigen test collected after RT-PCR	0	…	…	…	58	99.9% (94.0, 100%)	97.0% (91.0, 98.9%)	−1.2% (−7.3, 2.3%)
Symptom presentation[d]								
Symptomatic	17	88.4% (63.1, 97.1%)	99.9% (99.3, 100%)	8.6% (5.2, 13.0%)	0	…	…	…
Asymptomatic	34	49.9% (33.7, 66.0%)	91.2% (86.8, 94.6%)	…	263	100% (98.6, 100%)	98.7% (97.1, 99.3%)	…
Age[e]								
≤37 years	28	64.3% (45.2, 79.6%)	97.2% (94.6, 98.6%)	2.9% (−.9, 7.6%)	169	100% (97.8, 100%)	97.7% (95.2, 98.9%)	−0.7% (−3.4, 2.9%)
>37 years	23	60.8% (40.3, 78.2%)	94.2% (89.9, 97.0%)	…	94	100% (96.2, 100%)	98.5% (94.9, 99.5%)	…

Abbreviations: CI, confidence interval; COVID-19, coronavirus disease 2019; RT-PCR, reverse transcription–polymerase chain reaction.

[a]95% CI estimated using Generalized Estimating Equations with robust standard errors when >1 test pair per person was present; alternatively, Wald CIs were estimated.

[b]One rapid antigen test collection accuracy metrics estimated as the weighted average of the metrics for the first, second, and third rapid antigen test of the included series; serial collection (2 or 3 tests) sensitivity was estimated as the additive probability (positive any rapid antigen test); serial testing specificity was estimated as the multiplicative probability (negative for all rapid antigen test), posterior simulation of 1000 draws was used to propagate uncertainty through the equations.

[c]Difference in the accuracy metric between the stratified groups calculated on the draw level; uncertainty intervals estimated using percentile method.

[d]Symptomatic infection was defined as reporting 1 or more COVID-19–related symptoms (6) at time of rapid antigen test collected closest in time to the RT-PCR.

[e]Stratified according to mean age of the population (37 years of age).

from the rapid turnaround time and low cost of a single test, the collectively high diagnostic accuracy of serial collection, and the ability of serial collection strategies to detect events under continuous exposure scenarios. Although our findings speak predominantly to the value of serial collection resulting from a single exposure, serial collection provides additional benefit through capture of infections from exposures that occurred immediately prior to or following the first collected test [12]. The combination of these benefits thus may results in more rapid isolation of infected residents and, in turn, a reduction in facility-wide transmission.

Limitations and Strengths

Our study was subject to limitations typical of retrospective diagnostic validation analyses. First, race/ethnicity was missing for a large portion of the population and we were unable to test for differences in test accuracy by race. However, it is unlikely that race would impact the diagnostic accuracy of the rapid antigen test. Second, we relied on a reference outcome of RT-PCR positivity, which is an imperfect indicator of infection. Third, we did not have access to cycle threshold values and were unable to test the impact of viral load on rapid antigen test performance. Fourth, our accuracy estimates relied on collected tests that may be biased towards department-specific testing practices. However, we observed similar results when we selected the first, second, and third test of each series at random (Supplementary Figure 3; Supplementary Table 5). Finally, our study was conducted prior to the large Delta and Omicron waves of 2021/2022. While the diagnostic accuracy of rapid antigen tests likely varies between the different variants, we believe the benefits of serial collection will hold.

Our study had several strengths including our large sample of paired assays collected among a diverse population of Connecticut State correctional facility residents. This large sample allowed us to estimate and compare the diagnostic accuracy of 3 different collection strategies, including the 3-test collection strategy used by the Connecticut DOC. Our large sample also allowed us to examine characteristics associated with the accuracy of the rapid antigen test within correctional facility settings and speak to the use of different collection strategies based on these characteristics. Additionally, through the inclusion of numerous sensitivity analyses, we were able to show that our findings were not the result of the data cleaning or modeling assumptions we used within this analysis. Finally, we were able to include all unique rapid antigen test sets and account for within-person correlation in our uncertainty intervals using GEEs.

Conclusions

Compared with singularly collected tests, we found that serial collection of BinaxNOW rapid antigen tests resulted in meaningfully higher sensitivities and comparably high specificities

among residents in state correctional facilities. We found this held for both asymptomatic and symptomatic residents and regardless of rapid antigen test collection time relative to RT-PCR collection. These findings speak to the utility of serially collected rapid antigen tests within correctional facilities for asymptomatic and symptomatic screening, contact tracing, and during outbreak investigations. If used under such scenarios, rapid antigen testing may result in faster isolation of infected residents and reduce transmission within facilities.

Supplementary Data

Supplementary materials are available at *Clinical Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

Notes

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Author contributions. M. L. L. had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Concept and design: A. I. K., B. S. K., R. P. R. Acquisition, analysis, or interpretation of data: O. L. S., M. L. L. Drafting of the manuscript: M. L. L., O. L. S., A. J. R., A. I. K., D. A. T. C. Critical revision of the manuscript for important intellectual content: All authors. Statistical analysis: M. L. L. Administrative, technical, or material support: Houde. Supervision: A. I. K., B. S. K., R. P. R., D. A. T. C.

Data Use Agreement. The data used in this study belongs to the Connecticut Department of Correction. Qualified researchers may submit a data share request for de-identified patient-level data by contacting the corresponding author with a detailed description of the research question.

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Potential conflicts of interest. A. I. K. serves as an expert panel member for Reckitt Global Hygiene Institute, a scientific advisory board member for Revelar Biotherapeutics, a consultant for Tata Medical and Diagnostics and Regeneron Pharmaceuticals, and an unpaid leadership or fiduciary role on the Board of Directors for the American Society of Tropical Medicine and Hygiene and has received grants from Merck, Regeneron Pharmaceuticals, and Tata Medical and Diagnostics for research related to COVID-19, all of which are outside the scope of the submitted work. D.A.T.C. reports contracts or grants from Merck for research unrelated to this manuscript. All other authors report no potential conflicts. All authors have submitted the ICMJE Form for Disclosure of Potential Conflicts of Interest. Conflicts that the editors consider relevant to the content of the manuscript have been disclosed.

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