turnaround times. For frontline pandemic workers, those conditions might have contributed to accelerated staff burnout and reported staff challenges.

The SARS-CoV-2 pandemic offers a One Health case model, given that both humans and animals may become infected and environmental detection is possible (e.g., wastewater) (*5*,*6*). As recently demonstrated, human testing facilities might struggle to meet emergency public health demands without additional support; however, laboratories that regularly test other zoonotic and nonzoonotic pathogens can help meet testing needs. Many of the responding VDLs reported mutually beneficial outcomes from participating in human SARS-CoV-2 testing, particularly in the form of new interagency relationships, shared information, and improved recognition. Similar coordinated, collaborative efforts might be particularly useful in mitigating future pandemics and improving disease response outcomes (*7*,*8*).

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Model for Interpreting Discordant SARS-CoV-2 Diagnostic Test Results

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We devised a model to interpret discordant SARS-CoV-2 test results. We estimate that, during March 2020–May 2022, a patient in the United States who received a positive rapid antigen test result followed by a negative nucleic acid test result had only a 15.4% (95% CI 0.6%–56.7%) chance of being infected.

During the COVID-19 pandemic, nucleic acid amplification tests (NAATs) and rapid antigen tests (RATs) have been widely used to direct patient care and control transmission (*1*). NAATs, such as reverse transcription PCR, tend to have higher sensitivity and

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specificity than RATs (*2*) but often are more costly and take much longer to process (*3,4*). Thus, RATs increasingly have been used across the United States for at-home symptom-based testing and asymptomatic screening in healthcare, educational, and public event settings (*5*).

During June 2020–April 2022, healthcare providers recommended a confirmatory NAAT after a positive RAT because of high false-positive rates for RATs when community disease prevalence was low (*6,7*). When a patient received a negative confirmatory NAAT result, clinicians had to decide which of the results was erroneous and suggest a course of action.

In this study, we describe a statistical model that can guide the interpretation of discordant test results. The model considers test sensitivity and specificity and estimated community prevalence of the virus. By using community prevalence, the model can estimate the probability that an initial RAT result was a false-positive after a negative confirmatory NAAT result (Appendix, https://wwwnc.cdc.gov/EID/article/30/2/23-0200-App1.pdf).

As a case study, we considered BinaxNOW (Abbott Laboratories, https://www.abbott.com), a test widely used in 2021. BinaxNOW had an estimated test sensitivity of 84.6%; we also considered various NAAT false-negative rates depending on how long after BinaxNOW a NAAT was administered: 68% at 0 days, 37% at 1 day, 24% at 2 days, and 21% at 3 days (*2*). For a patient who received a positive RAT result and then a negative NAAT result, we estimated the probability that the RAT result was erroneous and the patient was not infected (Figure, panel A). That probability was >80% if community prevalence was <200 new weekly COVID-19 cases/100,000 population, the Centers for Disease Control and Prevention (CDC) threshold for low community prevalence (*8*), and generally declined as disease prevalence increased (Figure, panel A). However, a tradeoff exists between NAAT accuracy and speed of diagnosis. For instance, if RAT and NAAT were administered on the same day, the RAT false-positive probability was 89.6% (95% CI 80.5%–100%) when community COVID-19 levels were low according to CDC
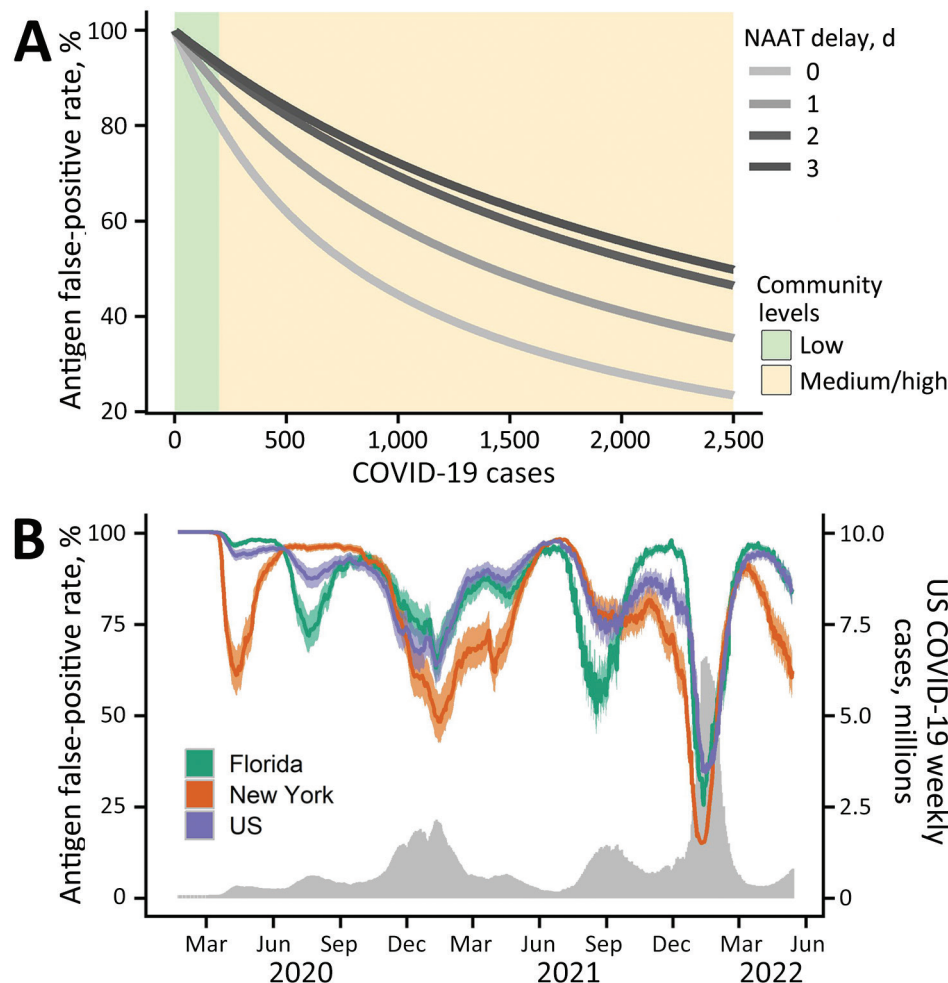

Figure. Estimated probability that a positive RAT result is erroneous given a subsequent negative NAAT in a model for interpreting discordant SARS-CoV-2 diagnostic test results. A) Estimated RAT false-positive percentages for levels of community transmission ranging from 0–2,500 COVID-19 cases per 100,000 population. Green and yellow shading correspond to the Centers for Disease Control and Prevention threshold for low and medium or high community levels (*8*). Line color corresponds to different numbers of days between the initial RAT and confirmatory NAAT, ranging from same day (lightest gray) to 3 days later (black). B) Estimated RAT false-positive percentages for the United States (purple), Florida (green), and New York (orange) during March 2020–May 2022, assuming the NAAT is administered 1 day after the RAT and that 1 in 4 cases were reported. Shading reflects uncertainty in Centers for Disease Control and Prevention estimated COVID-19 infection underreported, ranging from 1 in 3 to 1 in 5. The gray time series along the bottom indicates the daily 7-day sum of reported COVID-19 cases in the United States. NAAT, nucleic acid amplification test; RAT, rapid antigen test.

Table. Probability that a RAT is false-positive in a model for interpreting discordant SARS-CoV-2 diagnostic test results*

No. days between RAT and NAAT	Estimated RAT false-positive rate, % (95% CI)
0	73.4 (49.2–100)
1	82.5 (63.4–100)
2	88 (73.3–100)
3	89.2 (75.9–100)
4	89.6 (76.6–100)
5	88.8 (75.0–100)
6	88.4 (74.1–100)
7	86.7 (71–100)

*The model assumes that a NAAT was negative after a RAT and that NAAT was performed after specified time delay. Estimates assume that the antigen test was performed when patient symptoms first appeared and had a test sensitivity of 84.6% and specificity of 98.54%, which corresponds to the estimated values for BinaxNOW (Abbott Laboratories, https://www.abbott.com) (Appendix Table 1, https://wwwnc.cdc.gov/EID/article/30/2/23-0200-App1.pdf). The NAAT false negative rate for each delay was drawn from a previous study (3). NAAT, nucleic acid amplification test; RAT, rapid antigen test.

guidelines. However, if the NAAT was administered 3 days after the RAT, the corresponding probability increased to 96.4% (95% CI 93.0%–100%) (Appendix Table 4). Our confidence in the negative NAAT result peaked when the NAAT was administered 4 days after the RAT (Table; Appendix Figure 1, panel B). Barring other external information (e.g., symptomicity), clinicians can be 89.6% (95% CI 80.5%–100%) confident that the initial RAT result was false-positive when a community is in low risk according to CDC guidelines and 70.5% (95% CI 62.0%–80.5%) confident the same RAT was false-positive when the community is at medium or high risk (Appendix Tables 2–4, Figure 1, panel A).

During May 2020–May 2022, we estimate that RAT false-positive probability in the United States ranged from 34% (95% CI 29%–41%) to 97.7% (95% CI 97.2%–98.3%), assuming a 25% (95% CI 20%–33%) case reporting rate (Figure, panel B) (9). The probability of an erroneous RAT was lowest during the Omicron surge in the winter of 2021–22, when community prevalence was estimated to be highest. At the Omicron peak, we estimate RAT false-positive probabilities of 15% (95% CI 11%–20%) for New York, 25% (95% CI 21%–32%) for Florida, and 34% for (95% CI 29%–41%) the United States (Figure, panel B). The relative trends are similar for other commonly used antigen tests, but the estimated false-positive rates depend on test sensitivities and specificities for each test (Appendix Figures 2, 3).

Rapid and reliable diagnoses of severe infectious diseases is critical for clinical care and infection control. However, the first 2 years of the COVID-19 pandemic revealed enormous barriers to deploying inexpensive, rapid, and accurate tests to combat a newly emerging or rapidly evolving

pathogen. We developed this framework during fall 2021 to guide decision-making by patients, physicians, and public health officials in the Austin, Texas, USA metropolitan area. The University of Texas used this model for decision-making regarding when patients might need to visit a clinician. Our framework is limited by the accuracy of the estimates of the RAT and NAAT test sensitivity and specificity and the estimated community disease prevalence, which we drew from transmission estimates from the first 2 years of the pandemic. If community prevalence was higher than we estimated, which could be the case in the early weeks of the pandemic, our model could overestimate the RAT false-positive rate.

In conclusion, we developed a model to estimate false-positive RAT rates during the COVID-19 pandemic. The model inputs can be readily modified to guide the interpretation of discordant tests as COVID-19 continues to evolve and as RATs become more widely used for other diseases, such as influenza or respiratory syncytial virus (10).

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SARS-CoV-2 Infection in Beaver Farm, Mongolia, 2021

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We report an outbreak of COVID-19 in a beaver farm in Mongolia in 2021. Genomic characterization revealed a unique combination of mutations in the SARS-CoV-2 of the infected beavers. Based on these findings, increased surveillance of farmed beavers should be encouraged.

The COVID-19 pandemic that began in 2019 remains uncontained, and fatalities and multiple waves of infection continue to occur worldwide (1). The causative agent, SARS-CoV-2, has been detected in humans and several animal species, including domestic, wild, and laboratory animals (2,3). Because SARS-CoV-2 can be transmitted from humans to animals and back to humans, understanding the dynamics of infection in animals can contribute to the creation of more comprehensive response strategies.

We identified SARS-CoV-2 infection in beavers (*Castor fiber*) farmed for conservation reasons in Mongolia and report on serologic and whole genome sequence data from this outbreak. The beaver farm, located in the Bayanzurkh district in Ulaanbaatar, Mongolia, reared 32 adults and 16 kits in 2021. They were housed indoors in a large area separated by waist-high walls, with space for multiple animals. One of the 7 employees of the farm had influenza-like symptoms for several days and was diagnosed with COVID-19 on August 6, 2021. On August 9, the beaver farm reported the death of 2 beavers (one 6 months of age and one 2 years of age) after signs of coughing, nasal discharge, rasping on auscultation of the lungs and chest cavity, sluggish movement, and aversion to food. On August 13, research investigators collected nasal swabs, saliva, and 7 tissue samples

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Model for Interpreting Discordant SARS-CoV-2 Diagnostic Test Results

Appendix

Estimating the Probability of a False-Positive Rapid Antigen Test

Our goal is to estimate the probability that a positive rapid antigen test (RAT) was a false-positive conditional on a subsequent negative nucleic acid amplification test (NAAT) result. Using Bayes' theorem, this is given by the following:

$$P(D-|A=1,N_i=0) = \frac{P(A=1,N_i=0|D-)\cdot P(D-)}{P(A=1,N_i=0)}$$

where *D*– denotes the disease state of the individual (minus and plus indicate uninfected and infected, respectively), *A* denotes the result of the antigen test and N_t denotes the result of the NAAT when administered *t* days after the antigen test (0 indicates negative and 1 indicates positive). We assume that the antigen and NAATs are independent of one another.

We then estimate the false positive rate as follows:

$$P(D-|A=1,N_i=0) =$$
$$\frac{P(A=1|D-)\cdot P(N_i=0|D-)\cdot P(D-)}{P(A=1|D-)\cdot P(N_i=0|D-)\cdot P(D-) + P(A=1|D+)\cdot P(N_i=0|D+)\cdot P(D+)}$$

with parameter estimates as described in Appendix Table 1. We assume that $P(D+)$ is equal to the prevalence of SARS-CoV-2 in the community.

Estimating SARS-CoV-2 Community Prevalence

To calculate regional community SARS-CoV-2 prevalence we used daily incident cases provided by the New York Times (*9*). Following a previously described methodology (*10*), we estimated the prevalence for a region, *r*, on the day, *t*, as follows:

$$P_r(D+)(t) = \frac{\sum_{i=t-6}^{t} \frac{C(i)}{\rho}}{N_r}$$

where C(i) is the reported incident cases on day *i*, *P* is the reporting rate, and N_r is the population estimate for the region. We assumed a reporting rate of 25% (20%–33%) during February 2020–June 2022 (*11*) and that infected cases were infectious for 7 days (*12*). We estimated the prevalence for New York, Florida, and the United States as a whole to show how regional variation in epidemic timing impacts the interpretation of discordant test results (Appendix Figure 1, panel B).

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Appendix Table 1. Assumed model parameters for statistical estimation RAT and NAAT

Parameter	Description	Value								Source
$P(A = 1\vert D-)$	RAT false-positive rate									
BinaxNow		0.0146								(1)
On/Go		0.02439								(2)
CareStart		0.0068								(3)
iHealth		0.019								(4)
CLINITEST		0.0071								(5)
$P(A = 1\vert D+)$	RAT sensitivity									
BinaxNow		0.846								(1)
On/Go		0.87								(2)
CareStart		0.9375								(3)
iHealth		0.943								(4)
CLINITEST		0.854								(5)
$P(N_i = 0\vert D-)$	NAAT true-negative rate	0.98								(6)
$P(N_i = 0\vert D+)$	NAAT false-negative rate by day	Day, value								(7)
		0	1	2	3	4	5	6	7	
		0.68	0.38	0.24	0.21	0.20	0.22	0.23	0.27	
$P(D+)$	Prevalence	0–5%								(8)

*$D-$, uninfected disease state; $D+$, infected disease state; NAAT, nucleic acid amplification test; $P(D+)$, SARS-CoV-2 rate in the community; RAT, rapid antigen test.

Appendix Table 2. Thresholds for requiring a clinical visit following a positive antigen test and a negative NAAT confirmatory test*

	% Community prevalence threshold for requiring clinical confirmation	
Desired confidence level, %	1 d between RAT and NAAT	3 d between RAT and NAATs
50	4.3	7.6
65	2.4	4.2
80	1.1	2
90	0.5	0.9
95	0.24	0.46

*Because clinician visits can be burdensome to clinics during a COVID-19 surge and financially costly and disruptive to patients, we recommend requiring a clinician visit when community prevalence exceeds the values provided in the table based on a patient's desired confidence level. For example, if a patient had a positive RAT and negative confirmatory NAAT and wanted to be at least 50% sure that the RAT was a false positive before seeing a clinician, then we would recommend seeing a clinician if the community prevalence was at least 4.3% for a 1-day delay or 7.6% for a 3-day delay between the tests. NAAT, nucleic acid amplification test; RAT, rapid antigen test.

Appendix Table 3. Probability that a positive BinaxNOW RAT is a false-positive given a subsequent negative NAAT, depending on the prevalence of SARS-CoV-2 in the community*

Disease prevalence, %	% Confidence for false-positive RAT after negative NAAT	
	1 d between RAT and NAATs	3 d between RAT and NAAT
0.15	97	98
0.3	94	96
0.5	90	94
1	82	89
2	69	80
3	60	72

*BinaxNOW (Abbott Laboratories, https://www.abbott.com). NAAT, nucleic acid amplification test; RAT, rapid antigen test.

Appendix Table 4. Probability that a positive antigen test is a false-positive after negative NAAT, depending on community prevalence levels*

Community levels	% Mean confidence per no. days between RAT and NAAT (95% CI)		
	0	1	3
Low	89.6 (80.5–100)	93.8 (88.1–100)	96.4 (93.0–100)
Medium or high	70.5 (62.0–80.5)	80.9 (74.5–88.0)	88.4 (84.1–93.0)

*NAAT, nucleic acid amplification test; RAT, rapid antigen test.
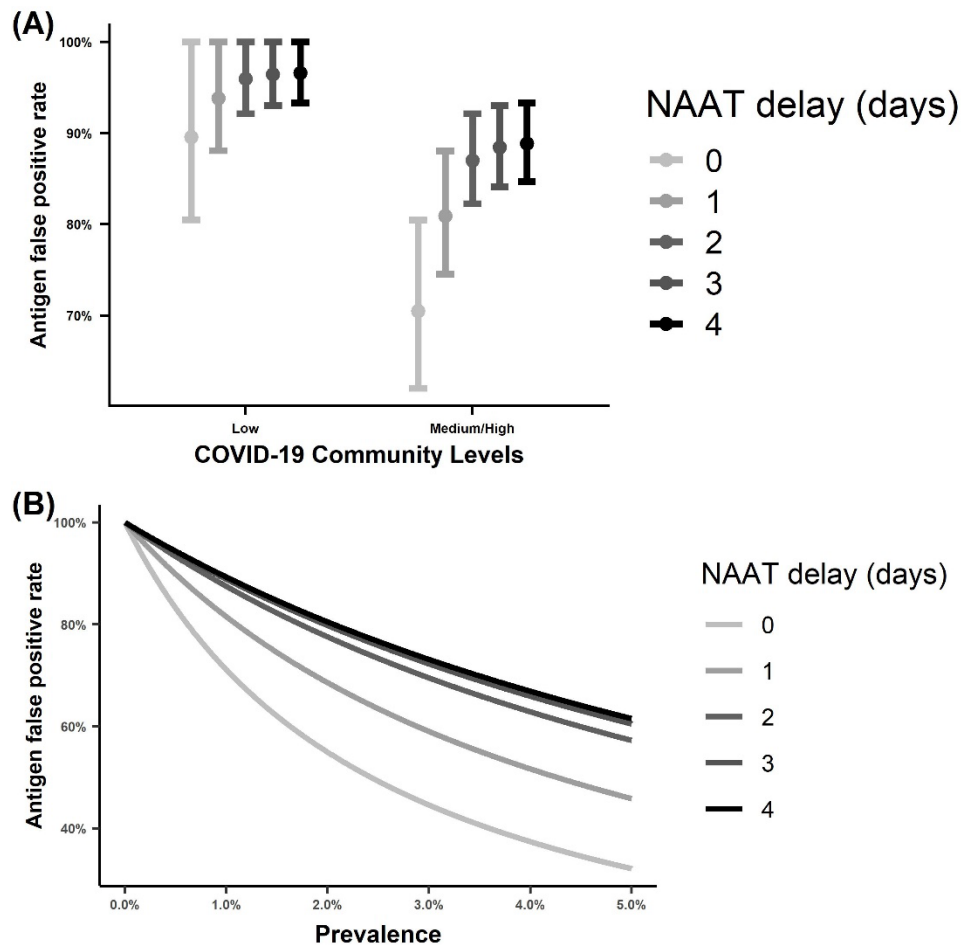
Appendix Figure 1. The probability that a RAT is a false-positive given a subsequent negative NAAT. A) The mean probability that <200 cases (low) and ≥200 cases (medium/high) per 100,000 population are RAT false-positive given a subsequent negative NAAT. Error bars indicate the lowest and highest probability RAT false-positive rates for SARS-CoV-2 community transmission level, assuming that 1 in 4

(95% CI 3–5) infections are reported. B) The probability that a positive RAT is a false-positive given a subsequent negative NAAT, depending on the prevalence of SARS-CoV-2 in the community. Color indicates the number of days between the initial RAT and confirmatory NAAT. NAAT, nucleic acid amplification test; RAT, rapid antigen test.
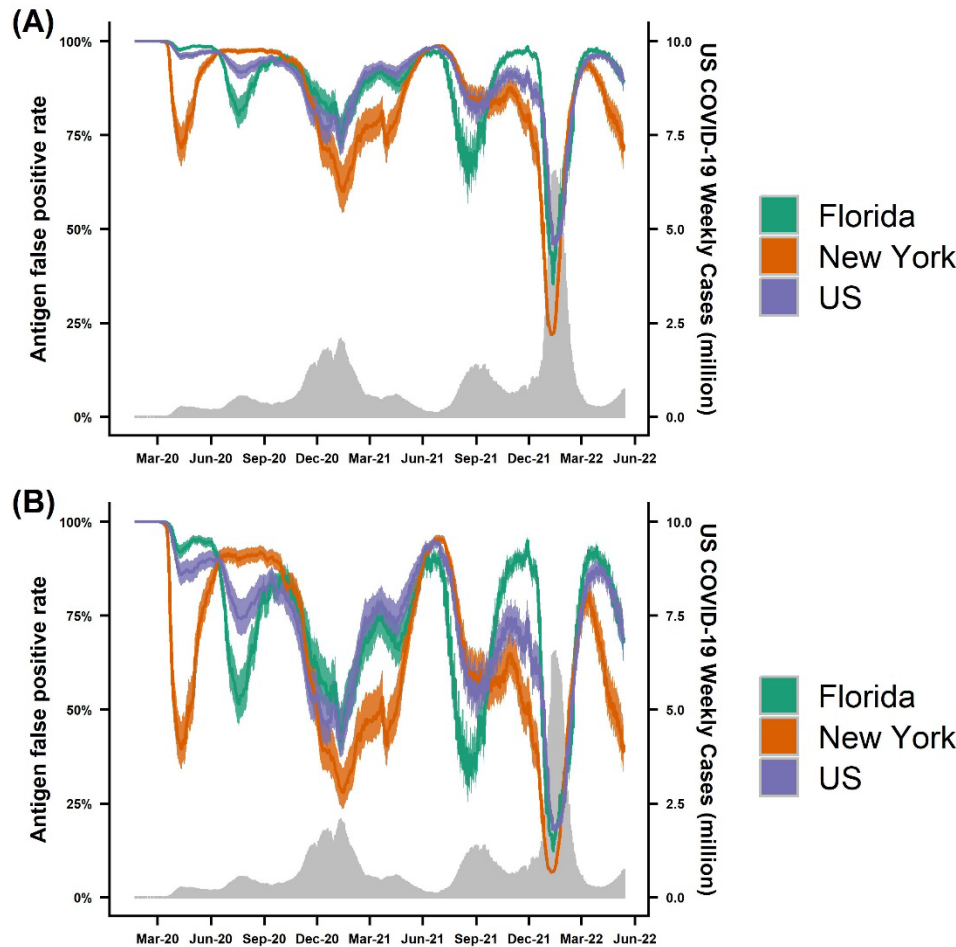
Appendix Figure 2. Estimated RAT false-positive probability rates during March 2020–May 2022, assuming the NAAT is administered 1 day after the RAT and that 1 in 4 infections were reported (*9*). A) On/Go test; B) CareStart test. Colors correspond to the United States (purple), Florida (green), and New York (orange). Shading reflects uncertainty in Centers for Disease Control and Prevention estimated COVID-19 infection underreported, ranging from 1 in 3 to 1 in 5. The gray time series along the bottom indicates the daily 7-day sum of reported COVID-19 cases in the United States. NAAT, nucleic acid amplification test; RAT, rapid antigen test.
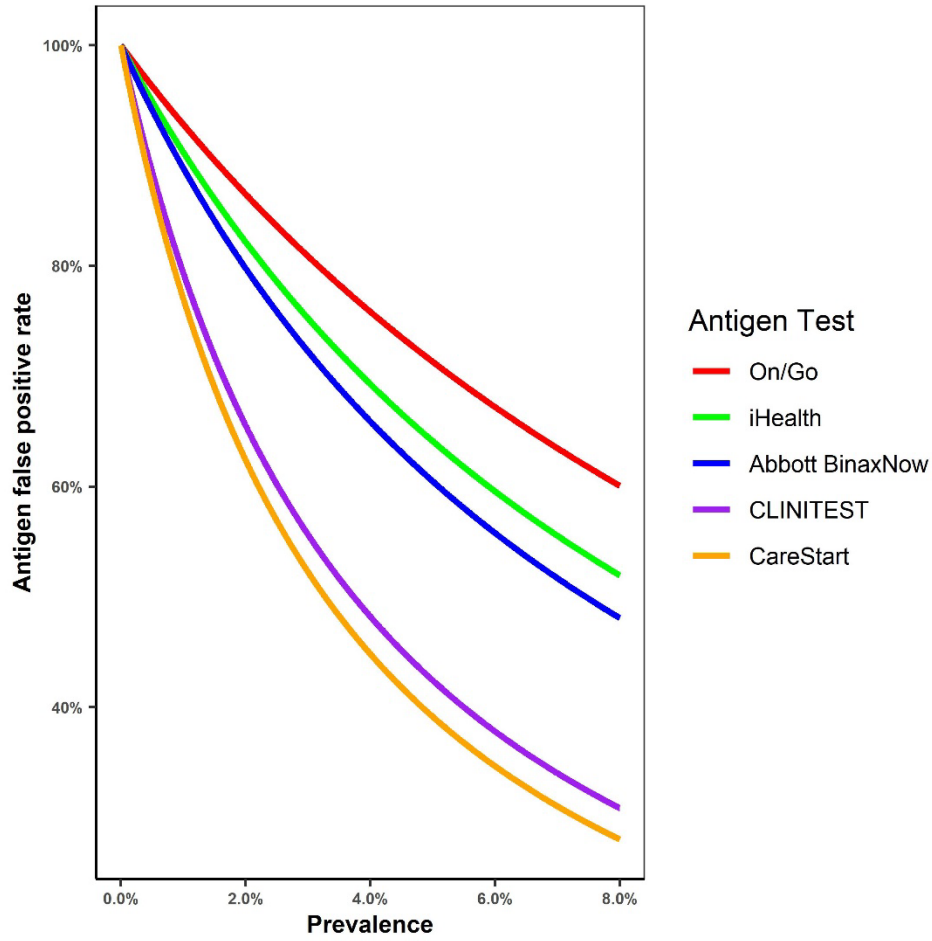
Appendix Figure 3. Estimated rapid antigen test false-positive probability for different community disease prevalences based on the chosen test. Color indicates the specific antigen test, with test sensitivity and specificity as described in Appendix Table 1. BinaxNow (Abbot, https://www.abbott.com); CareStart (Access Bio, https://accessbio.net); CLINITEST (Siemens Healthineers, https://www.siemens-healthineers.com); iHealth (https://www.ihealthlabs.com); On/Go (Access Bio).