Viral testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) of all patients admitted to the hospital is an appealing objective given the recognition of asymptomatic or minimally symptomatic infections. Yet such testing requires that all admitted patients be classified as persons under investigation (PUIs) until their test results are known. If an outside laboratory is used for the SARS-CoV-2 testing, the delay in obtaining results for these PUIs may cause significant personal protective equipment (PPE) use, postpone some care for non-coronavirus diseases, and produce anxiety among staff and other patients. Rapid in-house testing of all admitted patients may resolve these issues but may be limited by the supply of reagents. To address this challenge, we piloted a pooled testing strategy for patients at low risk for SARS-CoV-2 admitted to a community hospital.

**METHODS**

From April 17, 2020, to May 11, 2020, we implemented a pooled testing strategy using the GeneXpert® System (Cepheid, Sunnyvale, California) at Saratoga Hospital, a 171-bed community hospital in upstate New York. Under normal procedures for this system, a single patient swab is placed in a vial containing viral transport media (VTM). An aliquot of this media is then transferred into a Xpert® Xpress SARS CoV-2 test vial containing viral transport media (VTM). An aliquot of this media is then transferred into a Xpert® Xpress SARS CoV-2 test cartridge and assayed on the GeneXpert® instrument in our laboratory. Obtaining immediate results allowed us to assign admitted patients to either a COVID-19 or a non–COVID-19 unit, improving the issues associated with PUIs. Unfortunately, we did not have enough test cartridges to sustain this strategy of rapid individual testing of all admitted patients, and supply lines have remained uncertain.

We sought to conserve our limited Xpert Xpress SARS CoV-2 test cartridges using the strategy of pooled testing, a technique reported in Germany and by the University of Nebraska. In this method, variable numbers of tests are pooled for a single analysis. If the test from the pooled vial is negative, these patients are all considered negative. If the pooled test is positive, all those patients need individual testing. This pooling method has been theorized to preserve test cartridges when the expected frequency of positive results is low.

All patients admitted or placed on observation underwent SARS-CoV-2 PCR testing. The Emergency Department (ED) staff stratified patients into high or low risk to determine if they would be tested in a single send-out test (high risk) or a rapid in-house pooled group (low risk). High-risk patients were those with compatible history, physical exam, laboratory markers, and radiographic studies for COVID-19 disease. This often included increased supplemental oxygen requirement, multiple elevated inflammatory markers (including D-dimer, C-reactive protein, erythrocyte sedimentation rate, and ferritin levels), lymphopenia, and findings on chest radiograph or computed tomography scan including ground glass changes, multifocal pneumonia, or pneumonia. High-risk patients were admitted to the COVID unit or intensive care unit, had a send-out SARS-CoV-2 polymerase chain reaction (PCR) test, and were treated as a PUI until the results of their testing was known and correlated with their clinical course. Low-risk patients were those without complaints suggestive of COVID-19 infection and who may have had negative inflammatory markers, no significant lymphopenia, and negative imaging.

The samples from 3 admitted patients thought to be at low risk for COVID-19 using the clinical judgement of our ED staff
were pooled for testing. All samples were obtained using nasopharyngeal swabs by experienced staff. The swabs from these patients were placed into a single vial of 3 mL VTM, maintaining the recommended 1 swab per mL of VTM. An aliquot of this media was then transferred into an Xpert Xpress SARS CoV-2 test cartridge and assayed on the GeneXpert instrument in our laboratory following manufacturer’s instructions. Based on analytic laboratory studies of the Cepheid Xpert Express SARS-CoV-2 test, we assume a clinical performance comparable to other reverse-transcriptase PCR (RT-PCR) tests, which have so far demonstrated sensitivities of 60% to 80% and specificities of 95% to 99%. Validation studies were performed on pools made from samples obtained from admitted patients with previously known positive and negative samples tested at the New York State Department of Health, Wadsworth Center laboratory (Albany, New York). A total of 14 samples were used for the instrument validation study, including three samples for pooled testing. The cycle threshold (Ct) value is defined as the number of PCR cycles required for the signal to be detectable. Ct values for each nucleic acid target of a known positive sample tested singly and in the pool with known negative patients were compared. A small shift in Ct values was noted between single and pooled testing, demonstrating no decrease in analytic sensitivity and suggesting that we would experience no decrease in clinical sensitivity. We selected the pooling of 3 samples into 1 cartridge for several reasons: (1) 3-sample pools are well within the appropriate pooling size for the percentage positive rate in the population being tested. The use of larger pool sizes results in the need for more repeat testing when a positive result is obtained; (2) Given our supply lines, the projected savings would allow us to continue this strategy; and (3) Holding 3 patients in the ED until a pool was ready was manageable given our rate of admissions and ED volume.

The strategy required patients being held in the ED until a pooled group of 3 could be tested. On select occasions when holding patients in the ED to obtain a pool of 3 was not practical, 2 patients were tested in the pool. These decisions required close coordination between the laboratory, ED, and nursing staff.

RESULTS
This strategy resulted in 530 unique patient tests in 179 cartridges (172 with three swabs and 7 with two swabs). We had 4 positive pooled tests, requiring the use of 11 additional cartridges, for a positive rate of 0.8% (4/530) in this low-risk population (patients without COVID-19-related symptoms). There were no patients from negative pools who developed evidence of COVID-19 disease or tested positive for SARS-CoV-2 during their hospitalization. The total number of cartridges used was 190 and the number saved was 340.

DISCUSSION
The strategy of pooled testing for SARS-CoV-2 in patients admitted to our community hospital allowed us to continue rapid testing of admitted patients at low risk for COVID-19 disease during a period when supplies would otherwise not have been sufficient. We believe this strategy preserved PPE, led to a marked reduction in staff and patient anxiety, and improved patient care. Our impression is that testing all admitted patients has also been reassuring to our community. Like many others, we have observed that public fear of entering the hospital during this pandemic has caused delays in patients seeking care for non–COVID-19 conditions. We believe this strategy will help reduce those fears.

This strategy may require modification as the pandemic progresses. Our ED physicians were able to identify patients who they felt to be low risk for having COVID-19 disease based on signs, symptoms, and clinical impression during a time when we had an 8% positive rate among symptomatic outpatients and an estimated community positive rate in the range of 1% to 2%. If the rate of positive tests in our community rises, the use of pooling may need to be limited or the pool size reduced. If our supply of reagents is further limited or patient testing demand increases, the pool size may need to be increased. This will need to be balanced with our ability to hold patients in the ED while waiting for the pool size to be reached.

CONCLUSION
The strategy of pooled testing for SARS-CoV-2 has allowed us to continue to immediately test all admitted patients, thus improving patient care. It has required close coordination between multiple members of our laboratory and clinical staff and may require adjustment as the pandemic progresses. We believe it is a valuable tool during a time of limited resources that may have application in testing other low-risk groups, including healthcare workers and clients of occupational medicine services.

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