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Coronavirus Disease 2019 (COVID-19) Diagnostic Clinical Decision Support: A Pre-Post Implementation Study of CORAL (COvid Risk cALculator)

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Background. Isolation of hospitalized persons under investigation (PUIs) for coronavirus disease 2019 (COVID-19) reduces nosocomial transmission risk. Efficient evaluation of PUIs is needed to preserve scarce healthcare resources. We describe the development, implementation, and outcomes of an inpatient diagnostic algorithm and clinical decision support system (CDSS) to evaluate PUIs.

Methods. We conducted a pre-post study of CORAL (COvid Risk cALculator), a CDSS that guides frontline clinicians through a risk-stratified COVID-19 diagnostic workup, removes transmission-based precautions when workup is complete and negative, and triages complex cases to infectious diseases (ID) physician review. Before CORAL, ID physicians reviewed all PUI records to guide workup and precautions. After CORAL, frontline clinicians evaluated PUIs directly using CORAL. We compared pre- and post-CORAL frequency of repeated severe acute respiratory syndrome coronavirus 2 nucleic acid amplification tests (NAATs), time from NAAT result to PUI status discontinuation, total duration of PUI status, and ID physician work hours, using linear and logistic regression, adjusted for COVID-19 incidence.

Results. Fewer PUIs underwent repeated testing after an initial negative NAAT after CORAL than before CORAL (54% vs 67%, respectively; adjusted odd ratio, 0.53 [95% confidence interval, .44–.63]; *P* < .01). CORAL significantly reduced average time to PUI status discontinuation (adjusted difference [standard error], −7.4 [0.8] hours per patient), total duration of PUI status (−19.5 [1.9] hours per patient), and average ID physician work-hours (−57.4 [2.0] hours per day) (all *P* < .01). No patients had a positive NAAT result within 7 days after discontinuation of precautions via CORAL.

Conclusions. CORAL is an efficient and effective CDSS to guide frontline clinicians through the diagnostic evaluation of PUIs and safe discontinuation of precautions.

Keywords. COVID-19 diagnosis; electronic health record; diagnostic algorithm; clinical decision support system.

Isolation of persons under investigation (PUIs) for coronavirus disease 2019 (COVID-19) in healthcare settings is essential to prevent nosocomial transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Once COVID-19 infection has been excluded, prompt discontinuation of transmission-based precautions is critical to preserve hospital bed capacity, conserve personal protective equipment (PPE), and reduce adverse effects associated with isolation [1–3].

SARS-CoV-2 nucleic acid amplification tests (NAATs) are the reference standard for COVID-19 diagnosis, but they have imperfect sensitivity dependent on specimen source, collection technique, and symptom duration [4]. The Infectious Diseases Society of America recommends a repeated NAAT 24–48 hours after the first negative test result among symptomatic patients when clinical suspicion for COVID-19 remains intermediate or high [4]. Several reports describe COVID-19 diagnosed after 2 negative nasopharyngeal (NP) NAAT results [5, 6]. However, repeating a NAAT extends the duration of isolation and may delay treatment, and standardized frameworks to categorize patients by clinical suspicion have not been developed.

Among hospitalized PUIs, the stakes for accurate diagnoses are high, given the potential for nosocomial transmission [7–9]. Many medical centers have turned to infectious diseases (ID) physicians, infection preventionists, and hospital epidemiologists to guide COVID-19 evaluations and make case-by-case determinations regarding discontinuation of transmission-based precautions [10–12]. These specialists are in limited supply [13–17] and may not be available for 24/7 evaluation [13]. Approaches to increase the efficiency and accessibility of COVID-19 diagnostic evaluation are needed.

Clinical decision support systems (CDSSs) improve adherence to guideline-based care [18–20]. SARS-CoV-2 testing criteria, diagnostics, and literature on evaluation of PUIs have evolved rapidly; CDSSs can standardize evaluations through adoption of best practices. We created the COvid Risk cALculator (CORAL) CDSS, using a modified Delphi method informed by >4500 person-hours of ID physician–led case-by-case evaluation of PUIs. We describe the development and implementation of CORAL and outcomes from its use in >2000 inpatient encounters.

METHODS

Study Setting and Design

We conducted a pre-post intervention study of COVID-19 PUIs hospitalized at Massachusetts General Hospital during March–July 2020. Throughout the study period, all NAATs were performed on emergency use authorized assays, including a laboratory-developed quantitative polymerase chain reaction test (turnaround time 8–36 hours; through 23 March), Roche COBAS SARS-CoV-2 (6–18 hours; used from 23 March onward), and the Cepheid Xpert Xpress SARS-CoV-2 (2–4 hours; used from 30 March onward). (See full details regarding test availability in the Supplementary Methods and Supplementary Figure 1.)

In early March, SARS-CoV-2 NAAT was limited to inpatients with symptoms consistent with COVID-19. Admission NAAT screening for all patients began on 23 April. Patients were considered PUIs if they reported COVID-19 symptoms, had epidemiologic risk factors (ie, living in a congregate setting, experiencing homelessness, or receiving hemodialysis treatment), or if a history could not reliably be obtained. PUIs were isolated with enhanced respiratory isolation (ERI; gown, gloves, N95 or powered air purifying respirator, and eye protection), admitted to single-occupancy rooms, and marked as "CoV-Risk" in the electronic health record (EHR; Supplementary Table 1). Discontinuation of CoV-Risk status indicated that the patient was no longer a PUI and allowed for discontinuation of ERI. If clinical suspicion of COVID-19 remained high despite negative NAAT results, PUIs were labeled "CoV-Presumed" and maintained with ERI.

Pre-CORAL: ID physician review of PUIs

From 18 March to 23 April, ID physicians actively evaluated all hospitalized PUIs who had an initial negative NAAT before discontinuation of ERI. These physicians iteratively reviewed a list of PUIs in the EHR and proactively contacted frontline providers with diagnostic recommendations. From 24 April to 19 May, ID physicians passively evaluated all PUIs; frontline clinicians conducted guideline-based COVID-19 workup (Supplementary Figure 2) and requested ID physician review once complete. A team of 6–12 ID physicians a day, each contributing 4–12 hours daily, reviewed the EHR and, if needed, spoke to care teams to examine clinical details regarding the PUI's exposure history, epidemiologic risk factors, symptom types and duration, laboratory values, imaging studies, and response to treatment for alternative diagnoses. Based on this information, the ID physician recommended discontinuation of CoV-Risk status or additional work-up (eg, repeated SARS-CoV-2 NAAT from an NP or lower respiratory tract [LRT] specimen, serology, and chest computed tomography [CT]) (Supplementary Methods and Supplementary Table 2).

CORAL Components and Derivation

CORAL was developed as a diagnostic algorithm and clinical scoring system to incorporate symptoms, epidemiologic risk factors, and imaging findings (Supplementary Tables 3 and 4). It was designed to (1) guide licensed independent practitioners through the diagnostic workup of PUIs after an initial negative NAAT, (2) indicate when transmission-based precautions and isolation orders could be discontinued, and (3) triage more complex PUIs to ID physician review in the setting of clinical or radiographic features highly concerning for COVID-19 despite 2 negative NAAT results.

To be eligible for CORAL, patients must be adult (≥19-years-old) PUIs with ≥1 negative SARS-CoV-2 NAAT result and have chest imaging performed within the past 3 days. Classification of CT chest findings are based on Radiological Society of North America standardized categories, which were widely used at Massachusetts General Hospital during the study period [21]. There are 4 possible CORAL pathways, depending on the number of negative NAATs and available imaging: 1 NAAT plus chest radiography, 1 NAAT plus chest CT, ≥2 NAATs plus chest radiography, and ≥2 NAATs plus chest CT (Supplementary Figure 3). Scoring systems for these pathways were developed using a modified Delphi method (Supplementary Methods) [22, 23].

Technical Development of CORAL

CORAL, launched on 20 May, was developed using native EHR (Epic™ Inc, Verona, WI) functionality and can be used iteratively as the diagnostic evaluation progresses (Figure 1). Clinicians load CORAL into a SmartForm (ie, advanced note template) and then select answers, which generates a standardized note
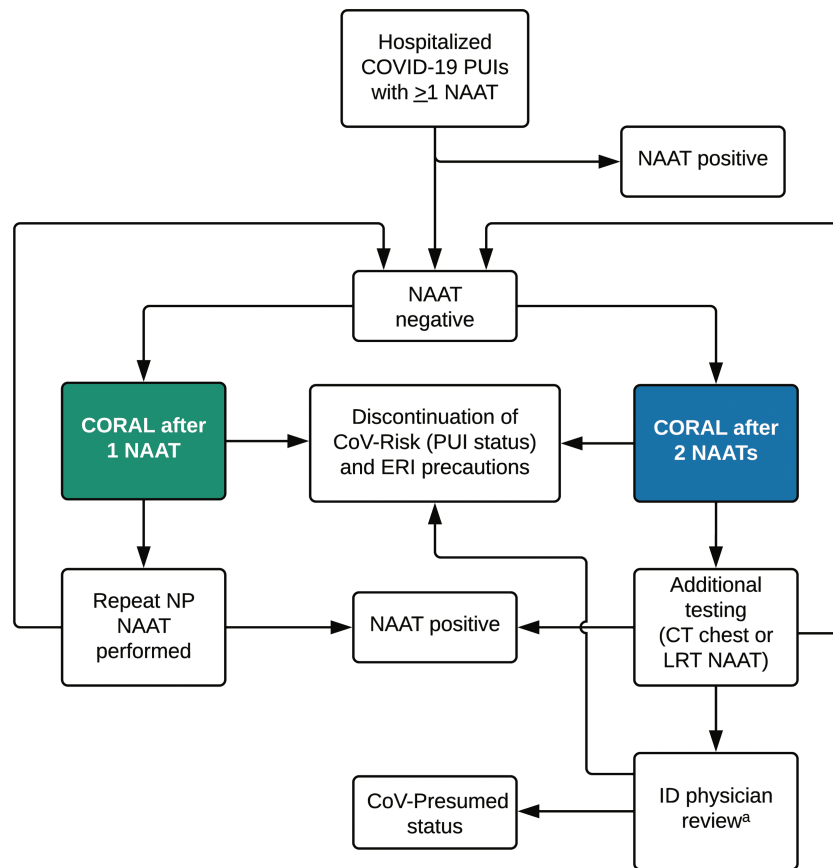
Figure 1. Overview of COvid Risk cALculator (CORAL) workflow. Persons under investigation for coronavirus disease 2019 (COVID-19) (PUIs) are eligible for CORAL if they have ≥1 nucleic acid amplification test (NAAT) with negative results and 1 imaging study performed. On completion of CORAL, PUIs are given a risk score which leads to either a prompt for discontinuation of PUI status with discontinuation of enhanced respiratory isolation (ERI) precautions, or a prompt for repeated nasopharyngeal NAAT, further diagnostics for COVID-19 workup, or infectious diseases (ID) physician review. (a If CORAL cannot be performed, clinicians are instructed to contact the ID physician for review.) See Study Setting and Design for explanation of how CoV-Risk and CoV-Presumed status was assigned. Abbreviations: CT, computed tomography; LRT, lower respiratory tract.

for the record (Supplementary Figure 4). Responses are scored once CORAL is completed; scores are not visible to the clinician. If the score is below a preset threshold, CORAL discontinues CoV-Risk status (Supplementary Figure 5). If the score is above the preset threshold, CORAL displays orders for recommended diagnostics. If additional workup cannot be obtained and clinical suspicion for COVID-19 remains high, CORAL prompts ID physician review.

Pre- and Post-CORAL Outcomes

We evaluated pre-CORAL outcomes among hospitalized patients with new CoV-Risk status from 18 March to 19 May. Allowing for a 1-week transition period for a hospital-wide CORAL education campaign, we evaluated post-CORAL outcomes from 27 May to 28 July. During both periods, we examined the proportion of PUIs with an initial negative NAAT result who underwent repeated NAAT and who required additional diagnostics beyond 2 negative NAAT results. We evaluated the time from the first (if only a single test was performed) or second negative NAAT result to discontinuation of CoV-Risk

status, total duration of CoV-Risk status during the hospitalization, and average ID physician person-hours dedicated to PUI evaluations. After CORAL, we described provider-documented patient characteristics from the first use of CORAL and CORAL recommendations.

After discontinuation of CoV-Risk status, repeated SARS-CoV-2 NAAT was recommended for patients with new or worsening symptoms concerning for COVID-19. We performed record review for patients with a positive NAAT result within 14 days after discontinuation of CoV-Risk in the same hospital encounter. This study was approved by the Mass General Brigham Institutional Review Board (no. 2012P002359).

Statistical Analysis

We conducted unadjusted and adjusted analyses for each outcome measure, comparing pre-CORAL with post-CORAL values. The pre-CORAL period included both the passive PUI evaluation and active PUI evaluation periods, which were analyzed together. We used χ^2 tests to compare unadjusted pre- and post-CORAL proportions of patients with repeated testing after

an initial negative NAAT result and additional workup after 2 negative NAAT results. We used logistic regression to adjust these comparisons for daily COVID-19 incidence among hospitalized PUIs as a surrogate for pretest probability. COVID-19 incidence was defined as the proportion of daily new COVID-19 diagnoses among all newly admitted PUIs. For continuous outcomes, we used *t* tests to compare unadjusted mean time from NAAT result return to discontinuation of CoV-Risk status and total duration of CoV-Risk status among PUIs. Pre- and post-CORAL means for these continuous outcomes were compared using a generalized linear model, adjusted for daily COVID-19 incidence.

RESULTS

COVID-19 Incidence and Demographics of Inpatient PUIs

On average, the proportion of new COVID-19 diagnoses among all newly admitted PUIs was 29% from 18 March to 19 May (before CORAL) and 3% from 27 May to 28 July (after CORAL) as the initial COVID-19 surge subsided. At the height of the surge in early April, >100 PUIs per day required ID review. Median age (interquartile range) among PUIs was similar before and after CORAL (63 [50–75]) vs 64 [51–77] years, respectively), as was the proportion of female PUIs (44% vs 40%). We report the epidemiology, symptoms, imaging findings, and additional diagnostics recommended for post-CORAL PUIs (Table 1); these structured EHR data were not available before CORAL.

Outcomes of PUIs

During the pre-CORAL period, 2443 of 3358 inpatient PUI encounters (73%) with ≥1 SARS-CoV-2 NAAT had a first negative NAAT result (Figure 2A). Of these, CoV-Risk status was discontinued without further testing in 764 of 2443 (31%), not discontinued owing to death or discharge in 39 of 2443 (1.6%), and converted to CoV-Presumed status in 4 of 2443 (0.2%). A second NAAT was performed in the remaining 1636 of 2443 encounters (67%) with a first negative NAAT result; 38 of 1636 (2.3%) repeated NAATs had newly positive results. Of the remaining 1598 encounters with 2 negative NAAT results, CoV-Risk status was discontinued without further workup in 1042 of 1598 (65%), and additional diagnostics were pursued in 485 of 1598 (30%). Additional testing resulted in positive NAATs results in 18 of 485 encounters (3.7%), conversion to CoV-Presumed status in 31 of 485 (6.4%), and discontinuation of CoV-Risk status in 383 of 485 (79%).

During the post-CORAL study period, the initial NAAT was negative in 2411 of 2485 inpatient encounters (97%) in which PUIs underwent SARS-CoV-2 NAATs (Figure 2B). CORAL was used at least once in 2303 of 2411 encounters (96%); its first use was after the first negative NAAT in 1580 of 2303 encounters (69%) and after a second negative NAAT in 723 of 2303 (31%). CoV-Risk status was discontinued with CORAL after 1 negative

NAAT in 1034 of 2303 encounters (45%) and after ≥2 negative NAATs in 1198 of 2303 (52%). PUIs underwent additional workup in 224 of 1245 encounters (18%) in which CORAL was used after 2 negative NAATs; of these, CoV-Risk status was discontinued with CORAL in 190 of 224 encounters (85%), discontinued with ID physician review in 21 of 224 (9.4%), and converted to CoV-Presumed status in 4 of 224 (1.8%). In encounters with ≥1 repeated NAAT after an initial negative result, subsequent NAAT yielded a new COVID-19 diagnosis in 12 of 1310 encounters (0.9%).

In the unadjusted analysis, repeated NAAT after 1 initial negative result was less frequent after CORAL than before CORAL (54% vs 67%, respectively; odds ratio [OR], 0.59 [95% confidence interval [CI]: .52–.66]; *P* < .01) (Table 2) and persisted after adjustment for COVID-19 incidence (adjusted OR [aOR], 0.53 [.44–.63]; *P* < .01). Additional diagnostics for COVID-19 beyond 2 negative NAATs were also less frequent after CORAL than before CORAL (19% vs 30%, respectively) in both unadjusted (OR, 0.53 [95% CI: .45–.63]) and adjusted (aOR, 0.42 [.33–.54]) analyses (both *P* < .01). These declines in repeated testing and additional diagnostics beyond 2 NAATs were not evident during the transition from active to passive ID physician review (24 April through 19 May); repeated testing and additional diagnostics were actually more frequent during this period despite decreasing COVID-19 incidence, which then led to lower ORs after adjustment for COVID-19 incidence (Figure 3A).

Duration of CoV-Risk Status

Among patients who had CoV-Risk status discontinued while in the hospital, the mean time in hours (standard deviation [SD]) from negative NAAT result return to discontinuation of CoV-Risk status was 5.3 (2.3) hours after CORAL, compared with 11.5 (3.6) hours before CORAL (unadjusted difference [standard error (SE)], −6.2 [0.5] hours; adjusted difference, −7.4 [0.8] hours; *P* < .01) (Table 3). The mean (SD) total duration of CoV-Risk status was 19.0 (5.9) hours after versus 36.1 (8.7) hours before CORAL (unadjusted difference [SE], −17.2 [1.3] hours; adjusted difference, −19.5 [1.9] hours; *P* < .01) (Table 3). In contrast, the mean time from negative NAAT result return to discontinuation of CoV-Risk status and the mean total duration of CoV-Risk status increased during the pre-CORAL period when transitioning from active to passive ID physician review and then declined in the post-CORAL period (Figure 3B).

ID Physician Workload

Despite declining COVID-19 incidence in late April and early May, daily numbers of PUIs remained high, as did ID physician workload (Figure 3C). Implementation of CORAL resulted in an immediate and dramatic reduction in ID physician workload. Before CORAL, PUI evaluations required a mean (SD) of 68.7 (12.1) person-hours/d (Table 2), which decreased to a

Table 1.   Characteristics of Patients Evaluated With the COvid Risk cALculator (CORAL)

	Outcome of 1st CORAL Use Within Encounter, No. (%)				
	1 Negative NAAT Result		≥2 Negative NAAT Results		
Characteristic	Resolved (n = 1034)	Repeated NAAT (n = 546)	Resolved (n = 647)	Further Chest Imaging ± LRT Sampling (n = 49)	ID Physician Review ± LRT Sampling (n = 27)
Epidemiology[a]					
Cannot obtain history	53 (5.1)	108 (19.8)	100 (15.5)	12 (24.5)	5 (18.5)
Close contact with confirmed COVID-19 in last 14 d	5 (0.5)	3 (0.5)	2 (0.3)	3 (6.1)	1 (3.7)
Preadmission circumstances					
Congregate setting	110 (10.6)	69 (12.6)	77 (11.9)	8 (16.3)	4 (14.8)
Experiencing homelessness	48 (4.6)	25 (4.6)	36 (5.6)	8 (16.3)	1 (3.7)
Private home	818 (79.1)	341 (62.5)	433 (66.9)	18 (36.7)	16 (59.3)
Receives hemodialysis	35 (3.4)	24 (4.4)	15 (2.3)	4 (8.2)	1 (3.7)
Symptoms[b]					
Respiratory symptoms					
Shortness of breath	158 (15.3)	280 (51.3)	143 (22.1)	20 (40.8)	16 (59.3)
Cough	45 (4.4)	132 (24.2)	74 (11.4)	19 (38.8)	6 (22.2)
Viral symptoms					
Fever (objective or subjective)	195 (18.9)	96 (17.6)	113 (17.5)	13 (26.5)	8 (29.6)
Chills	45 (4.4)	46 (8.4)	29 (4.5)	5 (10.2)	2 (7.4)
Headache	26 (2.5)	17 (3.1)	18 (2.8)	0 (0)	2 (7.4)
Sore throat	15 (1.4)	18 (3.3)	23 (3.6)	2 (4.1)	1 (3.7)
Muscle aches	21 (2.0)	24 (4.4)	19 (2.9)	2 (4.1)	3 (11.1)
Loss of taste (ageusia)	2 (0.2)	3 (0.5)	4 (0.6)	0 (0)	0 (0)
Loss of smell (anosmia)	3 (0.3)	4 (0.7)	0 (0)	0 (0)	0 (0)
Other symptoms	15 (1.5)	3 (0.5)	6 (0.9)	0 (0)	1 (3.7)
Chest radiographic findings					
Clear lungs	610 (59.0)	99 (18.1)	211 (32.6)	10 (20.4)	0 (0)
Focal consolidation, lobar collapse, likely atelectasis, or any changes that are stable to improved from prior imaging >2 wk earlier	128 (12.4)	141 (25.8)	122 (18.9)	6 (12.2)	0 (0)
Any other abnormality	52 (5.0)	219 (40.1)	112 (17.3)	33 (67.3)	0 (0)
Chest CT findings[c]					
No findings suspicious for COVID-19	234 (22.6)	1 (0.2)	134 (20.7)	0 (0)	0 (0)
Atypical or indeterminate for COVID-19	10 (1.0)	76 (13.9)	68 (10.5)	0 (0)	7 (25.9)
Typical for COVID-19	0 (0)	10 (1.8)	0 (0)	0 (0)	20 (74.1)
Mitigating factors					
Alternative diagnosis	NA	NA	429 (66.3)	13 (26.5)	7 (25.9)
Sputum NAAT negative	NA	NA	88 (13.6)	0 (0)	2 (7.4)
Tracheal aspirate NAAT negative	NA	NA	24 (3.7)	0 (0)	0 (0)

Abbreviations: COVID-19, coronavirus disease 2019; CT, computed tomography; ID, infectious diseases; LRT, lower respiratory tract; NA, not applicable; NAAT, nucleic acid amplification test.
[a]Questions cascaded based on previous answers; for example, if a patient had close contact, questions about living situation and dialysis were not asked (see Supplementary Material).
[b]Patients could report >1 symptom.
[c]Categories were based on Radiological Society of North America Reporting criteria [21].

mean of 3.1 (2.0) person-hours/d after CORAL (adjusted difference [SE], −57.4 [2.0] person-hours/d; $P < .01$).

**Diagnosis After Discontinuation of CoV-Risk Status**

In 360 of 2189 pre-CORAL encounters (16%), patients underwent repeated NAAT within 14 days of ERI discontinuation owing to new symptoms or required testing for discharge settings; 4 of 360 (1.1%) had COVID-19 diagnosed, all within 7 days of ERI discontinuation. Among 2232 encounters after discontinuation of CoV-Risk status with CORAL, 433 patients (19%) had clinician-directed repeated testing within 14 days of ERI discontinuation.

One patient of 433 (0.2%) had a positive NP NAAT result 9 days after initial negative NAAT result and ERI discontinuation by CORAL, as well as a positive total SARS-CoV-2 antibody test 11 days after admission. Details of the 5 patients are provided (Supplementary Table 5); no onward nosocomial transmission from these individuals to other patients was identified.
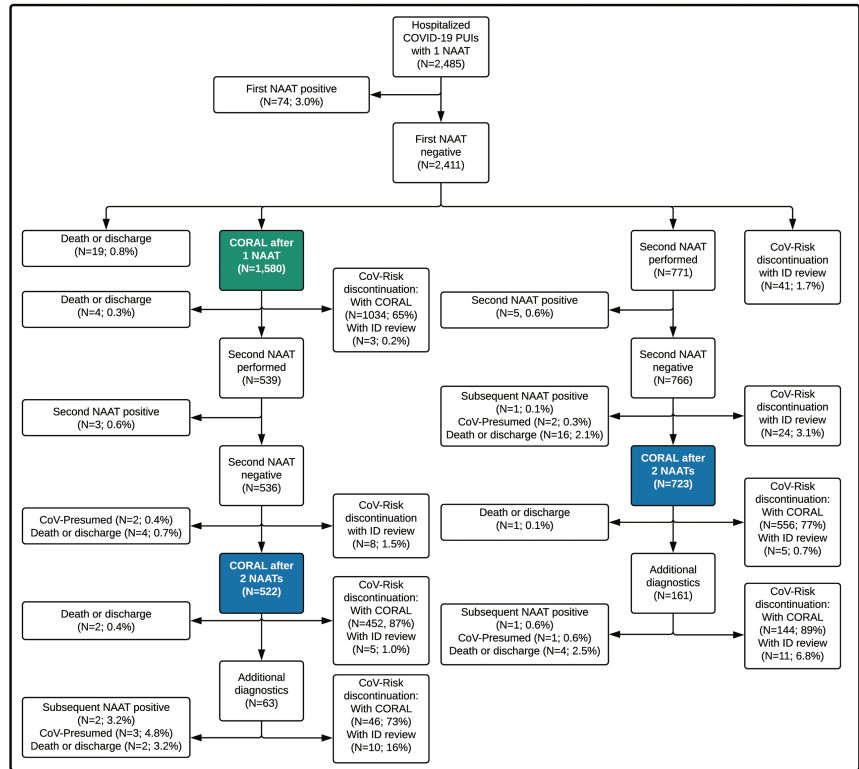
DISCUSSION

We describe the development and implementation of CORAL, a novel real-time diagnostic algorithm and CDSS to guide frontline clinicians through the evaluation of PUIs and assist

A. Pre-CORAL outcomes
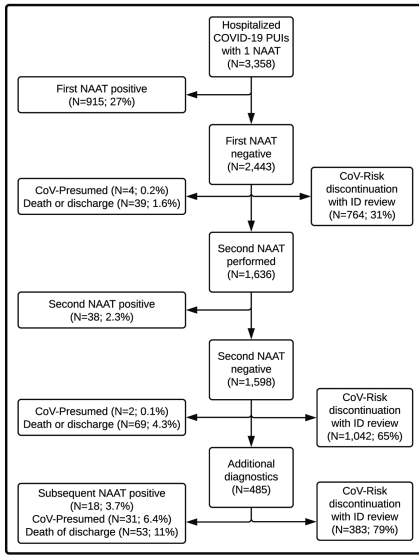
B. Post-CORAL outcomes

Figure 2. Outcomes before and after implementation of the COvid Risk cALculator (CORAL). Testing and CoV-Risk status discontinuation outcomes are demonstrated for the pre-CORAL (*A*) and post-CORAL (*B*) periods. In the post-CORAL period, outcomes are shown for persons under investigation for coronavirus disease 2019 (COVID-19) (PUIs) for whom CORAL was initially used after 1 (*green*) or 2 (*blue*) negative nucleic acid amplification test (NAAT) results. See Study Setting and Design for explanation of how CoV-Risk and CoV-Presumed status was assigned. Abbreviation: ID, infectious diseases physician.

with safe and efficient discontinuation of transmission-based precautions. As a structured diagnostic algorithm, CORAL decreased the use of repeated SARS-CoV-2 NAAT after a first negative NAAT result and the use of additional COVID-19 diagnostics beyond 2 negative NAAT results. CORAL reduced the duration of transmission-based precautions for PUIs compared with individualized ID physician review, supporting efforts to conserve PPE, preserve hospital capacity, and advance patient care.

Before CORAL implementation, individualized inpatient PUI evaluations were very resource-intensive [10]. Alternatives to case-by-case ID physician review such as indefinite continuation of ERI precautions, or algorithmic discontinuation of PUI status after 2 NAATs, were neither feasible nor an efficient use of laboratory or other resources. Sustaining individualized ID physician PUI evaluations required a considerable proportion of the ID workforce, at a time when demand for ID consultation was also high [24]. CORAL solved this critical problem, because it guided diagnostic evaluation and discontinuation of the PUI status 24 hours a day. CORAL was quickly adopted by clinicians, resulting in a significant decrease in ID physician person-power required and serving important roles in laboratory stewardship, PPE conservation, and improved bed allocation.

Table 2. COVID-19 Diagnostic Testing Utilization Before and After Implementation of the COvid Risk cALculator

Outcome	PUIs, %		OR (95% CI)		
	Before CORAL	After CORAL	Unadjusted	Adjusted[a]	P Value
Underwent repeated testing after initial negative NAAT result and repeated testing	67.0	54.3	0.59 (.52–.66)	0.53 (.44–.63)	<.01
Underwent additional diagnostic testing after 2 Negative NAAT results with additional diagnostic testing	30.4	18.8	0.53 (.45–.63)	0.42 (.33–.54)	<.01

Abbreviations: CI, confidence interval; CORAL, COvid Risk cALculator; NAAT, nucleic acid amplification test; OR, odds ratio; PUIs, persons under investigation for coronavirus disease 2019 (COVID-19).

[a]We adjusted all analyses for daily COVID-19 incidence among hospitalized PUIs.
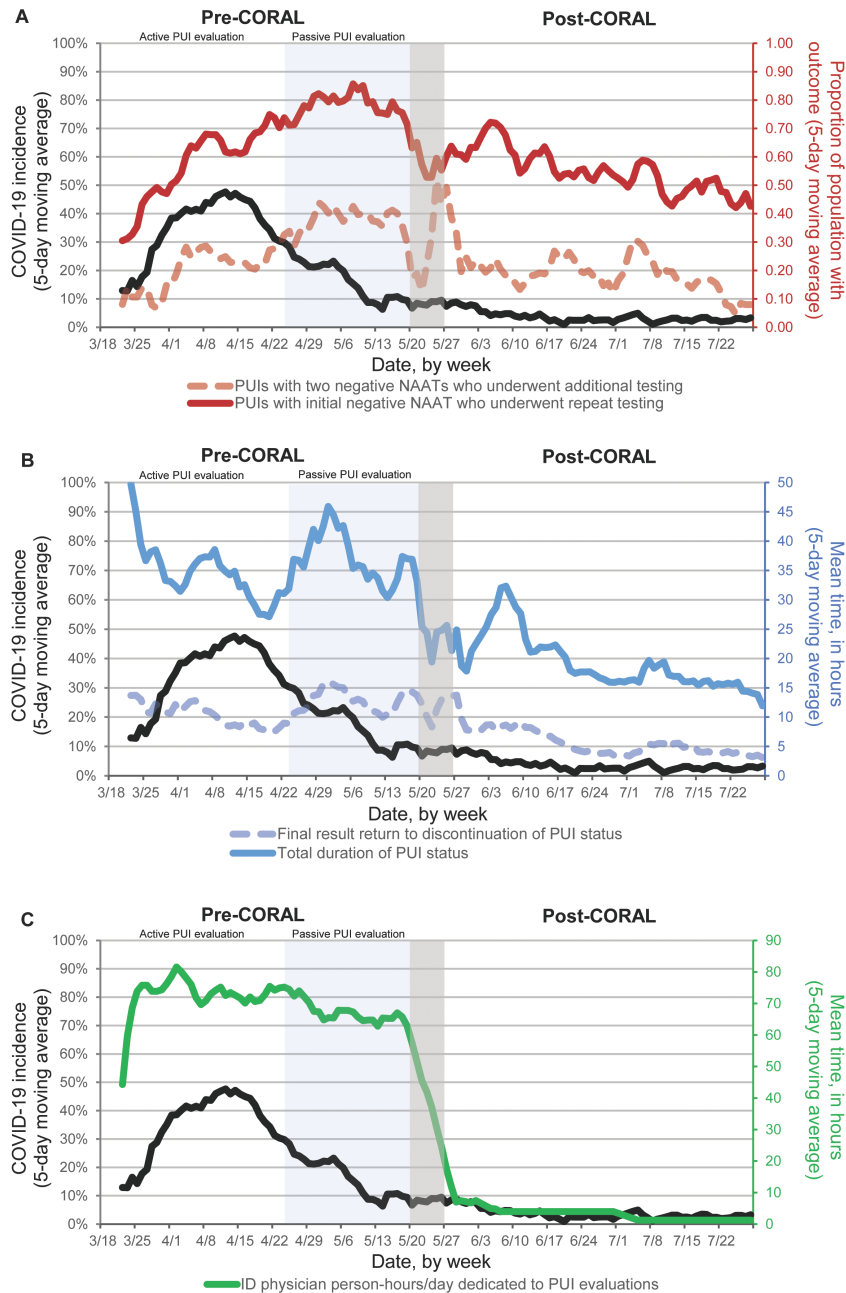
Figure 3. Daily changes in key outcomes in the periods before and after implementation of the COvid Risk cALculator (CORAL) relative to coronavirus disease 2019 (COVID-19) incidence. The pre-CORAL period (*left*) is shown with the active evaluation window for persons under evaluation for COVID-19 (PUIs), from 18 March to 23 April 2020, and the passive PUI evaluation window from 24 April to 19 May (Methods). CORAL was launched on 20 May 2020, followed by a 1-week transition period, with the post-CORAL period spanning 27 May to 28 July 2020. The incidence of new COVID-19 diagnoses among hospitalized PUIs, shown as a 5-day moving average, is shown in black (*left y-axis*) in all panels. (Dates are given in month/date format.) *A,* Proportion of PUIs with an initial negative nucleic acid amplification test (NAAT) result who underwent repeated testing (*solid red line; right y-axis*) and the proportion of PUIs with 2 negative NAAT results who underwent additional testing (*dashed red line; right y-axis*). *B,* Mean total duration of PUI status (*solid blue line; right y-axis*) and the mean time from final negative NAAT result return to PUI status discontinuation (*dashed blue line; right y-axis*). *C,* Mean infectious diseases (ID) physician person-hours/day dedicated to PUI evaluations (*solid green line; right y-axis*). Of note, we excluded patients who became PUIs during the pre-CORAL or wash-in period, but who had resolution of CoV-Risk status with CORAL, owing to the duration of their PUI status; the greater fluctuation in results around the end of the pre-CORAL and wash-in period is likely because fewer patients were contributing to the data set in those weeks.

Overall COVID-19 incidence declined before CORAL implementation, as public health interventions were implemented statewide [25]. Declining incidence may have contributed to decreased need for repeated NAATs and additional testing beyond 2 negative NAAT results, as pretest probability of COVID-19 declined. However, the difference in these key outcomes before and after CORAL was sustained after adjustment for COVID-19 incidence. Furthermore, in the late pre-CORAL period, we

Table 3. PUI Status Duration and ID Physician Work Hours Before and After Implementation of the COvid Risk cALculator

| | Mean (SD) | | Absolute Difference (SE) | | |
Outcome	Before CORAL	After CORAL	Unadjusted	Adjusted[a]	P Value
Time from final NAAT result return to PUI status discontinuation, h	11.5 (3.6)	5.3 (2.3)	−6.2 (0.5)	−7.4 (0.8)	<.01
Total duration of PUI status, h[b]	36.1 (8.7)	19.0 (5.9)	−17.2 (1.3)	−19.5 (1.9)	<.01
ID physician work hours, person-hours/d	68.7 (12.1)	3.1 (2.0)	−65.6 (1.5)	−57.4 (2.0)	<.01

Abbreviations: CORAL, COvid Risk cALculator; ID, infectious diseases; NAAT, nucleic acid amplification test; PUI, person under investigation for coronavirus disease 2019 (COVID-19); SD, standard deviation; SE, standard error.

[a]We adjusted all analyses for daily COVID-19 incidence among hospitalized PUIs. For total duration of PUI status, we were unable to additionally adjust for changes in test result return time owing to the introduction of additional in-house assays.

[b]Patients who did not have PUI status discontinued owing to death or discharge, or who were converted to CoV-Presumed status (defined in Study Setting and Design) or confirmed to have COVID-19 by subsequent NAAT were excluded from the 2 analyses regarding the duration of PUI status.

also observed paradoxical increases in these outcomes, as well as time from final result return to discontinuation of CoV-Risk status and overall duration of CoV-Risk status, despite declining COVID-19 incidence. These increases corresponded to a shift from a system of active to passive PUI evaluation, which makes it more likely that the decreased testing use and duration of CoV-Risk status were directly attributable to the standardization of and 24/7 access to diagnostic guidance through the CORAL CDSS, rather than declining COVID-19 incidence.

Implementation of a CDSS has benefits beyond direct clinical guidance. The CDSS captures structured data entered by clinicians, which can be used to refine the scoring algorithm. Second, as frontline clinicians must answer structured questions to complete CORAL, it also serves as an educational tool to teach clinicians about the diagnostic workup of COVID-19 [4]. In addition, the platform is easily extendable and could be modified to follow local ID expert and stakeholder consensus, provide differential guidance based on population prevalence, or incorporate emerging laboratory testing modalities, such as SARS-CoV-2 serology, which may also help assess patient transmissibility [26, 27].

Several other COVID-19 diagnostic risk scores based on combinations of patient epidemiology, laboratory values, imaging findings, symptoms, and time from symptom onset have been validated [28–31]. For example, the Corona-score algorithm relies on age, sex, chest imaging, and laboratory values; it demonstrates 82%–96% sensitivity to predict COVID-19 infection among patients presenting to the emergency department [30, 32]. While other scoring systems have demonstrated reasonable sensitivity for COVID-19 infection compared with a single NAAT, CORAL remains unique as the only algorithm, to our knowledge, that has been incorporated into routine, prospective clinician workflow via an EHR CDSS. CORAL guides clinicians through additional diagnostic recommendations after a negative test result, which other published tools do not incorporate [28–32]. Finally, since CORAL is embedded into Epic, it could be adopted by other health systems in the United States using this EHR or incorporated into other EHRs [33]. Alternatively, clinicians can apply the scoring system independently (Supplementary Methods).

The current study had several limitations. COVID-19 incidence declined before CORAL was implemented; however,

differences in outcomes before and after CORAL were sustained after adjustment for COVID-19 incidence to capture pretest probability. Delays in test turnaround time may have contributed to longer duration of CoV-Risk status in the early pre-CORAL period, but that duration was shorter post-CORAL compared with the late pre-CORAL period. Our evaluation of patients with COVID-19 diagnosed in the 14 days after discontinuation of CoV-Risk status is limited by clinician-directed testing of patients and may have been influenced by the lower COVID-19 incidence in the post-CORAL period. CORAL requires recent imaging and accurate history taking by frontline clinicians. Owing to changes in PUI definitions over time, patients in the pre-CORAL period were more likely to be at higher risk for COVID-19, given that testing was initially focused on symptomatic individuals; however, testing of all admitted patients regardless of symptoms started midway through the pre-CORAL period. Finally, this analysis was conducted at a single center with specific testing protocols and guidelines for discontinuation of transmission-based precautions. However, other facilities have similar protocols and guidelines [34, 35], and CORAL has since been implemented in 8 other affiliated facilities and used >19 000 times.

CORAL is an effective, efficient, and safe method to guide clinicians through the diagnostic steps of evaluating COVID-19 PUIs, enabling 24/7 discontinuation of transmission-based precautions in PUIs, and triaging complex patients for ID physician review. CORAL implementation markedly reduced ID physician-time for COVID-19 PUI evaluations and assisted in laboratory stewardship and PPE conservation. Healthcare facilities should consider implementing CDSS for PUI evaluations.

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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