*Clinical Infectious Diseases*

MAJOR ARTICLE

# Clinical Impact, Costs, and Cost-effectiveness of Expanded Severe Acute Respiratory Syndrome Coronavirus 2 Testing in Massachusetts

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**(See the Editorial Commentary by Rosenberg and Holtgrave on pages e2918–20.)**

***Background.*** We projected the clinical and economic impact of alternative testing strategies on coronavirus disease 2019 (COVID-19) incidence and mortality in Massachusetts using a microsimulation model.

***Methods.*** We compared 4 testing strategies: (1) hospitalized: polymerase chain reaction (PCR) testing only for patients with severe/critical symptoms warranting hospitalization; (2) symptomatic: PCR for any COVID-19–consistent symptoms, with self-isolation if positive; (3) symptomatic + asymptomatic once: symptomatic and 1-time PCR for the entire population; and (4) symptomatic + asymptomatic monthly: symptomatic with monthly retesting for the entire population. We examined effective reproduction numbers ($R_e$ = 0.9–2.0) at which policy conclusions would change. We assumed homogeneous mixing among the Massachusetts population (excluding those residing in long-term care facilities). We used published data on disease progression and mortality, transmission, PCR sensitivity/specificity (70%/100%), and costs. Model-projected outcomes included infections, deaths, tests performed, hospital-days, and costs over 180 days, as well as incremental cost-effectiveness ratios (ICERs, $/quality-adjusted life-year [QALY]).

***Results.*** At $R_e$ = 0.9, symptomatic + asymptomatic monthly vs hospitalized resulted in a 64% reduction in infections and a 46% reduction in deaths, but required >66-fold more tests/day with 5-fold higher costs. Symptomatic + asymptomatic monthly had an ICER <$100 000/QALY only when $R_e \geq 1.6$; when test cost was ≤$3, every 14-day testing was cost-effective at all $R_e$ examined.

***Conclusions.*** Testing people with any COVID-19–consistent symptoms would be cost-saving compared to testing only those whose symptoms warrant hospital care. Expanding PCR testing to asymptomatic people would decrease infections, deaths, and hospitalizations. Despite modest sensitivity, low-cost, repeat screening of the entire population could be cost-effective in all epidemic settings.

**Keywords.** COVID-19; testing; PCR; cost-effective; SARS-CoV-2.

Massachusetts experienced a major coronavirus disease 2019 (COVID-19) outbreak beginning in March 2020 after a biotechnology convention, which was subsequently fueled by transmission in communities living in multigenerational and multifamily housing [1]. In the United States, restricted testing capacity early in the pandemic led states such as Massachusetts to test only severely symptomatic people and/or those with a known exposure [2]. While some have argued that testing must be highly sensitive in order to be of value to guide reopening [3], others have argued that sensitivity can be sacrificed if tests are rapid, low-cost, and frequent [4, 5]. Despite the variable clinical sensitivity of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) polymerase chain reaction (PCR) testing, expanded testing programs could reduce transmissions by increasing isolation of infectious people, thereby reducing hospitalizations and deaths. Widely available testing could also allow for the safer resumption of economic and social activity

Received 23 July 2020; editorial decision 14 September 2020; published online 18 September 2020.

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**Clinical Infectious Diseases® 2021;73(9):e2908–17**

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DOI: 10.1093/cid/ciaa1418

by providing surveillance for any "second wave" of infection [6]. Such resumptions of public life may also benefit those with non–COVID-19–related health issues who may avoid seeking care due to concerns about acquiring COVID-19 [7].

To date, no national testing strategy has been articulated [8]. Since new infections peaked in late April 2020 [9], Massachusetts has used test positivity rates as a key indicator to guide gradual reopening, after implementing strategies to reduce transmission risk [6]. In Massachusetts and elsewhere, planning is essential for utilization of key limited resources, such as testing and hospital beds, since mitigation strategies need to be able to pivot rapidly as epidemic growth scenarios change. Our goal was to examine the clinical and economic impact of screening strategies on COVID-19 in Massachusetts.

## METHODS

### Analytic Overview

We developed a dynamic state-transition microsimulation model, the Clinical and Economic Analysis of COVID-19 Interventions (CEACOV) model, to reflect the natural history, diagnosis, and treatment of COVID-19. We modeled 4 testing strategies for all Massachusetts residents (excluding those residing in long-term care facilities): (1) hospitalized: PCR testing only of those who develop severe illness (ie, warranting hospital care), reflecting common practices in Massachusetts through late April 2020 [2]; (2) symptomatic: hospitalized and PCR for people with any COVID-19–consistent symptoms who self-isolate if positive; (3) symptomatic + asymptomatic once: symptomatic and a 1-time PCR for the entire population; and (4) symptomatic + asymptomatic monthly: symptomatic + asymptomatic once and retesting every 30 days of those who test negative and remain asymptomatic (Supplementary Figure 1). For those who are not hospitalized, we assume that a positive PCR test leads to self-isolation in the community. We projected clinical outcomes (infections, COVID-19–related mortality, quality-adjusted life-years [QALYs]), and COVID-19–related resource utilization (tests, hospital and intensive care unit [ICU] beds, self-isolation days), and costs for Massachusetts (6.9 million people, excluding long-term care facility residents) over a 180-day horizon. We report incremental cost-effectiveness ratios (ICERs: difference in cost divided by difference in QALYs [$ / QALY]) from a healthcare sector perspective (Supplementary Methods). The threshold at which interventions are considered cost-effective is a normative value that varies by setting; for the sake of interpretability, we define a strategy as "cost-effective" if its ICER is below $100 000/QALY [10].

### CEACOV Model Structure

#### *Cohort and Disease Progression*

At model start, a closed preintervention cohort is seeded with a user-defined proportion of age-stratified individuals (0–19, 25–59, ≥60 years) who are either infected with or susceptible to SARS-CoV-2. If infected, individuals face daily age-stratified probabilities of disease progression through 7 health/disease states, including latent infection, asymptomatic illness, mild/moderate illness, severe illness (warranting hospitalization), critical illness (warranting intensive care), recuperation, and recovery (Supplementary Figure 2). We assume that recovered individuals are immune from repeat infection for the 180-day modeled horizon [11]. Susceptible and recovered individuals may also present for testing with symptoms due to non–COVID-19 conditions ("COVID-19–like illness").

#### *Testing*

Individuals can experience a daily probability of undergoing SARS-CoV-2 testing. Each PCR testing strategy includes test sensitivity/specificity, turnaround time, and testing frequency.

#### *Transmission*

In the model, infected individuals have an equal probability of contacting susceptible individuals and transmitting SARS-CoV-2. The effective reproduction number ($R_e$) captures the average number of secondary cases per infected individual in the cohort; based on Massachusetts data, this was estimated to be 0.9 in late April 2020 (Supplementary Methods and Supplementary Table 1). People with a positive test result or symptom screen can isolate in the community or in the hospital, which further decreases transmission.

#### *Resource Use*

The model tallies tests, COVID-19–related use of hospital and ICU bed-days, as well as days spent self-isolating.

### Model Inputs

#### *Cohort and Disease Progression*

We derived the initial distribution of COVID-19 disease severity by age from the Massachusetts Census and Department of Public Health (Table 1) [12, 13]. Disease progression and COVID-19–related mortality are derived from data from China and Massachusetts and calibrated from mid-March to 1 May 2020 to deaths in Massachusetts (excluding those occurring in long-term care facilities) (Table 1 and Supplementary Table 1) [13–18].

#### *Testing and Associated Transmission Reduction*

PCR test sensitivity and specificity are assumed to be 70% and 100%, respectively (Table 1) [20, 21]. In all strategies, patients with severe or critical illness are eligible for diagnostic testing and are hospitalized regardless of PCR test result. Transmission is reduced by 90% for hospitalized people due to infection control and isolation practices (Table 1 and Supplementary Methods). In the expanded PCR-based strategies, self-isolation among those in the community with a positive PCR test leads to a 65% transmission reduction [29]; those who test negative do not self-isolate (incorporating the potential for transmissions

**Table 1. Input Parameters for a Model of Coronavirus Disease 2019 and Severe Acute Respiratory Syndrome Coronavirus 2 Testing in Massachusetts**

| Parameter | Value | |
|---|---|---|
| Cohort characteristics | | |
| Initial age distribution of cohort, % [12] | | |
| 0–19 y | 25 | |
| 20–59 y | 56 | |
| ≥60 y | 19 | |
| Initial distribution of health states on 1 May 2020, % [13][a] | | |
| Susceptible | 89.38 | |
| Latent | 0.52 | |
| Asymptomatic | 0.91 | |
| Mild/moderate illness | 1.49 | |
| Severe illness | 0.04 | |
| Critical illness | 0.02 | |
| Recuperation | 0.01 | |
| Recovered | 7.63 | |
| Health state transition probabilities, by ultimate stage of disease, daily [14–16, 18][b] | | |
| Asymptomatic | | |
| Latent to asymptomatic | 0.565 | |
| Asymptomatic to recovered | 0.099 | |
| Mild/moderate | | |
| Latent to asymptomatic | 0.565 | |
| Asymptomatic to mild/moderate | 0.221 | |
| Mild/moderate to recovered | 0.095 | |
| Severe | With Hospital Care | Without Hospital Care |
| Latent to asymptomatic | NA | 0.565 |
| Asymptomatic to mild/moderate | NA | 0.221 |
| Mild/moderate to severe | NA | 0.143 |
| Severe to recovered | .091 | 0.063 |
| Critical | | |
| Latent to asymptomatic | NA | 0.565 |
| Asymptomatic to mild/moderate | NA | 0.221 |
| Mild/moderate to severe | NA | 0.284 |
| Severe to recovered | 0.026 | 0.000 |
| Severe to critical | 0.105 | 0.143 |
| Critical to recuperation | 0.049 | 0.000 |
| Recuperation to recovered | 0.161 | 0.000 |
| COVID-19–related mortality while critically ill, probability, daily [19] | With hospital care | Without hospital care |
| 0–19 y | 0.00001 | 0.118 |
| 20–59 y | 0.004 | 0.166 |
| ≥60 y | 0.050 | 0.203 |
| Development of COVID-19–like illness symptoms among susceptible and recovered, probability, daily [19] | | |
| Mild/moderate illness | | |
| 0–19 y | 0.00005 | |
| 20–59 y | 0.00005 | |
| ≥60 y | 0.00008 | |
| Severe illness | | |
| 0–19 y | 0.00032 | |
| 20–59 y | 0.00036 | |
| ≥60 y | 0.00053 | |
| Critical illness | | |
| 0–19 y | 0.00009 | |
| 20–59 y | 0.00010 | |
| ≥60 y | 0.00015 | |
| Presentation to hospital care with severe symptoms, probability[c] | 0.80 | |
| Test characteristics | | |
| PCR test [20, 21] | | |
| Sensitivity[d], % | 70 | |
| Specificity, % | 100 | |
| Turnaround time, d | 1 | |
| Test acceptance, probability | | |
| Asymptomatic/mild illness/moderate illness | 0.80 | |
| Critical/severe illness | 1.00 | |

**Table 1. Continued**

| Parameter | Value | |
|---|---|---|
| Transmissions | | |
| $R_e$ | | |
| 1–30 May 2020 | 0.9 | |
| By health state, probability, daily [22–24][e] | | |
| Latent | 0.0000 | |
| Asymptomatic | 0.2024 | |
| Mild/moderate illness | 0.1948 | |
| Severe illness | 0.0135 | |
| Critical illness | 0.0107 | |
| Recuperation | 0.0135 | |
| Recovery | 0.0000 | |
| Transmission reduction after test result, %[f] | Test Positive | Test Negative |
| Asymptomatic | 65 | 0 |
| Mild/moderate illness | 65 | 0 |
| Severe/critical/recuperation[f] | 90 | 90 |
| Costs (2020 USD) | | |
| SARS-CoV-2 PCR assay [25] | 51 | |
| Hospital bed, daily [26–28] | 1640 | |
| Intensive care unit, daily [26–28] | 2680 | |

Abbreviations: COVID-19, coronavirus disease 2019; NA, not applicable; PCR, polymerase chain reaction; $R_e$, effective reproduction number; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; USD, United States dollars.

[a]Derived from model validation and calibration as described in the Supplementary Materials.

[b]Average days spent in each health state stratified by clinical disease progression severity are presented in Supplementary Table 1. Health state transitions are shown in Supplementary Figure 2.

[c]Assumption; includes those with COVID-19 disease and those with COVID-19–like illness.

[d]Test sensitivity is 0% in the latent phase and otherwise does not vary by disease states.

[e]Daily transmission rates contribute to $R_e$.

[f]Assumptions for transmission reductions following test result are detailed in the Supplementary Materials. In severe/critical/recuperation states, transmission reduction is due to hospitalization and thus is applied to all patients regardless of test result.

associated with false-negative tests). PCR test acceptance is assumed to be 80% for those who are asymptomatic or have mild/moderate illness at the time of testing, and 100% for those with severe or critical illness.

### *Epidemic Scenarios*

The analysis of screening strategies begins after the period of model validation and calibration (mid-March through late April; Supplementary Methods). For the first month of the simulation, corresponding to 1 May 2020 to 31 May 2020, $R_e$ remains 0.9 (Supplementary Table 1). To account for the uncertain trajectory of the epidemic as reopening plans are implemented, we model 3 scenarios representing epidemics with distinct $R_e$ values in the absence of expanded testing (ie, hospitalized), beginning on 1 June 2020: (1) slowing (1 June 2020, $R_e$ = 0.9), suggesting epidemic growth would remain the same as during May (eg, stay-at-home advisory and nonessential business closures); (2) intermediate (1 June 2020, $R_e$ = 1.3), suggesting modest increase in epidemic growth; and (3) surging (1 June 2020, $R_e$ = 2.0), suggesting an $R_e$ closer to late March/early April Massachusetts estimates ($R_e$ = 2.6–5.9; Supplementary Table 1). We also identified threshold values for the $R_e$ at which policy conclusions would change. Transmission probabilities are based on time spent in each health state (Table 1).

### *Costs and Cost-effectiveness*

PCR test cost is $51 [25]. Patients requiring hospitalization accrue per-day costs (hospital: $1640; ICU: $2680) [26–28]. We use projected deaths to estimate quality-adjusted discounted life-years lost per strategy (Supplementary Methods) [30].

### Sensitivity and Scenario Analyses

In each of the 3 epidemic growth scenarios, we vary PCR sensitivity (30%–100%), test acceptance (15%–100% for asymptomatic or mild/moderate symptoms), transmission reduction after a positive test (33%–100%), presentation to hospital with severe disease (50%–100%), ICU survival (20%–80%), testing program costs (including additional outreach costs of offering PCR testing even if declined, $1–$26), and hospital care costs ($820–$3880). In multiway sensitivity analyses, we vary key parameters simultaneously. In additional analyses, we examined implementation of these testing strategies on 1 April 2020 vs 1 May 2020; the $R_e$ threshold at which conclusions about the preferred strategy shifted ($R_e$ = 1.3–2.0); the frequency of retesting in symptomatic + asymptomatic monthly (up to daily); patterns of presenting with COVID-19–like illness; and, the impact of costs associated with lost productivity due to hospitalization or positive PCR test results and averted mortality. Further details of the methods, as well as model calibration and validation, are shown in the Supplementary Materials.

## RESULTS

### Base Case Outcomes

#### *Clinical Outcomes*

All of the expanded screening strategies would reduce infections and deaths compared to the hospitalized strategy. In all epidemic scenarios, symptomatic + asymptomatic monthly would lead to the most favorable clinical outcomes, and hospitalized would lead to the least favorable outcomes; in the slowing scenario, symptomatic + asymptomatic monthly vs hospitalized resulted in 209 500 vs 577 700 infections (64% reduction) and 1700 vs 3100 deaths (46% reduction) (Table 2). As $R_e$ increases, compared to hospitalized, more expansive screening strategies would lead to greater reductions in infections and deaths (Table 2). As $R_e$ increases, the expanded screening strategies, compared with hospitalized, would result in a greater reduction in peak prevalence and lower reduction in the susceptible proportion of the population (Figure 1A–C).

#### *Resource Utilization and Costs*

In all epidemic growth scenarios, symptomatic would lead to lower total costs compared to hospitalized. In the slowing scenario, symptomatic + asymptomatic monthly would lead to the greatest reduction in cumulative bed-days compared to hospitalized (77 300 vs 126 000 hospital bed-days [39% reduction] and 45 600 vs 76 600 ICU bed-days [40% reduction]) but would require >66-fold times more tests/day (192 200 vs 2900) at 5-fold higher total costs ($2.0 billion vs $439 million) (Tables 2 and 3).

In the slowing and intermediate scenarios, peak hospital bed use is similar across all strategies. In the surging scenario, however, all other PCR-based strategies would reduce peak hospital and ICU bed use compared to hospitalized: hospital beds (7100 vs 2300–4600) and ICU beds (4100 vs 1200–2500) (Table 3). Supplementary Table 2 reports results per million people.

#### *Cost-effectiveness Outcomes*

Under all epidemic growth scenarios considered, symptomatic would be clinically superior and cost-saving compared to hospitalized (Table 2). Symptomatic + asymptomatic monthly would have an ICER <$100 000/QALY compared to symptomatic only in the surging scenario ($33 000/QALY). ICERs increase steeply as $R_e$ declines (Table 2).

### Sensitivity and Scenario Analyses

#### *Clinical Outcomes and Resource Use*

The impact of variation in clinical model input parameters on infections and deaths would be greatest in the surging scenario (Supplementary Figure 3*A–F*). Varying rates of presentation to hospital care and ICU survival would lead to large changes in mortality, which remain substantial (slowing scenario: 1300–2400 deaths/180 days) even under optimistic assumptions (ie, 100% presentation to hospital with severe illness or 80% ICU survival) (Supplementary Figure 3*D–F*). If expanded PCR testing started 1 April 2020, compared to 1 May 2020, we project that PCR-based strategies would have averted 103 000–176 900

**Table 2. Clinical and Cost-effectiveness Outcomes for a Model of Coronavirus Disease 2019 Infection and Testing in Massachusetts**

| Scenario | Undiscounted Incident Infections, No.[a] | Undiscounted Deaths, No.[a] | Discounted Total QALYs Lost, No.[b] | Undiscounted Healthcare Costs, USD[a,c] | Discounted ICER, USD/QALY[c] |
|---|---|---|---|---|---|
| Slowing scenario (1 June 2020, $R_e$ = 0.9) | | | | | |
| Symptomatic | 315 700 | 2200 | 11 900 | 342 787 000 | … |
| Hospitalized | 577 700 | 3100 | 16 400 | 439 495 000 | Dominated |
| Symptomatic + asymptomatic once | 268 100 | 2000 | 10 500 | 605 505 000 | 194 000 |
| Symptomatic + asymptomatic monthly | 209 500 | 1700 | 8900 | 2 024 106 000 | 908 000 |
| Intermediate scenario (1 June 2020, $R_e$ = 1.3) | | | | | |
| Symptomatic | 680 600 | 3400 | 18 300 | 488 896 000 | … |
| Symptomatic + asymptomatic once | 579 200 | 3000 | 16 100 | 727 290 000 | 110 000 |
| Hospitalized | 1 696 800 | 6800 | 36 100 | 849 882 000 | Dominated |
| Symptomatic + asymptomatic monthly | 333 700 | 2100 | 11 400 | 2 091 084 000 | 287 000 |
| Surging scenario (1 June 2020, $R_e$ = 2.0) | | | | | |
| Symptomatic | 3 374 200 | 13 700 | 72 600 | 1 608 128 000 | … |
| Symptomatic + asymptomatic once | 3 258 100 | 13 000 | 68 800 | 1 831 196 000 | Dominated |
| Hospitalized | 4 444 300 | 18 300 | 97 200 | 2 090 289 000 | Dominated |
| Symptomatic + asymptomatic monthly | 1 884 000 | 7100 | 37 700 | 2 757 024 000 | 33 000 |

Strategies are listed in order of increasing cost as per cost-effectiveness analysis convention. Infections, deaths, and life-years lost are rounded to the nearest 100. Costs and ICERs are rounded to the nearest 1000. In-text results describing percentages are calculated from unrounded results.

Abbreviations: ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life-year; $R_e$, effective reproduction number; USD, United States dollars.

[a]Includes 180-day horizon between simulated days 1 May 2020 and 1 November 2020.

[b]Total life-years lost were estimated from coronavirus disease 2019–related deaths occurring over 180 days. Details are shown in the Supplementary Materials.

[c]Incremental cost-effectiveness ratios are calculated by dividing the difference in total healthcare-related costs by the difference in total QALYs lost compared to the next most expensive strategy. Dominated strategies are either more expensive and less effective than another strategy (strong dominance) or a combination of 2 other strategies (weak dominance). Total QALYs lost are discounted at 3%/year; because all healthcare costs occur in year 1, costs are not discounted in the base case. Additional details of calculating ICERs are shown in the Supplementary Materials.

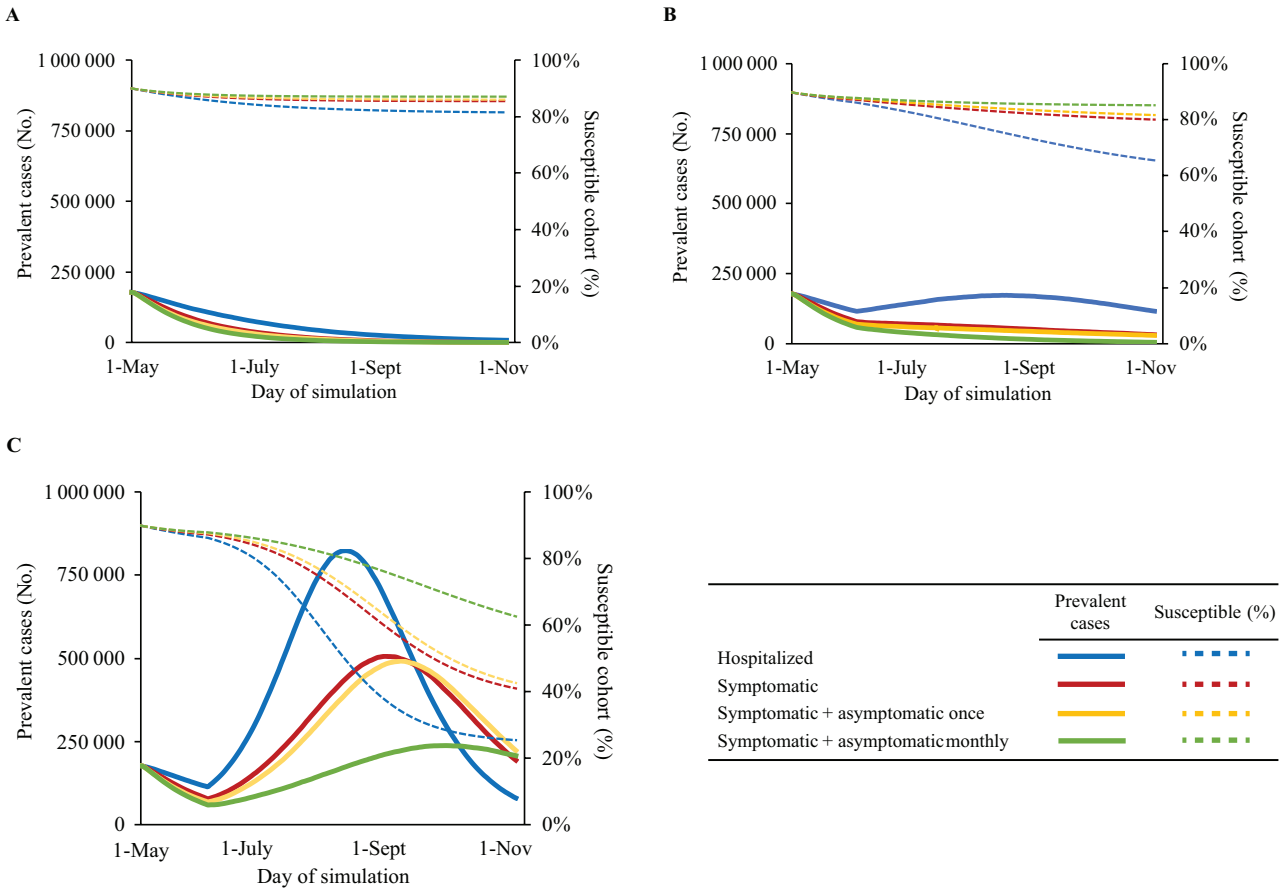


**Figure 1.** Model-projected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection prevalence and proportion of susceptible cohort. For the modeled strategies, prevalent coronavirus disease 2019 cases over time are plotted as solid lines on the left vertical axis, while the percentages of the cohort remaining susceptible to infection over time are plotted as dotted lines on the right vertical axis. People with SARS-CoV-2 are no longer considered prevalent when they have recovered (Supplementary Figure 1). Results shown represent the population of Massachusetts. Testing strategies are denoted by different shaded lines. *A*, Slowing scenario in which the effective reproduction number ($R_e$) on 1 June 2020 is 0.9. *B*, Intermediate scenario in which $R_e$ on 1 June 2020 is 1.3. *C*, Surging scenario in which $R_e$ on 1 June 2020 is 2.0. Abbreviation: $R_e$, effective reproduction number.

infections (Supplementary Figure 4*A–C*) and 90–260 deaths in April alone (Supplementary Figure 4*D–F*).

### *Cost-effectiveness*

In 1-way sensitivity analyses, the economically preferred strategy in each epidemic scenario was most sensitive to test acceptance, the transmission reduction after a positive PCR test, and PCR test costs (Supplementary Tables 3–11). In the surging scenario, symptomatic + asymptomatic monthly would not be cost-effective if we assume low test acceptance (15%), half the transmission reduction after a positive test (33%), or triple PCR test costs ($154). Symptomatic + asymptomatic monthly would become cost-effective in the intermediate and slowing scenarios only with reductions in test costs (intermediate: ≤$13; slowing: ≤$5). If costs decrease for PCR assays, many combinations of program and assay costs symptomatic + asymptomatic monthly strategy would be cost-effective or cost-saving (Supplementary Figure 5).

Holding other parameters equal to the base case, symptomatic + asymptomatic monthly would become cost-effective at an $R_e \geq 1.6$ (Supplementary Table 12). The frequency of repeat testing with symptomatic + asymptomatic monthly is also influential; in the surging scenario, symptomatic + asymptomatic monthly would no longer be cost-effective if tests occur more frequently than every 30 days (Supplementary Table 13); however, if test costs were ≤$3, then testing as frequently as every 14 days would be cost-effective in all epidemic scenarios (Figure 2). While total costs would vary widely with rates of COVID-19–like illness, cost-effectiveness conclusions would not change (Supplementary Table 14). Conclusions are similar even when costs associated with lost productivity or averted COVID-19–related mortality are included (Supplementary Table 15).

## DISCUSSION

Using a microsimulation model, we projected the COVID-19 epidemic in Massachusetts from 1 May 2020 to 1 November 2020 under slowing, intermediate, and surging epidemic

**Table 3. Clinical and Resource Utilization Outcomes for a Model of Coronavirus Disease 2019 Infection and Testing in Massachusetts**

| Scenario | PCR Tests per Simulation, d, Mean | PCR Tests, Total | Hospital Bed-days | | ICU Bed-days | | Cumulative Self-isolation Days |
|---|---|---|---|---|---|---|---|
| | | | Cumulative | Peak | Cumulative | Peak | |
| Slowing scenario (1 June 2020, $R_e$ = 0.9) | | | | | | | |
| Hospitalized | 2900 | 521 800 | 126 300 | 2200 | 76 600 | 1000 | … |
| Symptomatic | 4800 | 861 500 | 91 200 | 2200 | 55 500 | 900 | 1 731 000 |
| Symptomatic + asymptomatic once | 35 100 | 6 318 200 | 87 100 | 2200 | 51 600 | 900 | 1 948 900 |
| Symptomatic + asymptomatic monthly | 192 200 | 34 593 900 | 77 300 | 2200 | 45 600 | 900 | 2 251 900 |
| Intermediate scenario (1 June 2020, $R_e$ = 1.3) | | | | | | | |
| Hospitalized | 2900 | 530 400 | 257 500 | 2200 | 149 100 | 1000 | … |
| Symptomatic | 5900 | 1 053 100 | 133 100 | 2200 | 80 700 | 900 | 2 802 000 |
| Symptomatic + asymptomatic once | 36 300 | 6 534 100 | 123 200 | 2200 | 70 800 | 900 | 2 897 300 |
| Symptomatic + asymptomatic monthly | 193 500 | 34 823 700 | 93 400 | 2200 | 56 300 | 900 | 2 942 600 |
| Surging scenario (1 June 2020, $R_e$ = 2.0) | | | | | | | |
| Hospitalized | 3100 | 549 300 | 639 800 | 7100 | 377 300 | 4100 | … |
| Symptomatic | 13 900 | 2 498 800 | 469 200 | 4600 | 264 600 | 2500 | 10 974 100 |
| Symptomatic + asymptomatic once | 46 800 | 8 418 900 | 442 900 | 4300 | 250 600 | 2500 | 11 326 700 |
| Symptomatic + asymptomatic monthly | 209 300 | 37 672 900 | 265 700 | 2300 | 144 600 | 1200 | 10 694 400 |

Includes events occurring during the 180-day horizon between simulated days 1 May 2020 and 1 November 2020. Strategies are listed by increasing number of tests utilized. PCR tests, hospital bed-days, ICU bed-days, and self-isolation days are rounded to the nearest 100. In-text results describing percentages are calculated from unrounded results. Cumulative self-isolation days are estimated in addition to the hospitalized strategy.

Abbreviations: ICU, intensive care unit; PCR, polymerase chain reaction; $R_e$, effective reproduction number.

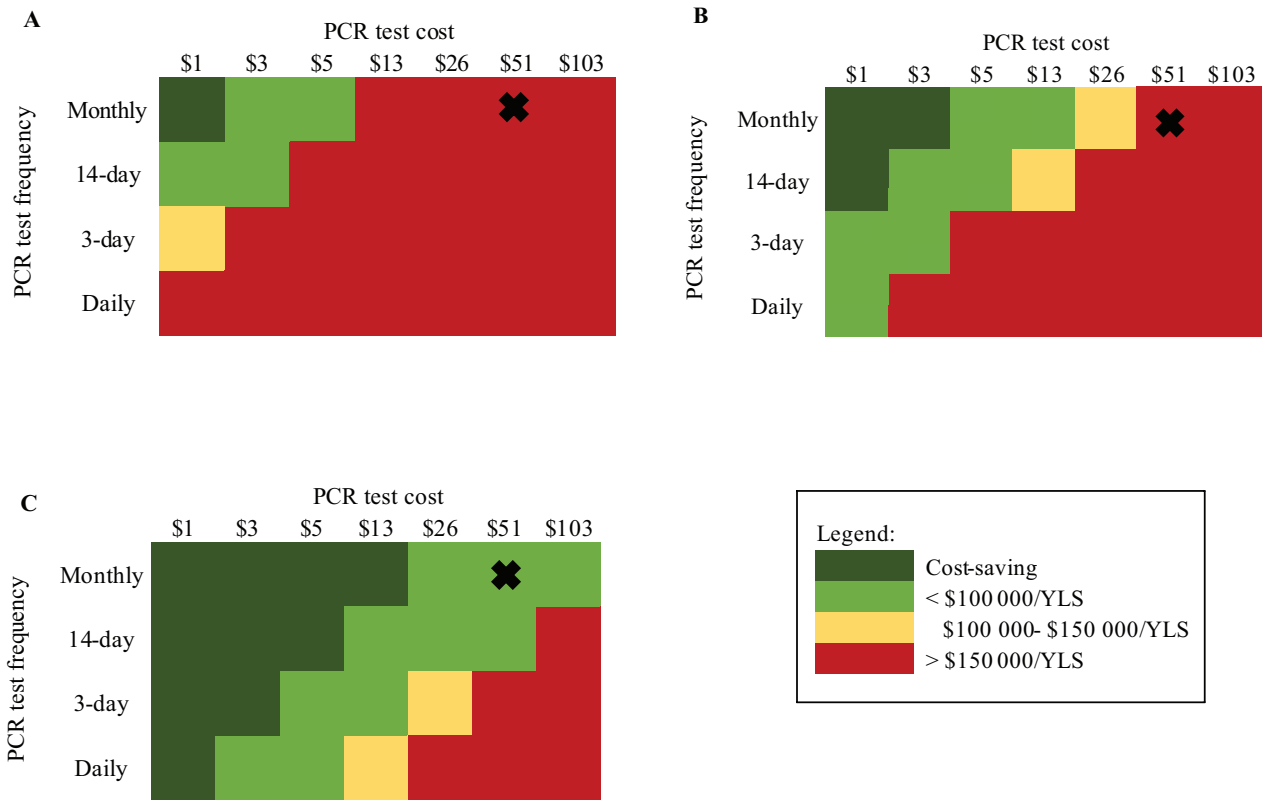


**Figure 2.** Two-way sensitivity analyses: polymerase chain reaction (PCR) test cost and frequency. In this 2-way sensitivity analysis, PCR test cost and frequency were varied. Incremental cost-effectiveness ratios are reported in $/quality-adjusted life-year for symptomatic + asymptomatic monthly testing vs the next least costly strategy. "X" represents the base case. *A*, Slowing scenario in which the effective reproduction number ($R_e$) on 1 June 2020 is 0.9. *B*, Intermediate scenario in which $R_e$ on 1 June 2020 is 1.3. *C*, Surging scenario in which $R_e$ on 1 June 2020 is 2.0. Abbreviations: PCR, polymerase chain reaction; YLS, years-of-life saved.

growth scenarios, to examine the clinical and economic impact of 4 testing strategies.

Expanded PCR testing beyond those with severe symptoms would reduce morbidity and mortality across a range of epidemic scenarios. In all $R_e$ scenarios, we estimate substantial reductions in mortality (1.8- to 2.6-fold lower) with symptomatic + asymptomatic monthly compared to hospitalized. Our $R_e$ values encompass published estimates for Massachusetts during the study period [31–33]. Importantly, the slowing scenario likely reflects Massachusetts's response through June 2020 [9], and the surging scenario provides important insight for elsewhere in the United States where infections are increasing.

We further estimate that if expanded PCR testing had been widely available in Massachusetts from 1 April 2020 to 1 May 2020, 103 000–176 900 infections and 90–260 deaths would have been averted during that 1 month alone. Given the average time from infection to hospitalization and death (~9 days and ~28 days, respectively), earlier expanded testing might also have facilitated timely recognition of epidemic trends and closure policies. Policies that reduce $R_e$ at scale (eg, stay-at-home advisories), as occurred in Massachusetts even while PCR testing was scarce, are likely to be more effective than any of the modeled testing strategies [34, 35]. Similar to conclusions from other studies [22, 31, 36–38], our findings suggest that looser restrictions on social distancing regulations (which can lead to a higher $R_e$) would require more aggressive testing, paired with individual behavioral measures, to control the epidemic.

All the expanded screening strategies would lead to reductions in key hospital resource use as well as fewer days spent self-isolating compared to hospitalized. In Massachusetts, an estimated 9500 hospital beds and 1500 ICU beds were available at the peak of the surge capacity, of which 3800 and 1440 were used [9, 39]. None of the modeled scenarios exceeded peak hospital bed capacity; however, we projected that 23%–75% of available hospital beds would be needed by people with COVID-19. In all scenarios, we projected peak ICU bed use close to or exceeding capacity (1200–4100). While some assumptions are uncertain (eg, proportion of people presenting to the hospital with severe disease, probability of ICU survival), the substantial burden of severe and critical illness we project in all scenarios has important implications for healthcare globally, as resources redirected for COVID-19–related illness may jeopardize the ability to care for other diseases.

In all examined epidemic growth scenarios, symptomatic testing would be cost-saving compared to hospitalized. At any $R_e$ >1.6, symptomatic + asymptomatic monthly would be the most efficient use of resources, unless test acceptance is very low (15%). Importantly, at these higher $R_e$ values, screening the entire population only once would be an inefficient strategy without repeat screening for those testing negative. ICERs were highly sensitive to PCR test costs. If low-cost testing were available at $5/test, it would be cost-effective or cost-saving to offer repeat testing in all epidemic scenarios. In the absence of rapid, low-cost, widely available testing, states will also need to prepare themselves to pivot testing strategies as the epidemic shifts.

In the slowing and intermediate scenarios, as of July 2020, Massachusetts would have test capacity to conduct the economically preferred symptomatic strategy (approximately 12 000/day estimated tests conducted statewide vs 4800–5900 model-projected tests) [9]. However, in the surging scenario, the projected average of 203 100 tests/day (36.6 million/180 days) required to conduct the cost-effective symptomatic + asymptomatic monthly strategy would greatly exceed current capacity; notably, daily testing of the entire population in this scenario led to >3 million projected tests/day. Large-scale testing has been achieved early in the epidemic in some settings: In March 2020, South Korea was testing 20 000 people/day [40]. Newer high-throughput machines may process thousands of tests per day, rendering such an approach potentially feasible in the near future [41]. Additionally, the number of tests used for people without COVID-19 is uncertain. We assumed high rates of COVID-19–like illness (adding approximately 2800 tests/day) in the base case; however, it is likely, particularly in summer months, that fewer people would seek testing. Given that the economically preferred strategy changes depending on $R_e$, implementation of the most cost-effective testing strategy will require careful planning and real-time epidemic monitoring in each setting to adapt to changing $R_e$. Furthermore, while currently an aspiration, low-cost, rapid turnaround testing, even with current imperfect test sensitivity, would be cost-effective even in low $R_e$ settings. While critical supply chain issues and other factors precluded widespread testing in the United States early in the pandemic, even now, expanding testing capacity must remain a focus of national efforts. Given that scaling current technologies may not be feasible in all settings, additional innovative strategies including pooled, rapid antigen, and home self-testing should be examined [42, 43].

The impact of any testing strategy depends on the actions that policymakers, employers, and individuals take in response. Compared to testing only those with severe symptoms, monthly routine testing averted only 58%–64% of infections, whereas daily testing averted 75%–91% of infections. Our results emphasize how policies that support isolating people infected with COVID-19 are essential; when an individual is less adherent to self-isolation after a positive test (ie, lower transmission reduction), the benefits of testing are greatly reduced. In Iceland, broad testing led to only 6% of the population being tested, with 34% of an invited random sample presenting for testing [44]. In the surging scenario, at low test acceptance rates (15%) among those with no or mild symptoms, symptomatic + asymptomatic monthly would no longer be cost-effective. In Massachusetts, SARS-CoV-2 testing often does not require co-pays, and sufficient personal protective equipment permits safe testing [1, 2]. Nevertheless, people may avoid testing due to concerns such as physical discomfort, missing work, or stigma. While the Family Medical and Leave Act may provide support for those eligible who test positive (or if family members test positive), not all

workers may be aware of their rights or have compliant employers [45]. Federal and setting-specific incentives for infected people to self-isolate should be considered (eg, childcare or workplace incentives) [46].

This analysis has important limitations. First, we assume homogenous population mixing. This assumption may over- or underestimate the benefits of PCR testing; however, we have calibrated our model to reflect observed data, using a transmission multiplier. When relevant, we selected values or made assumptions that would provide a conservative estimate of the benefits of testing (PCR sensitivity, test cost, transmission reduction after a negative test) and then varied these values widely in sensitivity analyses. Second, we do not address supply chain lapses, which could impact the feasibility of implementing these strategies. Third, we exclude several factors that may result from expanded testing that would render these strategies even more cost-effective, including averting quality-of-life reductions due to COVID-19–related morbidity or self-quarantine-related mental health issues [47], preventing school closure-related workforce gaps [48], increasing economic purchasing, and enabling economic activity to reopen due to reduced COVID incidence [36]. We also assume that transmissions vary with a constant daily rate by disease state; emerging data suggest that infectivity may be highest early after acquisition of the virus [49]. If true, testing strategies that diagnose people in early or asymptomatic stages of infection would be of higher value. Finally, we do not model contact tracing, which is likely to be a critical tool to respond to a patchwork of surging outbreaks over time.

Testing people with any COVID-19–consistent symptoms would be cost-saving compared to testing only those whose symptoms warrant hospital care. Expanding SARS-CoV-2 PCR testing to asymptomatic people would reduce infections, deaths, and hospital resource use. Despite modest sensitivity, low-cost, repeat screening of the entire population could be cost-effective in all epidemic settings.

## 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

***Author contributions.*** All authors contributed substantively to this manuscript in the following ways: study and model design (all authors), data analysis (A. M. N., A. C. B.), interpretation of results (all authors), drafting the manuscript (A. M. N., A. C. B., A. M., P. K.), critical revision of the manuscript (all authors), and final approval of submitted version (all authors).

***Acknowledgments.*** The authors gratefully acknowledge Christopher Alba, Giulia Park, and Tijana Stanic for their assistance in preparing the manuscript for publication.

***Disclaimer.*** The content is solely the responsibility of the authors; the study's findings and conclusions do not necessarily represent the official views of the National Institutes of Health (NIH), the Wellcome Trust, or other funders.

***Financial support.*** This work was supported by the Eunice Kennedy Shriver National Institute for Child Health and Human Development, National Institutes of Health (NIH) (grant number K08 HD094638 to A. M. N.); the National Institute of Allergy and Infectious Diseases, NIH (grant numbers T32 AI007433 to A. M. and R37AI058736-16S1 to K. A. F.); and the Wellcome Trust (210479/Z/18/Z to G. H.).

***Potential conflicts of interest.*** E. L. reports advisory fees for osteoarthritis-related work from Pfizer and Lilly, outside the submitted work. M. S. reports an investigator-initiated research grant from ViiV Pharmaceuticals, outside the submitted work. M. W. reports personal fees from Quadrant Health Economics and Precision HEOR, outside the submitted work.

All other authors report no potential conflicts of interest. 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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