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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

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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

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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

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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.

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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.

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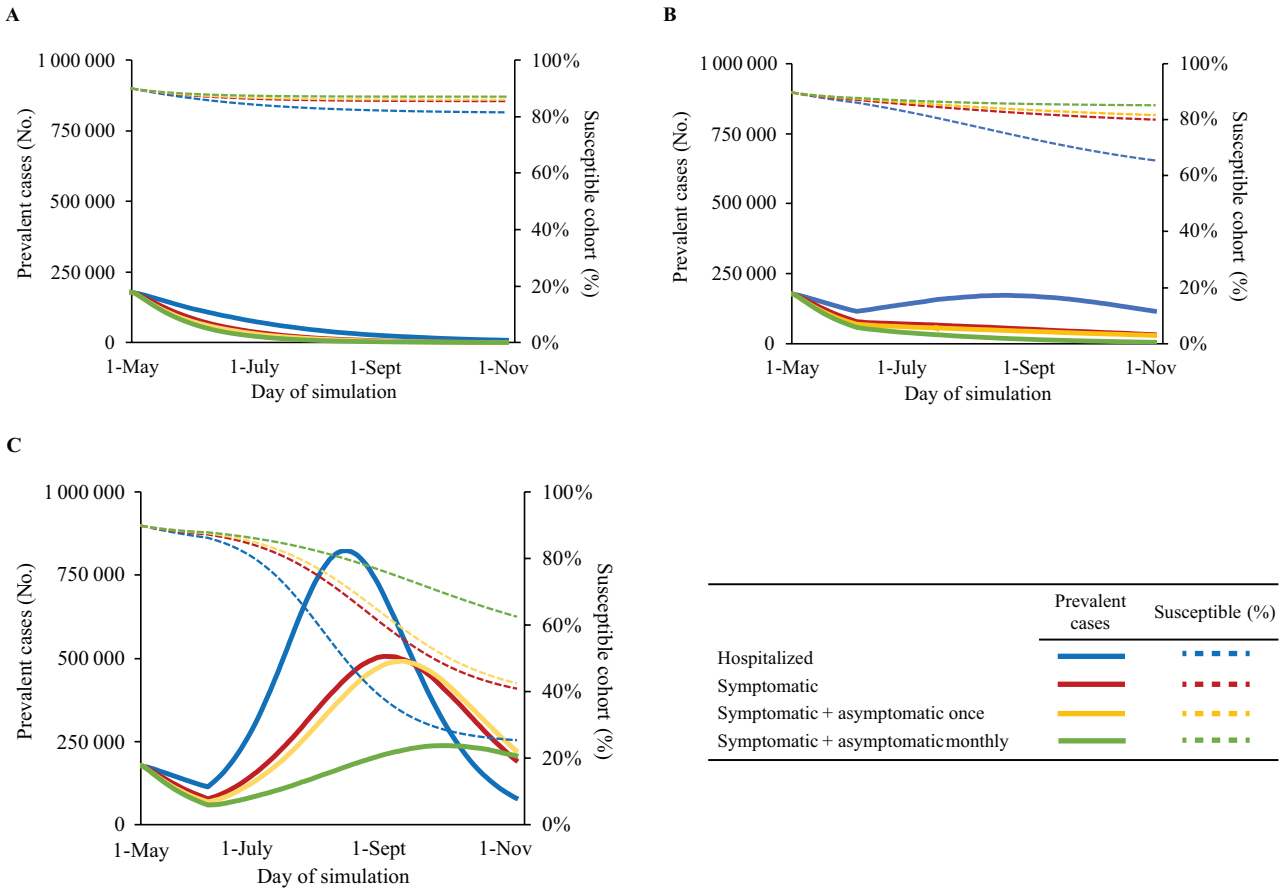


Figure 1. Model-projected severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection prevalence and proportion of susceptible cohort. For the modeled strategies, prevalent coronavirus disease 2019 cases over time are plotted as solid lines on the left vertical axis, while the percentages 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

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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.

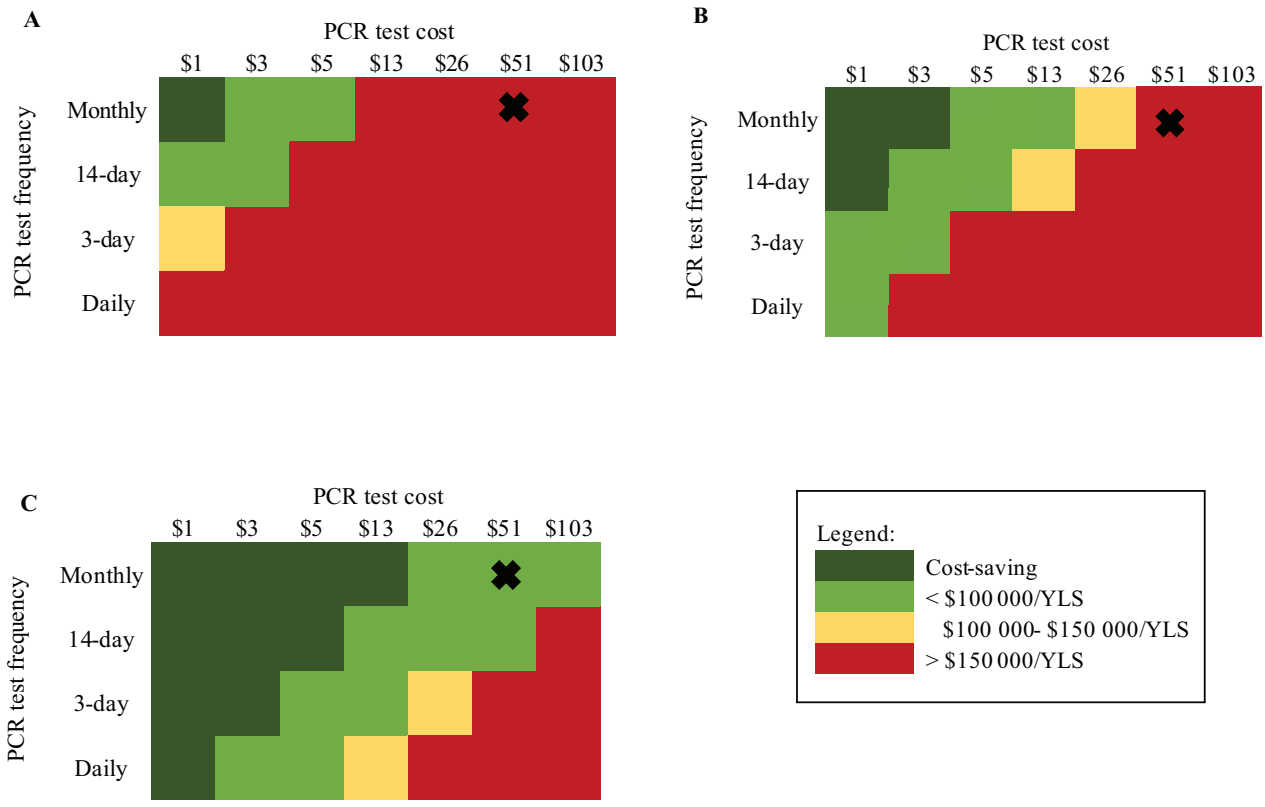


Figure 2. Two-way sensitivity analyses: polymerase chain reaction (PCR) test cost and frequency. In this 2-way sensitivity analysis, PCR test cost and frequency were varied. Incremental cost-effectiveness ratios are reported in $/quality-adjusted life-year for symptomatic + asymptomatic monthly testing 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.

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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

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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).

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