Widespread and frequent testing is essential to controlling COVID-19 in the United States

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More than six months into the US COVID-19 epidemic, the nation is still struggling to gain control of transmission [1]. As with other infectious diseases, testing for SARS-CoV-2 infection is a critical tool for containing spread, as it enables persons who are infected to isolate and their contacts to quarantine and get tested, often assisted by contact tracing efforts. Early epidemic growth has in part been ascribed to insufficient diagnostic testing, due to lapses in laboratory capacity, valid PCR assay availability, testing material availability, and effective targeting criteria [2]. Alleviation of these factors has led to a marked increase in testing, yet absent meaningful national coordination, US jurisdictions have been left to determine their own answers to these crucial questions: Whom should we test, and how frequently should they be tested, to achieve epidemic control in the most affordable and logistically feasible way?

In their recent publication, *Neilan et al* address these questions for Massachusetts, constructing a microsimulation model extensively parameterized with local epidemiologic, natural history, and cost inputs, which are honestly probed across sensitivity analyses [3]. Four strategies of descending stringency were primarily assessed, testing those needing hospitalization only, who are symptomatic only, who are symptomatic but also testing asymptomatic persons once, and who are symptomatic and testing asymptomatic persons monthly. These were evaluated across three epidemic trajectories, from slow decline, to moderate and "surging" growth. Given this year has illustrated how quickly epidemic circumstances can change within locations, this analysis provides robust findings applicable within and between places for optimizing strategies. *Neilan et al* report that, relative to reserving testing to those hospitalized, testing symptomatic persons was broadly effective at reducing transmissions and deaths, while being cost-effective across epidemic scenarios. Asymptomatic monthly screening, while most effective in reducing epidemic burden, at current PCR testing costs was only cost-effective in the surging scenario but was cost-effective across all epidemiological scenarios if per unit testing costs were reduced.

The finding of substantial incidence reductions owing to testing of asymptomatic persons is the logical endpoint of accruing evidence for the substantial proportion of transmissions attributable to asymptomatic infections [4]. Despite this, CDC's testing guidelines have recently oscillated on the value of asymptomatic testing, reportedly due to political interference in CDC's time-honored, expert-driven guidelines creation process [5]. The findings of *Neilan et al* provide strong model-based evidence in support of the impact of asymptomatic testing, across health and economic outcomes, and help to refute the political charade that more testing is a bad thing.

Another valuable lesson is that although testing broadly beyond those symptomatic is beneficial for epidemic control and potentially economical, this necessitates a marked expansion of the number of tests conducted. In the surging scenario for monthly testing, Massachusetts would need to conduct >200,000 tests per day, far outpacing current healthcare and laboratory system capacity. For comparison, New York State only in September 2020 achieved conducting >100,000 tests in a day, in its population nearly three times that of Massachusetts [6]. This lack of mass-scale testing capacity unfortunately means that population-wide asymptomatic screening is not yet a possibility in any US jurisdiction. A natural advancement is to shift testing paradigms away from reliance on laboratory-based PCR methods, with collection methods requiring skilled workers, to more cheaper and scalable approaches. In solving for the per-test costs at which monthly testing would be cost-effective in the two non-surging epidemic scenarios, finding ≤$13 for the moderate growth and ≤$5 for the slow growth scenarios, *Neilan et al* provided useful targets for such approaches, which may include pooled RT-PCR testing of self-collected saliva, point-of-care PCR and antigen tests, and rapid self-tests.

Even if testing materials and systems were ample and/or affordable, the conduct of the associated statewide testing campaigns will be complex to execute. To this point, the large-scale asymptomatic testing programs being deployed at workplaces and college campuses this fall offer fertile material for translation to the jurisdiction scale.

The finding that under the most favorable comparison involving the 4 main strategies, incidence was reduced by only 64% is an important reminder of the limits of testing alone in controlling epidemic spread. HIV models have demonstrated that frequent screening can still permit transmissions to occur, not just due to the failure to detect infected persons before they transmit onwards, but also because of gaps at each stage of our continuua of care after a diagnosis is made [7]. In the case of HIV, this manifests through imperfect linkage and retention of diagnosed persons to effective care and treatment. In the case of COVID-19, this may manifest as non-adherence and other gaps in isolation procedures, which *Neilan et al* have modeled as partial efficacy of isolation in both hospital and community settings, based on literature inputs. The recent case of University at Illinois illustrated this principle. Despite having a comprehensive campus testing program, willingness to ignore isolation procedures for some diagnosed persons (for any number of possible reasons, constraints, or situations) contributed to a temporary campus shutdown [8]. Given the impact of testing to reduce transmission can be compromised by an imperfect system downstream, further research and interventions are needed to decrease transmission likelihood post-diagnosis.

Interestingly, *Neilan et al* looked backwards to estimate the human toll of our lack of preparedness. Limited testing to primarily those severely ill may have led to an additional 176,900 infections and 260 deaths in Massachusetts. This provides an important warning about the need for future investments and planning, lest we lose more lives. As the authors astutely suggest, a national COVID-19 testing strategy is needed, and we extend that call to assert the need for an overarching national strategy to tackle COVID-19. Although elements of a national strategy exist across plans of multiple agencies, the US still lacks a comprehensive and coordinated approach and that is developed in concert with communities most affected. The 2010 and 2015 National HIV/AIDS Strategies offer a strong roadmap for a National COVID-19 strategy [9]. Inspired by such roadmaps, and guided by advances in testing and treatment, including these timely findings from *Neilan et al*, we can significantly cut SARS-CoV-2 transmission in the United States, even absent a vaccine.

Finally, we note *Neilan et al* used $100,000 as a cost-effectiveness threshold for cost-per-QALY-saved. This has historically been a common cut-point in the literature, but it is increasingly viewed as a rigid and relatively conservative threshold. WHO has recommended the use of up to three times the per-capita gross domestic product as a cost-effectiveness threshold [10]. For the US, this is approximately $195,354 (2019 dollars) [11]. Using such a threshold, testing strategy costs somewhat higher would still be cost-effective. Even given this alternative threshold, we submit that at times society must make intentional investments to truly turn the corner and achieve control, elimination, or eradication of an infectious agent [12]. Given the public health devastation, the COVID-19 pandemic would seem to qualify for investments beyond traditionally held cost-effectiveness thresholds. The analysis by *Neisan et al* provides us with important insights should society choose to make the higher level of investment in the near term, to benefit society in the long term. In short, to combat COVID-19 we need both coordination and investment - we can do it.

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