Working Paper

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The Value of Environmental Surveillance for Pandemic Response

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About This Working Paper

Environmental sampling surveillance (ESS) technologies can be used during disease outbreaks as early warning systems, informing public health decisions and saving lives. However, such systems can be costly and complicated to harness for decision-making, so it is important to identify when and how to employ ESS systems to maximize their benefits. This paper simulates a COVID-19-like pandemic to quantify the net-benefits of ESS systems through better-targeted nonpharmaceutical interventions (NPIs) under different scenarios. We project the net monetary benefits yielded by ESS systems relative to conventional detection systems under a base-case scenario reflecting the context of the COVID-19 pandemic and alternative scenarios reflecting other potential pandemics. This model and approach can be used for prioritizing pathogens for ESS, deciding whether and how to expand systems to currently uncovered populations and determining how to scale surveillance systems' coverage over time.

Community Health and Environmental Policy Program

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Abstract

Environmental sampling surveillance (ESS) technologies, such as wastewater genomic surveillance and air sensors, have been increasingly adopted during the COVID-19 pandemic to provide valuable information for public health response. However, ESS coverage is not universal, and public health decision-makers need support to choose whether and how to expand and sustain ESS efforts. This paper introduces a model and approach to quantify the value of ESS systems that provide leading epidemiological indicators for pandemic response. Using the SARS-Cov-2 pandemic as a base-case scenario, we quantify the value of ESS systems in the first year of a new pandemic and demonstrate how the value of ESS systems depends on biological and societal parameters. Under baseline assumptions, an ESS system that provides a 5-day early warning relative to syndromic surveillance could reduce deaths from 149 to 132 per 100,000 population during the first year of a new SARS-Cov-2-like pandemic, resulting in a net monetary benefit of $1,620 per person. The system's value is higher for more transmissible and deadly pathogens but hinges on the effectiveness of public health interventions. Our findings also suggest that ESS systems would provide net-positive benefits even if they were permanently maintained and pandemics like SARS-Cov-2 happened once every century or less frequently. Our results can be used to prioritize pathogens for ESS, decide whether and how to expand systems to currently uncovered populations and determine how to scale surveillance systems' coverage over time.

Contents

About This Working Paper iii
Abstract iv
Figures and Tables vi
Chapter 1. Introduction 1
Chapter 2. Methods 3
  Model 3
  Nonpharmaceutical Intervention Policy 3
  Surveillance 4
  Population 5
  Base Case Scenario 5
  Outcomes 5
  Net Monetary Benefit 6
  Sensitivity Analyses 6
  Minimum Pandemic Frequency for Net-Positive Benefit 7
Chapter 3. Results 8
  Value of ESS Under Baseline Assumptions 8
  Sensitivity Analyses 11
  Minimum Pandemic Frequency for Net-Positive Benefit 13
Chapter 4: Discussion 14
  Limitations 15
  Conclusion 16
Appendix A. Supplementary Methods 17
  Disease Transmission Model 17
  Stochastic Implementation 17
  Inter-jurisdiction Mixing 19
  Health Costs 20
  Time-varying Infection Fatality Rates 21
  NPI Costs 21
  Calibration 22
Appendix B. Supplementary Figures and Tables 23
Abbreviations 28
References 29

Figures and Tables

Figures

Figure 1. Health Costs, Economic Costs, and NMB of Alternative Surveillance Systems 9
Figure 2. ESS Net Monetary Benefit as a Function of R0 and NPI Effectiveness 13
Supplementary Figure 1. Value of ESS System Under Alternative Scenarios 23
Supplementary Figure 2. Cost per Person vs Minimum Pandemic Frequency for Payoff 24

Tables

Table 1. Health and Economic Outcomes for Alternative Disease Surveillance Systems 10
Supplementary Table 1. Sensitivity Analysis Results 25
Supplementary Table 2. Baseline Parameter Values and Sources 27

Chapter 1. Introduction

Novel environmental sampling surveillance (ESS) technologies (e.g., wastewater genomic surveillance and air sensors) were increasingly adopted in the US and globally during the COVID-19 pandemic.[1] For example, wastewater-based surveillance (WBS) systems were used to provide an early warning system for pandemic response,[2] examine trends in disease prevalence and project future hospitalizations,[3] and detect new SARS-CoV-2 variants,[4] and this information was used to estimate the latent number of infections in COVID-19 transmission models.[5] However, ESS capabilities are nascent, and the coverage of wastewater surveillance is uneven worldwide.[6]

ESS may strengthen pandemic response in several ways. The first benefit is that ESS systems do not require testing of symptomatic individuals, reducing the lag from disease transmission to detection. WBS data provide a 4- to 10-day earlier warning of the start of COVID-19 waves than case data[7] and predict hospitalizations before case data.[8] This is a crucial aspect of ESS technologies, as they do not depend on access to healthcare, care-seeking, clinical decision-making, or testing availability. Secondly, ESS systems can monitor many communities simultaneously without requiring additional outreach or resources.

Although ESS systems may help improve pandemic response, and qualitative frameworks to guide the adoption of ESS systems exist,[9,10] their net benefits to society have yet to be quantified. Quantifying the value of ESS systems in monetary terms can be helpful for several reasons: i) it helps policymakers justify the decision to maintain those systems; ii) it may help policymakers choose when to expand sampling, where to sample, and which pathogens require sampling, iii) it requires one to explicitly articulate *how the system will be used* for decision-making, and iv) it also offers a clear decision rule to determine when ESS should trigger public health action: decision-makers should only act on early warning if the value of ESS information is positive – **that is, using the system to make a decision produces more societal benefits than costs**.

This paper introduces a parsimonious simulation model and approach to quantify the value that ESS systems produce through better-targeted nonpharmaceutical interventions (NPIs). Our model depicts a network of jurisdictions, each making sequential decisions to introduce or remove public health interventions using the information provided by their surveillance systems. In this paper, ESS systems are assumed to improve only two parameters relative to syndromic surveillance systems alone: i) they reduce the lag with each public health decision makers observe disease incidence, and ii) they reduce the case ascertainment bias inherent to the surveillance system. Hence, they change the information available for decision-making but do not reduce uncertainty about disease parameters. In our framework, "value" is defined as the net monetary benefit (NMB) of the system – i.e., the benefits afforded by the system (value of lives saved and disease averted with better-targeted interventions) minus the costs of operating the system *and* of public health interventions triggered by the ESS. We parameterize our model with disease characteristics and economic parameters reflecting the first year of the COVID-19 pandemic and explore scenarios to clarify the conditions under which ESS systems provide the most or the least NMB.

Chapter 2. Methods

Model

We developed a stochastic metapopulation model that simulates the dynamics of a new pandemic over a set of n jurisdictions (Supplementary Methods). In this paper, jurisdictions are parameterized to have the average population size of a US county (approximately 100,000 individuals), but the approach generalizes to other jurisdiction sizes. The model describes the dynamics of a new pandemic, assumes no pre-existing immunity to the new pathogen, and individuals are assumed to acquire sterilizing immunity after infection that endures the timeframe of the simulation (one year). We parametrize the model to represent the COVID-19 pandemic as a base case (Supplementary Table 2).

Nonpharmaceutical Intervention Policy

In our framework, the value of better surveillance accrues due to more timely and better-targeted public health non-pharmaceutical interventions (NPIs). Hence, first, we specify an NPI policy (i.e., a method for introducing public health interventions) that reacts to data produced by the surveillance system; then, we specify how better surveillance improves the performance of the NPI policy. Following the structure of tiered COVID-19 public health response plans such as California's Blueprint for a Safer Economy,[11] each jurisdiction $i \in \{1, \dots, n\}$ in our model introduces and removes nonpharmaceutical interventions (NPIs) based on estimated disease incidence $\hat{C}_{i,t}$ following a pre-specified policy. $x_{t,i}$ represents an NPI portfolio (i.e., a set of interventions such as mandating mask wearing, restricting in-person gatherings, etc.) in place in jurisdiction i, where $x_t = 0$ implies no intervention, and $x_t = x_{max}$ is the highest intervention level. Intermediate levels of intervention are denoted by $x_t \in \{1, \dots, 5\}$ and represent other policy portfolios with increasing effectiveness and costs. The jurisdiction-level target NPI $x^*_{i,t}$ is calculated as

$$x^*_{i,t} = \min\left(\frac{10^5\ \hat{C}_{i,t}}{N_i p_i d_i}, x_{max}\right) \tag{1}$$

where N_i is the population size in jurisdiction i, x_{max} is the maximum intervention level, set to 5 in this analysis, p_i is a case ascertainment bias (i.e., proportion of cases that are identified by surveillance) and d_i is a disease incidence threshold used to increase interventions by one level. Eq. 1 results in policy such that the target jurisdiction-level NPI level increases proportionally to disease incidence until it reaches a maximum intervention level x_{max}. Public health decisions take time to be made, interventions take time to be implemented, and policymakers do not update policies instantaneously; hence $x^*_{i,t}$ is only a target intervention level. We model this process accounting for those decision and implementation lags. In the model, the actual intervention level taking place $\mathbf{L}_{t,i} \in \{0,1,\dots,x_{max}\}$ evolves discretely and depends on an exponentially weighted moving average of past surveillance data (Supplementary Methods). In this paper, NPIs' sole effect is to suppress disease transmission. Further, NPIs are assumed to have a linear effect on reducing infectious contacts, hence $n \times n$ time-varying contact matrix $\boldsymbol{\beta}_t$ becomes $\boldsymbol{\beta}_t = (1 - \tau\mathbf{L}_{t,i})\boldsymbol{\beta}_b$, where $\boldsymbol{\beta}_b$ is the baseline contact matrix in the absence of interventions and $\tau \in (0,1/x_{max})$ is the marginal NPI effectiveness to reduce transmission, and τx_{max} is the maximum NPI effectiveness to reduce transmission (i.e., the fraction of infectious contacts reduced when society makes its highest effort to reduce transmission.

This model is purposefully parsimonious, and there are a few advantages to this formulation: i) eq. 1 has the same structure of real-world policies adopted during the COVID-19 pandemic, such as the California Blueprint for a Safer Economy,[11] ii) eq. 1 can be a function of any absolute disease incidence measure; hence the public health policy directly becomes itself a function of the surveillance system that produces the disease surveillance signal $\hat{C}_{i,t}$, iii) the effectiveness of NPIs to reduce transmission τ is a single parameter, which can be traced to the existing literature on NPIs, and iv) more generally, $x^*_{i,t}$ can represent any policy that endogenously reacts to the surveillance system in jurisdiction (or sub-population) *i*. For instance, $x^*_{i,t} = 1$ could include testing of asymptomatic individuals in jurisdiction i which in turn reduces their transmissibility.

Surveillance

The estimated disease incidence $\hat{C}_{i,t}$ is a stochastic, lagged estimate of the true disease incidence and is affected by the surveillance system in place in each jurisdiction. In this analysis, $\hat{C}_{i,t}$ evolves daily as a binomial draw:

$$\hat{C}_{i,t} \sim B(-\Delta S_{i,t-l_i}, p_i) \tag{2}$$

where $-\Delta S$ is the unobserved daily rate of new infections. A surveillance system's performance may be parsimoniously represented by two variables: a case ascertainment rate parameter $p_i \in (0,1)$ and a surveillance lag l_i, expressed as the number of days from infection to detection (i.e, the time it takes for an unobserved exposure event that leads to an infection to be reflected in the epidemiological time-series tracked by public health officials). While surveillance systems that rely on clinical testing have lower, and potentially time-varying p_i, environmental sampling systems have higher p_i because they detect a disease signal from all the population within the catchment area where the system operates. Hence, our framework estimates the indirect effect that reducing the surveillance lag l_i and increasing the case ascertainment rate p_i has through NPIs.

Population

The model simulates disease spreading through six US interconnected jurisdictions that independently make nonpharmaceutical decisions. Individuals can travel and work across jurisdiction lines, and the six jurisdictions each have a population of 100,000 individuals. Travel rates and inter-jurisdiction mixing rates were set to reflect the level of travel and mixing observed in the US Northeast metropolitan areas (Supplementary Methods). Mortality parameters were chosen to reflect mortality rates observed in the United States during the first year of the COVID-19 pandemic.

Base Case Scenario

We parameterize our model to represent the COVID-19 pandemic during its first year. Supplementary Table 1 contains parameter values and supporting references. The baseline scenario with conventional surveillance assumes a syndromic surveillance system based upon confirmed case counts. The syndromic surveillance system entails a thirteen-day time span from exposure to the pathogen to case detection by the public health authority. This thirteen-day lag covers the disease incubation phase (6.6 days)[12] and testing and reporting delays (6 days).[13]

The conventional surveillance system is assumed to have a constant 30% case ascertainment rate in our baseline scenario, which is within the range of case ascertainment rates estimated during the COVID-19 pandemic in the US.[14] In reality, case ascertainment rates from syndromic surveillance are not constant because they depend on the patients' choice to get tested. Public health officials countered those biases by attempting to adjust case rates for the test positivity in their decisions.[11] We do not model those time-varying testing self-selection processes in this paper; hence our assumption that case ascertainment rates are constant favors syndromic surveillance systems and serves as a boundary condition for the purposes of this analysis.

SARS-Cov-2 concentration with wastewater has been shown to lead new COVID-19 cases by 4-10 days,[15] which is consistent with a 3.5 day incubation period estimate.[12] Hence, in our base-case scenario, we assume the environmental sampling system can provide absolute, unbiased disease incidence estimates that lead the case counts by 5 days. We explore longer and shorter lead times, from 2 to 10 days in sensitivity analyses. Moreover, this analysis assumed that all the populations within the jurisdictions are covered by the ESS system (or equivalently, that the sampled population is a representative sample of all the population within the jurisdiction.). The Supplemental Materials also include detailed information about other model inputs, including the health costs of infection and economic costs of interventions.

Outcomes

The primary health outcome of this study is the average mortality per 100,000 population caused by the infectious pathogen. We also compute the cost of illness due to disease, using

COVID-19 parameters as the base-case scenario. We also account for economic costs caused by the nonpharmaceutical interventions introduced (discussed in the Supplementary Appendix). All outcomes are computed over one year from the pandemic onset and are averages computed across the jurisdictions in our model. Since the model is stochastic, we simulate the model 1,000 times and present means and 95% prediction intervals (calculated with the 2.5% and the 97.5% percentiles) of each outcome across stochastic replications.

Net Monetary Benefit

Although ESS systems can improve health outcomes by allowing a swift response to the outbreak, the use of NPIs also carries significant costs, which need to be accounted for in the analysis since a more responsive surveillance system may result in earlier and longer intervention periods and higher intervention costs. As noted above, for this analysis, we use a net monetary benefit measure of value and, therefore, measure the value of ESS systems by computing the health costs of the outbreak Y_h, which include the cost of death and illness per person caused by the disease, and the costs of NPIs per person Y_{npi}, which are a function of model parameters θ, and the surveillance system used in the outbreak (Supplementary Appendix I). The overall cost of the outbreak per person is the sum of the two costs $Y = Y_h + Y_{npi}$. Let $\boldsymbol{s}' = (p_i, s_i)$ represent the surveillance system configuration of a single jurisdiction and $\boldsymbol{s}$ the baseline surveillance system configuration for all jurisdictions. We compute the NMB of ESS systems as

$$NMB_{s'}|\theta = \underbrace{E[Y|\theta, \boldsymbol{s}'] - E[Y|\theta, \boldsymbol{s}]}_{Net\ benefit\ of\ ESS} \quad \underbrace{-Y_s}_{Net\ cost\ of\ ESS} \tag{4}$$

where Y_s is the marginal cost of the improved surveillance system $\boldsymbol{s}'$, and the expectation is taken across stochastic model replications. Also, ESS systems are not assumed to resolve any uncertainty around exogenous parameters in θ. If that were the case, it would be possible to estimate the value of information (VOI) provided by wastewater surveillance systems using an expected value of partial perfect information method.[16] Nevertheless, if Y_s set to zero, eq. 4 yields the maximum (per person) dollar value policymakers society should be willing to invest in installing and maintaining the surveillance system for a specific outbreak.

Sensitivity Analyses

We investigate the sensitivity of the net monetary benefit estimates by varying model parameters one at a time. This exercise aims to assess the robustness of the net monetary benefit of ESS systems to our base-case assumptions. Our sensitivity analysis explored key epidemiological parameters (R0 and the infection fatality rate), economic inputs (NPI costs), the effectiveness of NPI interventions (presented as the percent reduction in infectious contacts induced by the highest intervention level, or τx_{max}), and the stringency of interventions (parameter d_i in eq. 1). We also performed a separate sensitivity analysis with a finer-grained experimental design combining three levels of R0 (1.25, 2.5 and 3.75) and twenty evenly spaced NPI effectiveness values exploring the full range of $\tau x_{max} \in (0,1)$ to shed light on the non-linear, monotonic relationship between NPI effectiveness and NMB (Figure 2).

Minimum Pandemic Frequency for Net-Positive Benefit

Eq. 4 computes the NMB of the system conditioning on the occurrence of a pandemic. That is, if a pandemic with characteristics θ were to happen, Eq. 4 yields the NMB of the system if it is used with policy parameters also encoded in θ. It is likely impossible to obtain a defensible joint probability distribution of θ for all possible pandemics; hence it is also unfeasible to provide a meaningful expected net monetary benefit estimate that accounts for the likelihood of all such pandemics. To provide a straightforward approximation of the likelihood needed of a pandemic such that an ESS system provides net-positive benefit, we simply find $p_\theta -$ the annual probability of θ that would render the ESS' net monetary benefits equal to a set net cost of ESS per person. $\frac{1}{p_\theta}$ is the "frequency" of the pandemic that would make the net benefits of the ESS system equal to the net costs of the ESS system *if the system was designed for a single pathogen*. The minimum pandemic frequency for a positive expected net benefit $1/p_\theta$ can be obtained by dividing the system's benefits by its annual costs. We present the minimum pandemic frequency for positive net benefit for an ESS system that costs from 5 dollars to 100 US dollars per year per person.

Chapter 3. Results

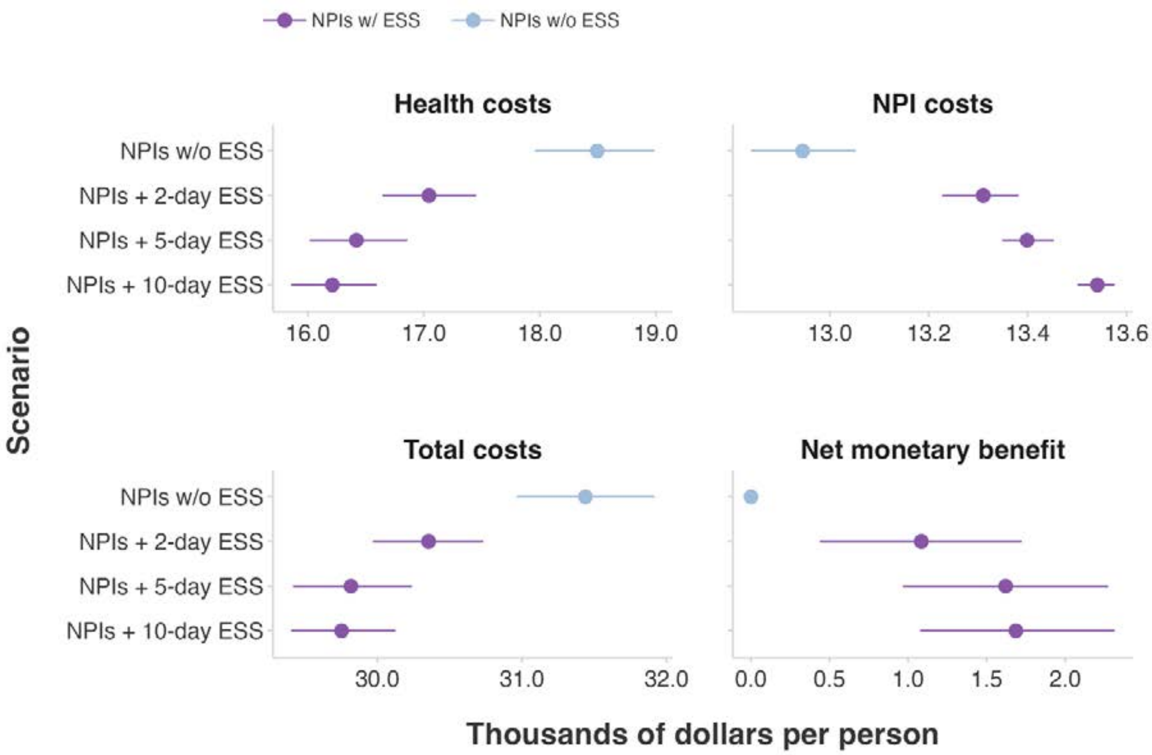
Value of ESS Under Baseline Assumptions

Assuming no NPIs are implemented ("No NPIs" scenario), a new COVID-19-like pandemic would cause substantial harm, causing 542 (536-548) deaths per 100,000 people [mean (95% prediction interval of stochastic replications)] over a one-year timeframe (Table 1). In the absence of any behavioral change, the unmitigated pandemic would infect 92.0 (92.0-92.0) percent of the population, costing 4,730 (4,730-4,730) dollars per person due to illness, and 61,800 (61,100-62,500) dollars due to deaths. The total health cost would be projected at 66,500 (65,800-67,200) dollars per person.

If policymakers followed our base-case NPI policy, the death toll of the pandemic would be reduced from 542 (536-548) to 149 (145-153) deaths per 100,000 population if a baseline syndromic surveillance system is used to trigger NPIs (NPIs w/o ESS scenario). Such an achievement would involve a substantial public health effort. Under baseline assumptions, this effort would require 325 (323-328) days of public health interventions, of which 113 (100-127) days are spent under the most restrictive policy intervention level. We project this effort to cost on the order of 12,900 (12,800-13,100) dollars per person (Figure 1). Based on those assumptions, the total cost of the pandemic would be reduced from 66,500 (65,800-67,200) to 31,400 (31,000-31,900) dollars per person.

Under baseline assumptions, ESS systems provide net-positive value to society because they enhance the effectiveness of NPIs (i.e., preventing illness and death) more than they increase the costs of additional interventions introduced due to the early warning. Even an early warning system that provides only a 2-day early warning relative to a conventional pandemic response system (NPI + 2-day ESS scenario) is projected to reduce the pandemic death toll from 149 (145-153) to 137 (134-141) deaths per 100,000 population. Health benefits increase if the system can provide earlier warning, but we observe a saturation effect beyond 5 days of early warning (Figure 1). A system that provides a 5-day early warning (NPIs + 5-day ESS scenario) would be projected to result in 132 (129-136) deaths per 100,000 population, and a 10-day early warning would result in 130 (127-134) deaths per 100,000 people.

Figure 1. Health Costs, Economic Costs, and NMB of Alternative Surveillance Systems



Notes: Dots represent the average value of each outcome across 1,000 replications, and 95% of the stochastic replications fall within the range represented by lines. Purple scenarios are the ones in which the ESS is used, whereas the blue scenario represents a case with conventional (i.e., syndromic) surveillance. This plot shows that better surveillance improves health outcomes reducing health costs, but also increases NPI costs per person. On balance, total costs (Health + NPI cost) are reduced with improved surveillance, resulting in a positive net-monetary benefit under baseline assumptions - even for a system that only provides a 2-day earlier warning.

Early warning would result in earlier public health intervention, increasing the number of days under NPIs from 325 (323-328) to 330 (330-330) days for a system providing a 5-day early warning signal. That said, the number of days at the *maximum* intervention level (i.e., a "lockdown") was projected to *decrease* with the early warning system in our base-case scenario, as earlier action prevented surges from reaching alarming levels that prompted blunt interventions. For example, a system that provided a 5-day early warning reduced the number of days under the maximum intervention level from 113 (100-127) to 70.8 (63.0-79.3) days. Still, the net effect of the ESS was to marginally increase NPI intervention costs, from 12,900 (12,800-13,100) to 13,400 (13,300-13,500) dollars per person, assuming a 5-day early warning system. Hence, the early warning system reduced the total pandemic costs from 31,400 (31,00-31,900) to 29,800 (29,400-30,200) dollars per person. The difference between the two costs is the net monetary benefit of the system, which is estimated at 1,620 (967-2,270) dollars per person in the first year of the pandemic (Table 1).

Table 1. Health and Economic Outcomes for Alternative Disease Surveillance Systems

Outcome	No NPIs	NPIs w/o ESS	NPIs + 2-day ESS	NPIs + 5-day ESS	NPIs + 10-day ESS
Epidemic size	92.0 (92.0-92.0)	29.0 (28.5-29.5)	27.1 (26.8-27.4)	26.2 (25.9-26.6)	26.1 (25.8-26.5)
Cost of illness	4,730 (4,730-4,730)	1,490 (1,460-1,520)	1,390 (1,380-1,410)	1,350 (1,330-1,360)	1,340 (1,320-1,360)
Deaths per 100,000 people	542 (536-548)	149 (145-153)	137 (134-141)	132 (129-136)	130 (127-134)
Deaths averted per 100,000 people	-393 (-400--385)	0 (0-0)	11.8 (6.05-17.4)	16.9 (11.0-22.4)	18.7 (13.3-24.1)
Cost of deaths	61,800 (61,100-62,500)	17,000 (16,500-17,500)	15,700 (15,300-16,000)	15,100 (14,700-15,500)	14,900 (14,500-15,200)
Health costs	66,500 (65,800-67,200)	18,500 (18,000-19,000)	17,000 (16,600-17,500)	16,400 (16,000-16,900)	16,200 (15,900-16,600)
Days of any NPI	0 (0-0)	325 (323-328)	329 (328-330)	330 (330-330)	337 (336-337)
Days of max NPI	0 (0-0)	113 (100-127)	71.2 (58.3-85.2)	70.8 (63.0-79.3)	51.1 (44.3-57.2)
NPI costs	0 (0-0)	12,900 (12,800-13,100)	13,300 (13,200-13,400)	13,400 (13,300-13,500)	13,500 (13,500-13,600)
Total costs	66,500 (65,800-67,200)	31,400 (31,000-31,900)	30,400 (30,000-30,700)	29,800 (29,400-30,200)	29,800 (29,400-30,100)
Net monetary benefit	-35,000 (-35,900--34,200)	0 (0-0)	1,080 (437-1,720)	1,620 (967-2,270)	1,690 (1,080-2,310)

Notes: All outcomes are computed at the end of the pandemic. Costs are expressed as 2020 dollars per person. Epidemic size is expressed as a percent of the population. Columns represents scenarios without NPIs (No NPIs), NPIs without ESS systems (NPIs w/o ESS), and NPIs informed by ESS systems with varying disease incidence detection lead times relative to syndromic surveillance (NPIs + n-day ESS). For instance, scenario NPIs + 5-day ESS represents an early warning system that produces a disease incidence measure that leads syndromic surveillance by five days.

Sensitivity Analyses

Epidemiological Parameters

A pathogen that is 50% more transmissible than wild-type SARS-Cov-2 would pose a greater challenge for pandemic response, causing 319 (308-327) deaths per 100,000 people even if mitigated with the same NPI policy considered in our base-case scenario (Supplementary Table 1, Supplementary Figure 1). Such a pandemic would cause a substantial societal cost of 53,300 (52,300-54,100) dollars per person. In those conditions, the ESS would be particularly valuable, reducing the pandemic's death toll to 269 (264-275) per 100,000 people and would provide an NMB of 4,660 (3,560-5,660) dollars per person. Conversely, a pathogen that is 50% less transmissible than SARS-Cov-2 would result in a lower death toll of 43.9 (41.9-45.9) without the ESS system, reducing the net monetary benefit of the system to 43.5 (-341-478) dollars per person. The value of the ESS system also depends on the infection fatality rate of the pathogen, but the net benefit of the ESS would be positive even for a pathogen that is half as deadly as SARS-Cov-2. All else being equal, the ESS would still yield an NMB of 657 (248-1,080) dollars per person in a pandemic caused by a pathogen that is 50% less deadly than SARS-Cov-2 and would yield 2,590 (1,680-3,430) dollars per person in responding to a pathogen that is 50% more deadly than COVID-19.

NPI Costs

NPI costs had a moderate effect on the value of surveillance systems. If NPI costs were 50% higher than assumed in our base-case scenario (i.e., if achieving the same NPI effectiveness were to cost 50% more than assumed under our base-case scenario), then the total cost of the pandemic would increase from 31,400 (31,000-31,900) to 37,900 (37,400-38,400) dollars per person with the conventional surveillance system. (Supplementary Figure 1, Supplementary Table 2). Despite that increase, the NMB of the system would only be reduced from 1,620 (967-2,270) to 1,390 (744-2,050) dollars per person because the ESS system only marginally increased the duration of interventions.

Policy Lags and Stringency

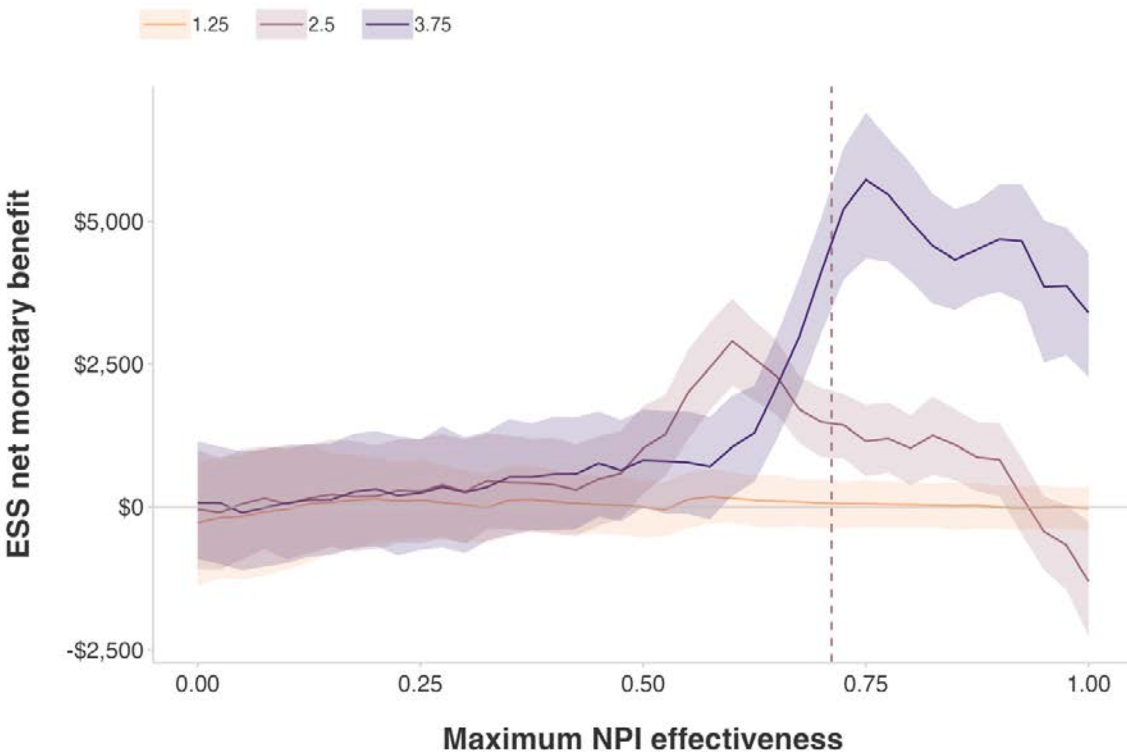
Although longer NPI decision and implementation lags have an overall negative effect on the total costs of the pandemic, longer decision lags would *increase* the net benefit of ESS systems for pandemic response because they would “buy time” for decision-makers to react. Our base-case scenario assumes that decision-makers take one week to decide and implement NPIs. If policymakers took two weeks to implement interventions, the total pandemic cost would increase from 31,400 (31,000-31,900) to 33,500 (32,900-34,000) dollars per person, assuming conventional surveillance. The early warning system effectively helps to compensate decision lags, reducing total costs to 30,900 (30,500-31,300) dollars per person, yielding an NMB of 2,570 (1,820-3,260) relative to conventional surveillance. Conversely, in contexts where NPI implementation is swift (i.e., decisions are made within 3 days), the NMB of ESS would be lower but still positive at 837 (259-1,390) dollars per person.

Policy stringency (i.e., how stringent the case thresholds are used to introduce or remove interventions) has a similar effect on the value of ESS relative to decision lags - the ESS provides the most value under the least desirable conditions for disease prevention. In a context where decision-makers are 50% more stringent than in our base-case assumptions (i.e., their case thresholds are half of its base-case), society can avert a substantial number of deaths, reducing mortality from 149 (145-153) to 83.9 (80.6-87.1) deaths per 100,000 population without the ESS. In that scenario, the ESS yields 1,100 (616-1,580) dollars per person of net benefit since more deaths would already be prevented through more stringent NPIs. Conversely, if policymakers were more lenient, policy choices would change the system's overall outcomes and result in a higher value of the enhanced surveillance system.

NPI Effectiveness

NPI effectiveness (i.e., the % reduction in infectious contacts induced by NPIs) had a non-linear and non-monotonic effect on the value of surveillance systems to pandemic response (Figure 2). If NPI effectiveness is 0%, an improved surveillance system has no value, as expected. The value of the enhanced surveillance system increases slowly with NPI effectiveness for maximum NPI effectiveness below around 50% and peaks when the maximum NPI effectiveness reaches 60%, enough to reduce the baseline R0 of 2.5 below 1 at the pandemic onset. In general, we find that the value of the ESS peaks at a maximum NPI effectiveness value of around $1-1/R0$. Beyond that point, increases in NPI effectiveness result in lower total pandemic costs, but the value of the surveillance system starts to decrease.

Figure 2. ESS Net Monetary Benefit as a Function of R0 and NPI Effectiveness



Notes: ESS net monetary benefit is a non-monotonic function of R0 (represented in different colors) and the maximum NPI effectiveness (i.e., the fraction of infectious contacts reduced by the maximum intervention level). The vertical dashed line represents the NPI effectiveness in our base-case scenario (see Supplementary Methods). Lines represent the average net monetary benefit of a 5-day early warning system, and shaded areas represent 95% prediction intervals computed over 1,000 stochastic replications.

Minimum Pandemic Frequency for Net-Positive Benefit

Under base-case assumptions, an ESS system that costs 10 dollars per person per year would provide net-positive benefits even if a SARS-Cov-2-like pandemic only occurred every 162 (97 – 227) years. Even a pandemic caused by a pathogen 50% less deadly than SARS-Cov-2 would only need to happen every 66 (25-108) years to justify the permanent operation of an ESS system with the characteristics assumed in this study (Supplementary Figure 2).

Chapter 4: Discussion

ESS systems could yield thousands of dollars of value per person in a new pandemic. Our simulation results demonstrate that ESS systems that provide early warning could provide benefits valued at low to mid-thousand dollars per person by helping prevent deaths and illness in a new pandemic (see Supplementary Table 1). Baseline results estimate these benefits to be $1,620 per person. The system's value results from earlier and improved alignment of interventions with the timing of epidemic progression. Benefits could be as high as $4,660 per person for more transmissible pathogens and are greater when diseases are more severe, interventions are less costly, and decision lags are longer. The relationships between the benefits of ESS and these parameters provide additional insights for taking advantage of ESS.

ESS helps to mitigate worst-case pandemic scenarios. The worse the pandemic, the more value early warning systems have. Hence, more transmissible and deadly pathogens should be prioritized for ESS. This is an intuitive yet important finding. The value of ESS increases linearly with mortality but non-linearly with transmissibility.

ESS helps mitigate the effects of poor adherence to NPIs and decision lags. Implementing earlier and more targeted interventions can provide policymakers with flexibility. Public health outcomes are better when interventions are implemented decisively, stringent, and adhered to by the public. Our results demonstrate that decision-making supported by ESS reduces the costs that accrue when adherence to NPIs drops or decision-making must be slower or favors less stringent interventions. As a result, ESS may afford policymakers options to better manage the net costs of a pandemic when managing uncertainty and competing demands of a pandemic.

The benefits of ESS may outweigh their costs even if a pathogen as severe and transmissible as SARS-CoV-2 were to emerge only once a century (or even less frequently). Our results describe benefits from ESS that are only realized when a pandemic occurs, but severe pandemics for which these benefits materialize may occur infrequently. Although the magnitude of benefits presented in these results vary, the net benefits of a permanent ESS system that costs 10 dollars per person may be justified even if a SARS-Cov-2-like pandemic were to occur as infrequently as once every 150 years. Experiences with ESS during the COVID-19 pandemic (i.e., wastewater surveillance) suggest that the implementation costs of the system could be under 5 dollars per person. Hence, this research suggests public health decision-makers have a rationale to install and maintain ESS systems even if a SARS-Cov-2 pandemic were not to happen in the next several decades.

The value of ESS must be evaluated in the context of the costs and benefits of the interventions it triggers. This analysis demonstrates that the value of an ESS is influenced by the characteristics of the disease event, the costs and effectiveness of response options, and how decisions are made to implement interventions. The primary benefit of the ESS is the reduction in deaths caused by a pandemic. The realization of reduced deaths is associated with higher economic costs of interventions. However, ESS can potentially reduce the duration of the most stringent interventions and costs associated with those severe measures that are not captured well in economic terms.

The net monetary benefit of ESS operationalizes existing guidance for adopting and using ESS systems. Qualitative frameworks to guide the adoption of ESS systems (primarily, wastewater-based surveillance) have been put forth by several entities,[9,10] and national and international surveillance networks have been set up to organize and sustain ESS activities.[17,18] For instance, the National Academy of Sciences published a report containing a framework with criteria for adopting wastewater-based surveillance. The criteria are (i) the public health significance of the threat, (ii) analytical feasibility for wastewater surveillance, and (iii) the usefulness of community-level wastewater surveillance data to inform public action.[9] Similarly, WHO's existing guidance also qualitatively articulates the sources of value of ESS systems and the rationale for their implementation.[10] The model and framework we propose complement and operationalize those guidance documents by quantifying the societal value of ESS systems.

Ultimately, the value of early warning hinges on the effectiveness of the public health interventions it informs. Low effectiveness and adherence to NPIs reduce the potential value of the ESS systems. As presented in Figure 2, the benefits of an ESS increase as NPI effectiveness increases until NPIs can contain the spread of a pandemic. However, the benefits of ESS are non-monotonic with NPI effectiveness. Once NPIs are effective enough to contain a disease outbreak, public health outcomes are improved, but the value of the ESS decreases. This threshold increases as disease transmissibility increases. As a result, the benefits of ESS to policymakers will be greatest for more severe diseases for which NPIs are justified. The benefit of ESS will be lower if the policymakers are not willing to introduce NPI interventions or the public is not willing to comply with them.

Limitations

Future research can address the following limitations of our analysis. First, this paper only simulated the first year of a COVID-19-like pandemic, against which the population has no immunity. We only simulate the benefit of the system before vaccines are expected to be available. We also do not simulate the introduction of new SARS-Cov-2 variant strains or other pathogens with different progression timeframes and viral shedding dynamics. ESS systems may be even more valuable for pathogens that are more transmissible, deadly, or that exhibit a longer infectious and asymptomatic periods. We also did not assess the system's value during the endemic phase in this study. However, this model and approach can be extended for those conditions.

We also assumed that ESS systems provide a leading, unbiased, absolute disease incidence estimate, which can be used to trigger public health action as disease incidence surpasses pre-defined thresholds. Implementing such a system might not be straightforward at this time, since the data reported by wastewater surveillance efforts provide RNA concentration estimates, which cannot be directly translated to an absolute disease incidence estimate. That said, wastewater data is being used by the CDC to forecast hospitalizations,[3] demonstrating that ESS could in principle be used to infer disease incidence.

Moreover, this paper evaluated the value of ESS by comparing a group of jurisdictions where no jurisdiction has access to ESS versus a group of jurisdictions where all have access to the same ESS and use the system consistently over one year. However, jurisdictions have heterogeneous surveillance systems and may not use them throughout the year. Future work might explore the marginal value of additional surveillance, both in space (i.e., surveilling additional jurisdictions currently not covered by the system) and in time (i.e., surveilling the system for longer). Future work might explore how to tailor and "right-size" surveillance systems for maximum net societal benefit. Finally, this study focused on the benefits of biosurveillance for a new pandemic. If intentionally implemented and flexible, ESS also provides benefits for managing endemic diseases. Future work could explore how options that provide these benefits could be integrated into pandemic ESS.

Conclusion

Environmental sampling surveillance systems could provide substantial public health value in mitigating the impacts of future pandemics. Our results demonstrate that ESS could yield net benefits valued at thousands of dollars per person by enabling timely and better-targeted public health interventions. We also demonstrate that ESS systems can provide net-positive benefits even if a pandemic on the same scale as COVID-19 occurred only once per century or less frequently. However, benefits hinge on the effectiveness of and adherence to non-pharmaceutical interventions. In summary, this analysis suggests that maintaining ESS capabilities is a good investment for pandemic preparedness and offers a framework for evaluating ESS system design and implementation decisions.

Appendix A. Supplementary Methods

Disease Transmission Model

Our analysis starts with a standard disease transmission model describing person-to-person transmission of SARS-Cov-2 across n jurisdictions. The state-space of the model is comprised of a set of health statuses $\mathbf{S}, \mathbf{E}, \mathbf{P}, \mathbf{I}, \mathbf{A}, \mathbf{R}$, each a $1 \times n$ vector representing the population in each of the following compartments: susceptible, exposed (but not infectious), pre-symptomatic (and infectious), asymptomatic, infected, and removed, respectively. Eqs. 1-6 describe a system of differential equations representing the model, and Supplementary table 2 contains parameter definitions, values and sources.

$$\dot{S} = -\lambda_t \odot S \tag{1}$$

$$\dot{E} = \lambda \odot S - \sigma E \tag{2}$$

$$\dot{P} = \sigma E - \delta P \tag{3}$$

$$\dot{I} = (1 - \rho)\delta P - \gamma_I I \tag{4}$$

$$\dot{A} = \rho\delta P - \gamma_A A \tag{5}$$

$$\dot{R} = \gamma_I I + \gamma_A A \tag{6}$$

$\dot{\mathrm{S}}, \dot{\mathrm{E}}, \dot{\mathrm{P}}, \dot{\mathrm{I}}, \dot{A}, \dot{\mathrm{R}}$ represent the time derivatives of each disease status and Greek letters represent progression rates. The force of infection λ_t is computed using a time-varying effective contact-rate vector $\boldsymbol{\beta}_t$ which will depend on contact rates within each stratum as well as nonpharmaceutical interventions (discussed later). Infectiousness of each disease status $\mathbf{P}$ and $\mathbf{I}$ are modulated by constants c_p and c_i and c_a.

$$\boldsymbol{\lambda}_t = \boldsymbol{\beta}_t\left(c_p\mathbf{P}_t + c_i\mathbf{I}_t + c_a\mathbf{A}_t\right) \tag{7}$$

Stochastic Implementation

Deterministic models may be appropriate for simulating large populations but may fail to accurately represent stochastic dynamics when the pandemic approaches or achieves local elimination. This was a common feature of the COVID-19 pandemic response when public health mandates momentarily reduced disease transmission to low levels. Moreover, this model seeks to represent the performance of surveillance systems even when disease transmission is low; hence, we implement the model as a discrete-time stochastic model. We simulate outflows for each disease state vector $\mathbf{X}$ drawing from a binomial distribution $\mathbf{out}_{\mathbf{X_t}} \sim Binomial\left(\mathbf{X}, 1 - exp(\mathbf{p})\right)$. We then carry over outflows from one disease state to the next. Hence, our disease state equations can be re-written as

$$\mathbf{S_{t-1}} \sim \mathbf{S_{t-1}} - B\left(\mathbf{S_{t-1}}, 1 - \exp\left(-\frac{\boldsymbol{\lambda}_{t-1}}{\mathbf{N}}\right)\right) \tag{8}$$

$$\mathbf{E_t} \sim \mathbf{E_{t-1}} + B\left(\mathbf{S_{t-1}}, 1 - \exp\left(-\frac{\boldsymbol{\lambda}_{t-1}}{\mathbf{N}}\right)\right) - B\big(\boldsymbol{E_{t-1}}, 1 - \exp(-\sigma)\big) \tag{9}$$

$$\mathbf{P_t} \sim \mathbf{P_{t-1}} + B\big(\boldsymbol{E_{t-1}}, 1 - \exp(-\sigma)\big) - B\big(\boldsymbol{P_{t-1}}, 1 - \exp(-\delta)\big) \tag{10}$$

$$\mathbf{I_{t-1}} \sim \mathbf{I_{t-1}} + B\left(\boldsymbol{P_{t-1}}, 1 - \exp\big(-\delta(1-\rho)\big)\right) - B\big(\boldsymbol{I_{t-1}}, 1 - \exp(-\gamma_I)\big) \tag{11}$$

$$\mathbf{A_t} = \mathbf{A_{t-1}} + B\big(\boldsymbol{P_{t-1}}, 1 - \exp(-\rho\delta)\big) - B\big(\boldsymbol{A_{t-1}}, 1 - \exp(-\gamma_A)\big) \tag{12}$$

$$\mathbf{R_{t-1}} \sim \mathbf{R_{t-1}} + B\big(\boldsymbol{A_{t-1}}, 1 - \exp(-\gamma_A)\big) + B\big(\boldsymbol{I_{t-1}}, 1 - \exp(-\gamma_I)\big) \tag{13}$$

where $B(\mathbf{n}, p)$ results in a binomial draw from population vector $\mathbf{n}$ with probability p. The model simulates outflows and inflows such that the outflows from one disease state are the same as the inflows to the following state, ensuring that the population size is constant.

Nonpharmaceutical Interventions

Following mitigation plans adopted during the COVID-19 pandemic, nonpharmaceutical interventions (NPIs) are modeled as a set of intervention portfolios organized within intensity levels with a marginal effectiveness τ at each intervention level $L \in \{1,2,3,\ldots,L_{max}\}$. In this analysis, we set L_{max}= 5, and τ is specified as an additive percent reduction in infectious contacts induced by a set of interventions introduced by public health decision-makers. For simplicity, this analysis uses a constant, additive marginal effectiveness of interventions. For instance, if $\tau = 0.15$, then introducing the first intervention level reduces potential infectious contacts by 15% relative to a no-intervention scenario, and introducing the second intervention level reduces infectious contacts by 30%. Under this specification, $\tau \in (0,1/L_{max})$. Under this specification, the time-varying contact rate matrix $\boldsymbol{\beta}_t$ is specified as

$$\boldsymbol{\beta}_t = (1 - \mathbf{L}_t\tau)\boldsymbol{\beta}_b \tag{14}$$

where $\boldsymbol{\beta}_b$is the baseline $n\ x\ n$ mixing matrix and the intervention level $\mathbf{L}_t$ is an $n\ x\ 1$ jurisdiction-dependent nonpharmaceutical intervention level. $\mathbf{L}_t$ can be either specified as an exogenous variable or an endogenous variable influenced, in part, by public health policy. Public health decision-makers follow epidemiological outcomes that are proportional to $\mathbf{L_t}$ (such as case counts) to decide the appropriate level of intervention. Thus, we specify a target NPI level $x^*_{i,t}$ as a linear function of disease incidence $\hat{C}_{i,t}$

$$x^*_{i,t} = \min\left(\frac{10^5\ \hat{C}_{i,t}}{N_i p_i d_i}, x_{max}\right) \tag{15}$$

where N_i is the population size in jurisdiction i, x_{max} is the maximum intervention level, set to 5 in this analysis, p_i is a case ascertainment bias (i.e., proportion of cases that are identified by surveillance) and d_i is a disease incidence threshold used to increase interventions by one level.

NPI Decision and Implementation Lags

To account for the time it takes for decisions to be made and implemented, the target intervention level $x^{*}_{i,t}$ affects the actual intervention level $\mathbf{L}_t$ with a lag. For instance, during the COVID-19 pandemic, California introduced interventions based on epidemiological data averaged over a week, and only introduced or removed interventions at pre-specified intervals.[11] We model this process with two adjustments that make the NPI policy more stable yet responsive. First, we make the target intervention level a state variable, which evolves as an exponentially weighted moving average of the instantaneous intervention target $x^{*}_{i,t}$ (i.e., $\frac{\mathbf{dL}^{*}}{dt} = (\boldsymbol{x}^{*}_{t} \text{-} \mathbf{L}^{*}_{t}) / 2$). This adjustment makes the NPI policy less-susceptible sudden changes driven only due to stochasticity. Second, the actual NPI is only revised in a pre-specified periodicity. Hence, we assume that intervention levels may increase once every a_{up} days, while they may be relaxed once every a_{down} days. In our base-case scenario, we set a_{up} to a week, and a_{down} to two weeks. The intervention level can increase or decrease by more than one unit within one revision. This feature allows increases in interventions (i.e., closures in response to increasing disease incidence) to occur faster than relaxations in interventions. On days that are not even multiples of a_{up} or a_{down}, NPIs are not changed.

Inter-jurisdiction Mixing

A baseline mixing matrix $\boldsymbol{\beta}_b$was created to represent the level mixing and inter-jurisdiction mixing across jurisdictions with the size of a US county. First, we partition overall mixing in three categories: Mixing at home k_h, mixing at work and travel, which may cross county lines k_{wt} and mixing at other modes that do not cross county lines k_o. These three proportions are taken from our prior work,[19] which used network data to identify the proportion of mixing occurring within each mode. Then, we create one mixing matrix for each mode, and the overall mixing matrix is the sum of mixing within each mode.

We simulate six jurisdictions divided into two blocks of three jurisdictions. Within the two blocks, we simulate high levels of commuting reflecting commuting data observed in the New York metropolitan statistical area. The relative levels of mixing at work and travel within and outside county lines were informed by commuting data from the US Census Bureau American Community Survey (ACS),[20] which showed that approximately 10% of county populations commuted to a neighboring county in the New York metropolitan statistical area. In addition to commuting to proximal counties, individuals also perform business and leisure trips to counties outside of their commuting. Data from the US Travel Association projects that about 2% of individuals perform non-commuting travel per day. Since our model considers six jurisdictions, with three jurisdictions in non-adjacent counties, the travel rate for other counties is set to 0.7% for each non-adjacent block.

Health Costs

This study adopts a societal perspective on health costs. We consider disability-adjusted life years (DALYs) lost across various disease states, the financial costs of hospitalization and treatment, and the cost of deaths. We estimate mortality costs using the Value of a Statistical Life (VSL) and morbidity costs using the Value of a Statistical Life Year, as adjusted for disability and duration of morbidity effects. VSL is defined as the valuation of mortality risk reduction[21] or the willingness of an individual to pay to reduce their risk of fatality.[16] It is important to note that using the VSL does not imply placing a value on any individual life. Instead, VSL is used in regulatory analysis to value the welfare impact of policies that reduce or increase fatalities.[11] We use the central VSL estimate published by the Department of Health and Human Services ($11.4 million for the year 2020)[22] multiplied by the number of deceased individuals to account for the mortality cost of the pandemic. Additionally, a 2020 estimate of the Value of the Statistical Life Year (VSLY) ($240,676) was used in calculating the cost of disease resulting from morbidity.[23]

Morbidity costs were computed for each disease state as:

$$C_{ij} = VSLY * w_j * d_j * p_j * R_i \tag{16}$$

Where VSLY the Value of the Statistical Life Year, w_j are the DALY weights of each disease state $j \in \{asymptomatic, mild, severe, critical, post - acute\}$, d_j is the duration of the disease states (as a fraction of a year), p_j is the proportion of infected individuals that experience disease state j, and R_i is the number of individuals who were infected by the end of the simulation in jurisdiction i.

DALY weights w_j were incorporated to account for disease costs resulting from morbidity (i.e., loss in quality of life due to time spent under different disease states). We used the following DALY weights estimated for infectious diseases (see table 2 in Salomon et al.[24]): Mild acute episode (0.006), severe acute episode (0.133), and post-acute effects (0.219) to represent morbidity effects of severe SARS-Cov-2. In addition, a DALY weight for critical acute episode – requiring intensive care unit care (0.655) – was used for hospitalization.[25]

Estimates of symptom duration d_j by disease state to be used in morbidity cost calculations were also selected based on the literature on COVID-19. The mild disease state duration value was set at 5 days,[26] the severe duration at 8.5 days,[27] the critical duration at 13 days,[16] and the post-acute (long COVID) duration at 365 days.[28] The three acute disease state durations were well established, but the post-acute duration was not consistently defined in the literature. The 365-day duration was chosen as a midpoint between the minimum duration to be considered long COVID (2-3 months) and the maximum, which is undefined because many of those infected continue to exhibit long COVID symptoms.[29]

Estimates of relative disease state prevalence p_j were also established based on the COVID-19 literature. A report on over 70,000 symptomatic cases in China found that 81% were mild, 14% were severe, and 5% were critical.[30] Asymptomatic cases accounted for approximately 33% percent of all infections.[31–33] Symptomatic percentages were adjusted to take this into account, setting final disease state prevalence percentages at 33% asymptomatic, 55% mild, 9% severe, and 3% critical. The prevalence of post-acute chronic symptoms or long COVID was also considered. The Long COVID Household Pulse Survey found that 30% of all adults who had COVID experienced long COVID symptoms and that 25% of all adults with long COVID have significant activity limitations.[34] Multiplied together, 7.5% of all adults who experienced COVID symptoms experienced debilitating long COVID. Considering the percentage of asymptomatic cases, the final disease state prevalence percentage of those infected with COVID who experience long (i.e., post-acute) COVID symptoms was set at 5%.

Hospital costs were also considered – hospital care being required for those experiencing severe or critical COVID. Severe was defined as requiring hospital care but not ICU care, while critical was defined as requiring hospital care, including ICU care and mechanical ventilation. Severe cases were found to cost $11,267, and critical cases $41,510.[35]

Time-varying Infection Fatality Rates

During a pandemic, providers learn about the pathogen and illness, developing improved standards of care, even absent pharmaceutical interventions. This has been the case for the treatment of hypoxemia and acute respiratory distress syndrome (ARDS) during the COVID-19 pandemic.[36] For example, initially, patients suffering from hypoxemia were usually laid in a supine position. However, in the Spring of 2020, evidence showed that initially simply placing patients in a prone rather than supine position and less aggressive intubation improved outcomes.[37,38] Implementing the new protocols likely reduced infection fatality rates and health system burden.[39] To account for this phenomenon, which argues for delaying the bulk of new infections from a new pandemic to when standards of care have been better developed, we allow infection fatality rates to be time-varying and decrease after the beginning of the pandemic, following the order of magnitude observed in the US after the first six months of the pandemic.[40]

NPI Costs

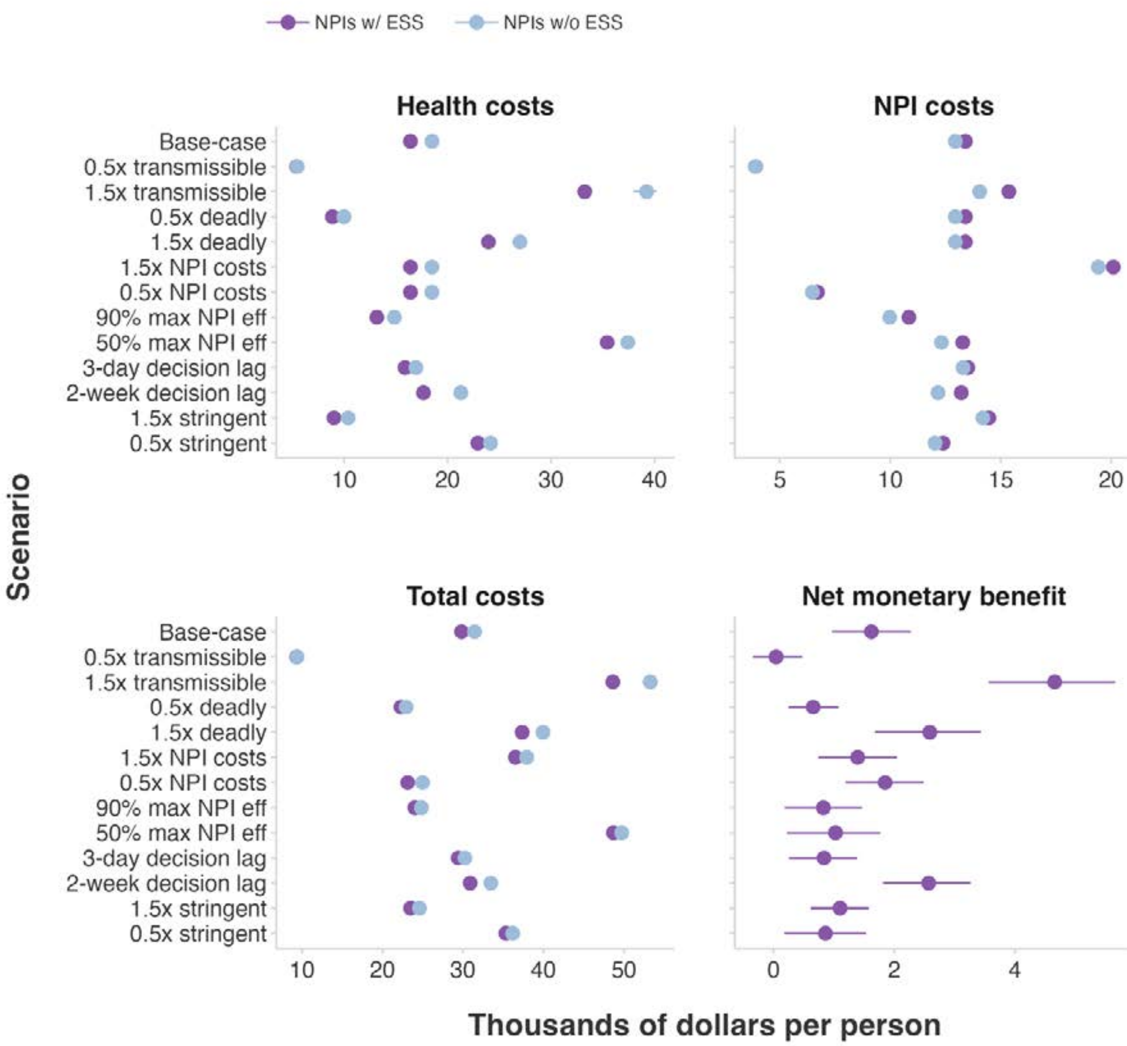
We draw from estimates of the economic costs of COVID-19 used in our prior work to approximate the economic costs caused by NPIs. Welburn and Strong[41] used a computable general equilibrium model to estimate the income (i.e., GDP) lost in several social distancing portfolios for each US state. Each intervention level modeled in the economic model mapped to social distancing strategies used in our epidemiological model.[19] Here, we use an analogous approach. The US state-level estimates from Welburn and Strong[41] suggested a 25% median GDP loss across all US states for the highest intervention level – i.e., closing non-essential businesses would cost one-quarter of GDP. We make the simplifying assumption that intervention costs are linear, so our baseline scenario assumes that an intervention level 5 costs 25% of GDP, and intermediate intervention levels cost proportionally less. This linearity assumption underestimates the value of ESS systems if NPIs have a marginally decreasing cost-effectiveness, which we argued elsewhere.[42,43] Since higher NPI costs imply higher costs of ESS adoption, the linear functional form provides a parsimonious upper bound for NPI intervention costs; hence, it results in a lower bound for the estimate of the value of ESS systems. The estimates we use only consider the direct economic costs of interventions and did not factor the loss of learning from school closures or other unquantified costs of NPIs. Hence, we test the sensitivity of our results in sensitivity analyses, allowing NPI costs to be 50% higher or lower than our base-case estimates to explore the sensitivity of results to those parameters.

Calibration

Whenever possible, we used parameter estimates from the literature (Supplementary Table 2). However, two of our model parameters need calibration so that the number of deaths in our base-case surveillance scenario matched the number of deaths observed in the US during the first year of the COVID-19 pandemic. We calibrate two parameters that cannot be directly observed from data: the intervention effectiveness τ and the disease incidence threshold for increasing the NPI intervention level by one unit d. Our calibration procedure used two empirical targets: i) the average number of COVID-19 deaths per 100,000 population from March 1st 2020 to March 1st 2021 in US states (144.45 deaths per 100,000 population), and ii) the median number of days spent at the highest intervention level adopted in US states, defined as a Policy Stringency of 95% or more relative to the maximum NPI stringency level, as measured by the Oxford COVID-19 NPI policy database (112 days).[44] We compute a mean square error distance function, equally weighing the deaths and the days under maximum intervention level, and searched the parameter space of $\tau \in (0.1, 0.18)$ and $d \in (5, 25)$ to minimize that distance function. In this calibration exercise, τ =0.142, and d =17.8, which are plausible values, and were not a corner solution within the range we specified for the parameter search.

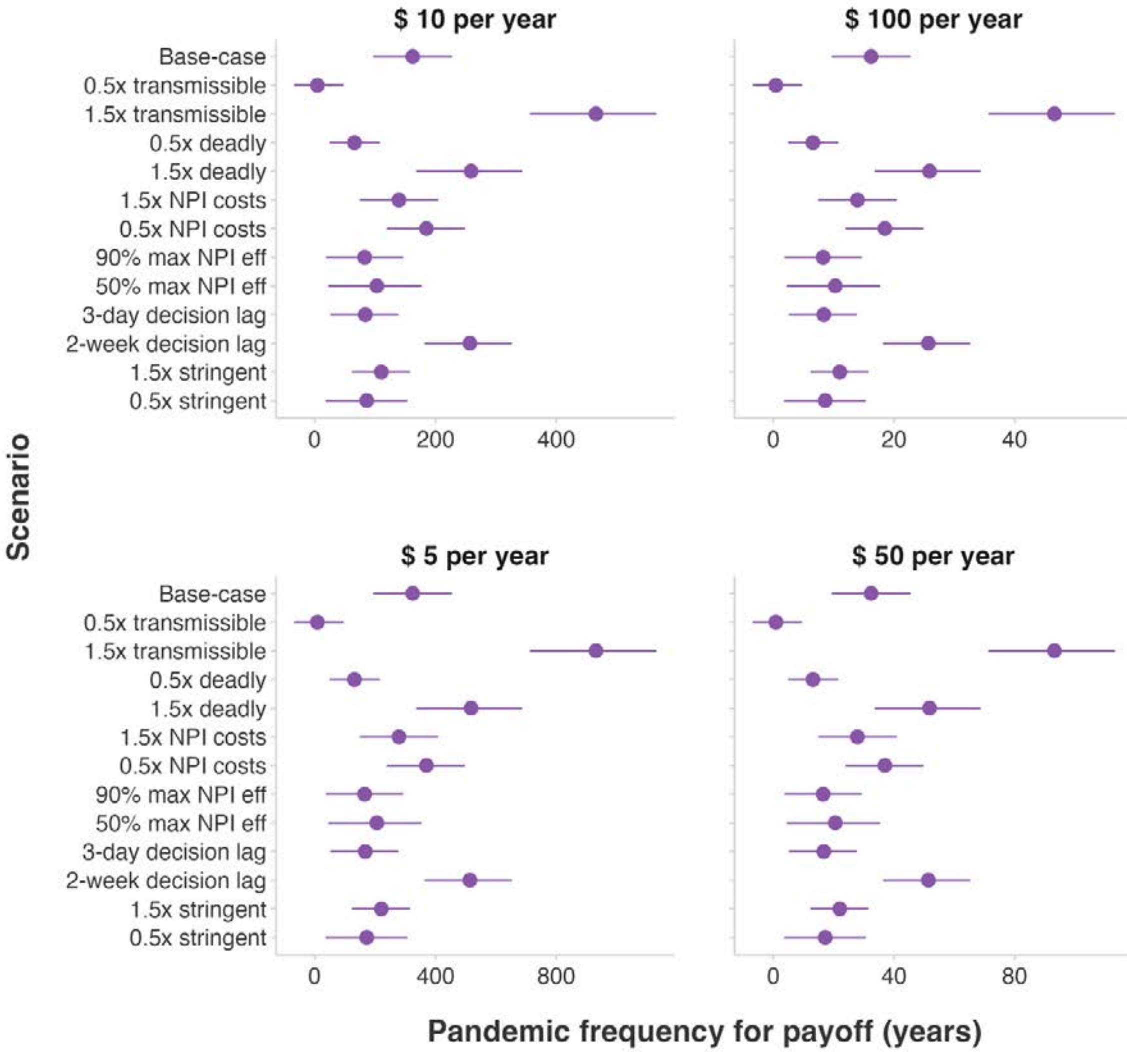
Appendix B. Supplementary Figures and Tables

Supplementary Figure 1. Value of ESS System Under Alternative Scenarios



Notes: Dots represent the average value of each outcome across 1,000 replications, and 95% of the stochastic replications fall within the range represented by lines. Purple scenarios are the ones in which a 5-day ESS is used, whereas the blue scenario represents a counterfactual scenario with conventional (i.e., syndromic) surveillance. In general, improved surveillance reduces health costs but increases NPI costs, but the net monetary benefit of the system remains above zero under most scenarios.

Supplementary Figure 2. Cost per Person vs Minimum Pandemic Frequency for Payoff



Notes: Dots represent the minimum pandemic frequency so that the system provides net monetary benefits. The average value of each outcome across 1,000 replications, and 95% of the stochastic replications fall within the range represented by lines. In general, even if SARS-Cov-2-like pandemics were to occur as infrequently as every 150 years, a system that costs less than 10 dollars per person per year would yield net-positive benefits.

Supplementary Table 1. Sensitivity Analysis Results

Scenario	EWS	Deaths per 100,000 people	Health costs	NPI costs	Total costs	Net monetary benefit
Base-case	N	149 (145-153)	18,500 (18,000-19,000)	12,900 (12,800-13,100)	31,400 (31,000-31,900)	0 (0-0)
Base-case	Y	132 (129-136)	16,400 (16,000-16,900)	13,400 (13,300-13,500)	29,800 (29,400-30,200)	1,620 (967-2,270)
0.5x transmissible	N	43.9 (41.9-45.9)	5,490 (5,260-5,720)	3,880 (3,780-3,980)	9,370 (9,090-9,650)	0 (0-0)
0.5x transmissible	Y	43.4 (41.5-45.3)	5,430 (5,200-5,650)	3,900 (3,810-3,990)	9,330 (9,040-9,610)	43.5 (-341-478)
1.5x transmissible	N	319 (308-327)	39,200 (38,000-40,200)	14,000 (13,800-14,300)	53,300 (52,300-54,100)	0 (0-0)
1.5x transmissible	Y	269 (264-275)	33,300 (32,600-33,900)	15,400 (15,300-15,500)	48,600 (48,000-49,200)	4,660 (3,560-5,660)
0.5x deadly	N	74.6 (71.9-77.2)	9,990 (9,670-10,300)	12,900 (12,800-13,100)	22,900 (22,600-23,200)	0 (0-0)
0.5x deadly	Y	66.1 (63.9-68.4)	8,880 (8,620-9,150)	13,400 (13,300-13,500)	22,300 (22,000-22,500)	657 (248-1,080)
1.5x deadly	N	224 (218-229)	27,000 (26,300-27,700)	12,900 (12,800-13,100)	39,900 (39,300-40,600)	0 (0-0)
1.5x deadly	Y	198 (194-203)	24,000 (23,400-24,500)	13,400 (13,300-13,500)	37,400 (36,800-37,900)	2,590 (1,680-3,430)
1.5x NPI costs	N	149 (145-153)	18,500 (18,000-19,000)	19,400 (19,300-19,600)	37,900 (37,400-38,400)	0 (0-0)
1.5x NPI costs	Y	132 (129-136)	16,400 (16,000-16,900)	20,100 (20,000-20,200)	36,500 (36,100-36,900)	1,390 (744-2,050)
0.5x NPI costs	N	149 (145-153)	18,500 (18,000-19,000)	6,470 (6,420-6,530)	25,000 (24,500-25,500)	0 (0-0)
0.5x NPI costs	Y	132 (129-136)	16,400 (16,000-16,900)	6,700 (6,670-6,730)	23,100 (22,700-23,600)	1,850 (1,190-2,490)
90% max NPI eff	N	120 (115-124)	14,900 (14,300-15,400)	9,970 (9,840-10,100)	24,800 (24,300-25,400)	0 (0-0)
90% max NPI eff	Y	106 (103-109)	13,200 (12,800-13,500)	10,800 (10,800-10,900)	24,000 (23,700-24,400)	826 (185-1,460)
50% max NPI eff	N	303 (297-308)	37,400 (36,800-38,000)	12,300 (12,200-12,500)	49,700 (49,200-50,300)	0 (0-0)
50% max NPI eff	Y	286 (281-291)	35,400 (34,900-36,000)	13,300 (13,200-13,400)	48,700 (48,200-49,300)	1,030 (223-1,770)
3-day decision lag	N	137 (133-140)	16,900 (16,500-17,300)	13,300 (13,200-13,400)	30,200 (29,800-30,600)	0 (0-0)
3-day decision lag	Y	128 (125-131)	15,900 (15,500-16,300)	13,500 (13,400-13,600)	29,400 (29,000-29,800)	837 (259-1,390)
2-week decision lag	N	172 (166-177)	21,300 (20,600-21,900)	12,200 (12,000-12,400)	33,500 (32,900-34,000)	0 (0-0)
2-week decision lag	Y	142 (139-146)	17,700 (17,200-18,100)	13,200 (13,200-13,300)	30,900 (30,500-31,300)	2,570 (1,820-3,260)
1.5x stringent	N	83.9 (80.6-87.1)	10,400 (10,000-10,800)	14,200 (14,100-14,300)	24,600 (24,200-25,000)	0 (0-0)
1.5x stringent	Y	72.7 (70.3-75.2)	9,020 (8,740-9,320)	14,500 (14,400-14,500)	23,500 (23,200-23,800)	1,100 (616-1,580)
0.5x stringent	N	195 (190-199)	24,100 (23,600-24,700)	12,000 (11,900-12,100)	36,200 (35,700-36,700)	0 (0-0)
0.5x stringent	Y	185 (181-189)	22,900 (22,500-23,400)	12,400 (12,300-12,500)	35,300 (34,900-35,800)	860 (178-1,530)

Notes: All outcomes are computed at the end of the first year of the pandemic. Costs are expressed as 2020 dollars per person. Epidemic size is expressed as a percent of the population. Uncertainty intervals encompass 95% of stochastic replications.

Supplementary Table 2. Baseline Parameter Values and Sources

Parameter	Description	Value	Sources
σ	Time from exposed to pre-symptomatic (latent period) [1/days]	3.3^{-1} days	12
δ	Time from pre-symptomatic to infected (incubation period – latent period) [1/days]	3.5^{-1} days	12
γ	Time from infected to removed [1/days]	7^{-1} days	12,45
ρ	Proportion of asymptomatic cases	35%	46
r_{t0}	Age-adjusted IFR at pandemic onset	0.733%[i]	40
p_{r^*}	Percent reduction in the IFR at time t_{r^*}	40%	40
t_{r^*}	Time at which IRR reaches pre-vaccine plateau (days after pandemic onset).	150[ii]	40
R_0	Basic Reproductive number	2.5	47
$VLSY$	Value of a statistical life year (2020 US dollars)	$240,676	
VSL	Value of a statistical life (millions of 2020 US dollars)	11.4	22
C_{max_npi}	Cost of the most-stringent NPI level as a fraction of GDP per capita	25%[iii]	19,41
Y	GDP per capita (used to approximate economic costs of NPIs).	$76,000	48
c_{lag}	Baseline time from symptom onset to case confirmation (days)	6[iv]	13
p	Case ascertainment rate for conventional surveillance.	30%[v]	14
τ	Incremental reduction in transmission rates per non-pharmaceutical intervention level	14.2%[vi]	calibrated
d	Incidence rate per 100,000 people (adjusted for case ascertainment rate) necessary for the introduction of nonpharmaceutical interventions	17.9	calibrated
k_h	Proportion of mixing at home	0.18	19
k_{wt}	Proportion of mixing at work and travel, which may cross county lines	0.46	19
k_o	Proportion of mixing at other modes (not crossing county lines)	0.36	19
a_{up}	Time lag (in days) to increase NPI intervention levels, which accounts for decision and implementation delays (3 minimum)	7	assumed
a_{down}	Time lag (in days) to decrease NPI intervention levels, which accounts for decision and implementation delays	14	assumed
L_{max}	Maximum intervention level	5	assumed

Notes: Parameter values reflect the COVID-19 pandemic assumptions.

[i] Age-adjusted IFR estimate at the outset of the pandemic for the United States. We use age-adjusted IFR estimates as to reflect the current population distribution, which is consistent with the use of VSL for valuing the costs of interventions.

[ii] Virtually all the 40% reduction in IFR observed during the first months of the COVID-19 pandemic in the US was observed during the first six months. IRR is assumed to evolve following at logistic function set to start at r at the beginning of the pandemic, reaches $(1-p_{r^*})r$ at time t_{r^*}, and passes at (1-0.5p_{r^*}) at time $t_{r^*}/2$.

[iii] Median of estimates for most-stringent intervention level from Welburn and Strong[41] across all US states.

[iv] Assuming case confirmation is the epidemiological indicator used for decisionmaking. A study comparing the timeliness of alternative epidemiological signals found that case data leads hospital admissions data by about one day,[49] hence the use of hospitalization data would not meaningfully change these results.

[v] Held constant throughout the simulation. Although the case ascertainment rate is not constant, it has been estimated between 20% and 40% throughout the pandemic in the United States.[14]

[vi] See the calibration section. The calibrated middle point is also consistent with the middle range of a literature review that found the effectiveness of the most-stringent NPIS in the US to be in the 70%-80% range.[50]

Abbreviations

CDC	Centers for Disease Control and Prevention
COVID-19	coronavirus disease 2019
ESS	environmental sampling surveillance
NMB	net monetary benefit
NPI	nonpharmaceutical intervention
RNA	ribonucleic acid
SARS-Cov-2	virus that causes the coronavirus disease 2019
WBS	wastewater-based surveillance

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