Economic optimization of a global strategy to address the pandemic threat

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Emerging pandemics threaten global health and economies and are increasing in frequency. Globally coordinated strategies to combat pandemics, similar to current strategies that address climate change, are largely adaptive, in that they attempt to reduce the impact of a pathogen after it has emerged. However, like climate change, mitigation strategies have been developed that include programs to reduce the underlying drivers of pandemics, particularly animal-to-human disease transmission. Here, we use real options economic modeling of current globally coordinated adaptation strategies for pandemic prevention. We show that they would be optimally implemented within 27 y to reduce the annual rise of emerging infectious disease events by 50% at an estimated one-time cost of approximately $343.7 billion. We then analyze World Bank data on multilateral "One Health" pandemic mitigation programs. We find that, because most pandemics have animal origins, mitigation is a more cost-effective policy than business-as-usual adaptation programs, saving between $344.0.7 billion and $360.3 billion over the next 100 y if implemented today. We conclude that globally coordinated pandemic prevention policies need to be enacted urgently to be optimally effective and that strategies to mitigate pandemics by reducing the impact of their underlying drivers are likely to be more effective than business as usual.

emerging infectious diseases | One Health | adaptation | mitigation | climate change

Pandemics of emerging infectious diseases (EIDs) are a major challenge to global health and economies (1, 2). Even in the absence of significant global mortality, pandemics can cost tens of billions of dollars when an emerging pathogen enters human travel networks (3). Estimates of the economic cost of an influenza pandemic range from $374 billion (in 2014 US$) for a mild pandemic (4) to $7.3 trillion for a severe pandemic with 12.6% loss of gross domestic product (GDP) and 142 million deaths extrapolated globally (5). Pandemics usually begin as outbreaks of EIDs caused by animal pathogens that spill over into people in conditions of increased contact through demographic or environmental changes (6, 7). When EIDs possess, or evolve, the ability to be transmitted among people and then spread through populations over large geographic regions, they are classed as pandemics. Analysis of global data on EIDs shows that pandemic risk is rising over time. Specifically, the frequency of EID events (the first emergence of a new disease or the point at which a known disease increases in incidence to become emerging) has increased significantly over the last five decades, after accounting for observer bias (8). This is likely a product of increasing pressure from the underlying socioeconomic and environmental factors (human population growth, land use change, international trade, and others) that cause them to emerge. It follows that, under business-as-usual policies, the economic damages that EIDs cause will rise exponentially in the future, given increasing economic reliance on international connectivity through travel and trade networks and the exploitation of these networks by emerging pathogens (2, 4, 9).

The underlying dynamics and our global response to pandemic emergence have many similarities to the problems associated with climate change. First, the underlying drivers of pandemics, like the rise in CO_2 levels, are increasing in a nonlinear fashion. Second, both climate change and pandemic emergence are a global commons problem, with both inflicting global damages (4, 10) and requiring globally coordinated policies for effective control (11–13). Finally, policies to address both phenomena suffer from geopolitical constraints and debate over adaptation (technological solutions after the fact) vs. mitigation (reduction of the underlying causes). For pandemic emergence, we consider adaptation policies as those that aim to reduce the impact of diseases after they have emerged and mitigation policies as those that aim to reduce underlying drivers of disease emergence and the frequency that new EIDs emerge. Most current (business-as-usual) pandemic control programs are adaptive and include programs that increase the capacity and speed of outbreak investigation and reporting (14), that set up emergency control measures such as social distancing and travel restrictions (9), or that stockpile drugs and vaccines (12).

Strategies have been developed to mitigate the pandemic threat by reducing the underlying causes (drivers) of disease emergence. In most cases, these are socioeconomic and demographic factors that alter transmission dynamics, evolution, and spread of microbes within and among animal and human populations (2, 8, 15). Pandemic mitigation programs include those that foster multisectoral collaboration among governmental or intergovernmental agencies for health, environment, and agriculture (the "one health" approach) (16); that conduct targeted pathogen discovery in wildlife, coupled with international

Significance

Emerging pandemics are increasing in frequency, threatening global health and economic growth. Global strategies to thwart pandemics can be classed as adaptive (reducing impact after a disease emerges) or mitigation (reducing the causes of pandemics). Our economic analysis shows that the optimal time to implement a globally coordinated adaptive policy is within 27 y and that given geopolitical challenges around pandemic control, these should be implemented urgently. Furthermore, we find that mitigation policies, those aimed at reducing the likelihood of an emerging disease originating, are more cost effective, saving between $344.0 billion and $360.8 billion over the next 100 y if implemented today.

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development programs to address underlying socioeconomic drivers (17, 18) and promote behavioral change in at-risk populations (7, 18); and that increase farm biosecurity to reduce the risk of novel zoonoses originating in wildlife or livestock, particularly in EID hotspot countries (14, 19).

In this paper, we model the economic damages associated with increasing frequency of disease emergence. We use real options modeling and data from prior pandemics and disease control programs to identify the optimal timing for implementation of global "business-as-usual" adaptive strategies to contain pandemic risk. We then use data from a Food and Agriculture Organization–World Health Organization–World Organization for Animal Health (FAO–WHO–OIE)–World Bank pandemic prevention program to examine whether mitigation strategies that curtail the underlying drivers of animal-origin EIDs are more cost effective in the long-term.

Methods

We used real options economic modeling (20) to analyze the optimal timing for implementation of a globally coordinated adaptive strategy to address the pandemic threat (*SI Text*). We analyzed the temporal pattern of EID events over the past six decades from ref. 8 and found the rise in EID events is nonlinear (Fig. S1). We calculated that, under business-as-usual policies, EID events will continue to increase by 5.371/y (*SI Methods*). We assumed that the nonlinear increase in the frequency of EID events will correlate with increased net damages to the global economy. This assumption reflects the expectation that underlying drivers of EIDs will continue to rise nonlinearly—e.g., population growth, agricultural intensification, and international connectivity of travel and trade (2, 4, 9). We calculated the present value to society of accrued damages under business as usual based on GDP losses in 2003 for Hong Kong, Singapore, Taiwan, and Vietnam due to pandemic severe acute respiratory syndrome (SARS) as detailed in *SI Methods*. We compared this to the present value of accrued damages following the implementation of a program of action that slows the rise in EIDs and reduces expected damages accrued in the future. This comparison includes the value of being able to wait and deploy a policy optimally in the future, which may lower the present value of damages to society following business as usual. It also includes the cost of the policy, which adds to the present value of accrued damages following the implementation of the policy (Fig. 1). We estimated costs of a business-as-usual policy to combat pandemics, using budgetary data from relevant US government agencies, which we extrapolated globally (Table S1).

To analyze the cost and optimal timeline required for an effective pandemic mitigation policy, we considered only zoonoses (diseases transmitted from animals to humans), which represent the majority (67%) of EIDs (8) and are responsible for almost all recent global pandemics (e.g., HIV/AIDS, SARS, and H1N1 influenza) (7, 21). We used published raw data from ref. 8 to estimate the rise in zoonotic EIDs over time (which is 3.2 annually) and the associated SD, over the same period (*SI Methods*). We estimated costs of an extensive avian influenza mitigation strategy proposed by FAO, OIE, WHO, the World Bank, and others [The "One World–One Health" strategic framework (19)], expanded to all zoonoses by the World Bank (22), and extrapolated these globally (*SI Methods*). This strategy targets the interfaces among animals and humans within different ecosystems. It employs different disciplines among different sectors to develop control and prevention measures, including building infrastructure for surveillance and diagnostics that would prevent novel emerging diseases in general. The strategy employs scenarios that assume low or high prevalence of diseases as a basis for development of preventive measures (22). We used baseline zoonotic damages from ref. 22 and our earlier estimates of expected damages associated with zoonotic pandemics (*SI Methods*) to examine how effective the low prevalence and high prevalence policy scenarios must be to implement today ($t^* = 0$). We assumed that the rate of emergence of novel pathogens will not be constrained by the size of the microbial pool in wildlife and livestock from which pandemics predominantly originate (7, 8, 23).

Results

Adaptation Policy. We considered four hypothetical policies for pandemic adaptation: Option "A" increases the current policy spending by a factor of 1.1 ($75.6 billion), option "B" targets increases the current policy spending by a factor of 2.5 ($171.9 billion), option "C" increases the current policy spending by a factor of 5 ($343.7 billion), and option "D" increases the current policy spending by a factor of 10 ($687.5 billion). We assumed that option A would reduce EID events by 10%, option B by 20%, option C by 50%, and option D by 75% to (m_2). The estimated costs (K), and estimates or assigned values for $\beta, \gamma, m_1, s_1, m_2, s_2$, and δ, are given in Table S2. We parameterized the model, using data from a series of recent outbreaks and analyses of global trends in disease emergence (Table S2). We used the published raw data from ref. 8 to estimate the rise in EIDs over time (drift rate) and associated SD (*SI Methods* and Fig. S1).

The four increasingly effective policy options reduce mean drift rate of EID events by 10%, 20%, 50%, and 75% to m_2 = 4.8839, 4.0282, 2.6855, and 1.3427, respectively, with corresponding increases in cost (K). Our model results show that as the targeted reduction in mean drift rate increases, the critical EID number I^* and the expected time to reach that value both increase. Intuitively, as the expected time to reach that value increases, damages increase, resulting in the policy becoming more effective by reducing the rate of increasing EIDs. As t^* grows, more EIDs are added to the total number of EIDs analyzed, and damage associated with this increase grows at a faster rate because damages increase at an increasing rate.

To illustrate the value each policy can generate, we ran 1,000 stochastic simulations of the damage-generating process given by our data and compared the optimal choices and total values from following the optimal decision rule for each of our four policies (*SI Methods*). Following ref. 20, 1,000 sample paths were generated by taking a time path of 1 y over the time period 2014–2074 and then calculating a trajectory for EID events, I, using the equation

$$I_t = I_{t-1} + 5.37111 + 3.627\varepsilon_t,$$

where 5.371 is the drift rate (m_1), 3.627 is the SD (s_1), and 394 is the initial I. ϵ_t is drawn from a normal distribution with mean

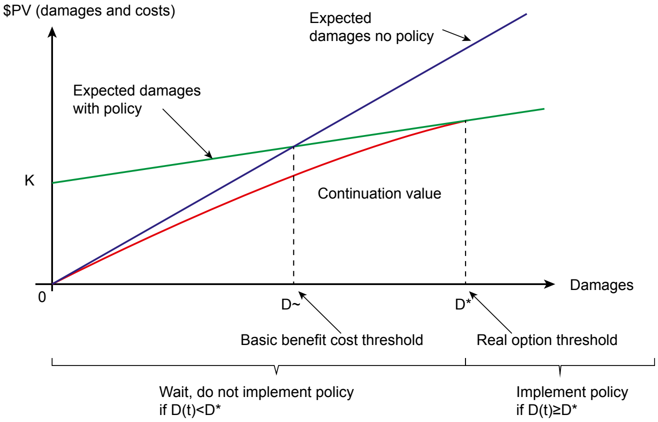

Fig. 1. Real options model. Shown is the structure of our real options model to enable optimal timing of business-as-usual global adaptive policy to reduce the rise in frequency of emerging infectious diseases (EIDs). The *y* axis represents the net present value of the expected damages of an EID outbreak plus the cost, *K*, of a policy if implemented. The *x* axis represents expected damages/time. The blue line represents expected damages following business as usual and the value of waiting is not considered. The green line represents the evolution of EID damages if a policy with cost, *K*, is implemented. If the value of waiting is ignored, *D*~ is the threshold at which a policy should be implemented. The red line, known as the "continuation value," illustrates the expected damages under business as usual, including the value of waiting. The decision model simply takes the currently experienced damage, a point on the *x* axis, and determines which of the three lines is lowest (has lowest expected present damages and costs). For damages less than *D** it is optimal to "continue" to wait. For all damages above *D** it is optimal to implement the policy. *D** is the optimal threshold. Full model development and simulations from the parameterized model are in *SI Text*.

Table 1. Adaptation policy results

Variable	Policy option A: $m_2 = 4.83$, K = \$75.6 billion	Policy option B: $m_2 = 4.03$, K = \$171.9 billion	Policy option C: $m_2 = 2.69$, K = \$343.7 billion	Policy option D: $m_2 = 1.34$, K = \$687.5 billion
D^*	\$26.7 billion	\$29.5 billion	\$38.2 billion	\$62.4 billion
I^*	475.2	492.2	536.7	621.75
t^*	15	18	27	42
E^*	\$812.7	\$759.1	\$726.0	\$753.2

Shown are D^*, critical damage level; I^*, EID events trigger; t^*, expected first-passage time; and E^*, expected net present cost, for the basic policy option (the expected net present value of damages plus the costs of the policies, where all policies are discounted back to 2014 dollars). Note that $\beta = 16.7$, $\gamma = 0.0057$, $m_1 = 5.371$, $s_1 = s_2 = 3.673$, and $\delta = 0.05$. E^* is averaged across 1,000 simulations.

zero and SD of one. The three trajectories of EID events were then used, along with baseline damages, the gamma parameter (Table S2), and the discount rate, to determine the evolution of expected conditional damages (Fig. S2).

For each of the 1,000 simulated expected damages (D), and for each of the four policies, we generated estimates of the threshold damages (D^*) (Fig. S3), below which it is optimal not to implement the program of action and above which it is optimal to implement the program (Table 1). We then calculated the critical number of EID events at which to implement a policy, I^*, and the expected first passage time, t^* (Table 1). We find that associated damages rise at an increasing rate relative to the rise in EID events. These simulations, coupled with the critical damage level to implement a policy (D^*), can then be used to determine the net present value of expected damages E^*, which includes the expected damages D and the costs of the policies, K. The average of the 1,000 simulations resulted in policy option C being the most valuable (i.e., the lowest E^*) (Table 1).

Expected net present cost E^*, which includes the "option value" (20), decreases as the policies become more effective except for the extremely effective policy, D, $m_2 = 1.34$ (Fig. S2 and Table 1). Thus, as damages increase due to an increase in EIDs, the policy becomes more valuable because of its potential to reduce expected discounted damages. However, for the most costly policy (D, where $m_2 = 1.34$), the net value of having a policy declines. Our results suggest that across the given options for globally coordinated adaptive policies, the best alternative is option C, which reduces mean drift rate of EID events by 50% and provides the lowest expected net present costs. With a more effective policy, the value of reducing discounted expected damages begins to decline due to the high cost of the extremely effective policy (Fig. S4).

For any of the policies, an increase in efficacy is defined as a larger decrease in drift rate (m_2) after the policy is implemented. Across the policies analyzed, more expensive policies are assumed to be effective. The influence of all parameters on the critical thresholds for specific policies is examined in *SI Methods*. For example, considering policy C, a less effective policy (higher drift after the policy is implemented) results in the critical thresholds for EIDs and passage time to implement the policy increasing at an increasing rate (Fig. S5). The implications are that as a policy becomes more effective (holding costs of the policy constant), the policy should be implemented at a lower critical EID threshold, which in the framework is at an earlier point in time.

Mitigation Policy. We examined the benefit of implementing the mitigation policy today by comparing damages from business as usual with damages if mitigation policies were implemented today (*SI Methods*). We find an average savings of \$344.0 billion for the low prevalence policy and an average savings of \$360.3 billion for the high prevalence policy (Table 2). The difference in savings between the two policies is \$16.3 billion. The difference in policy costs is only \$1.5 billion, illustrating increasing (10-fold) returns on the cost of the policy. For the low prevalence adaptive policy, the implementation of the policy must result in a 9.9% reduction in drift rate, resulting in a drift rate of 2.92 to justify implementation today. For the high prevalence policy, the implementation of the policy must result in a 10.5% reduction in drift rate, resulting in a drift rate of 2.90 to justify implementation today. Thus, mitigation policies need to be only minimally effective in reducing EID risk to be worth implementing (i.e., more cost effective than business as usual), with a difference of only 0.2% between m_2 and m_3 (Table 2).

Discussion

Our analysis uses prior work on global trends in emerging diseases to enumerate the nonlinear rise in pandemic risk and the likely exponential growth in their economic impacts in the future. Pandemic prevention, like climate change control policies (24), therefore has an optimal time during which an effective global response to the rise in EIDs can be mounted before damages rise beyond control capacity. Our analysis illustrates that the window of opportunity to deal with pandemics as a global community is within the next 27 y. Pandemic prevention therefore should be a critical health policy issue for the current generation of scientists and policymakers to address. Recent developments suggest that the timeframe is more urgent. The efficacy and rapidity of recent efforts to reduce pandemic impacts (e.g., influenza emergence) have been hindered by geopolitical constraints (25) and problems of sample ownership and intellectual property rights (26). Recently, new policies have been adopted to improve pandemic preparedness, including expansion of the International Health Regulations (IHR), a globally coordinated reporting mechanism (13), and transboundary or multilateral outbreak response mechanisms (27). However, mutually agreed IHR targets have been achieved in less than 30% of countries that have adopted the IHR (28), so that the timeframe for implementation of this

Table 2. Mitigation policy results and savings from the policy

Variable	Low prevalence policy: $m_2 = 2.92$, K = \$37.4 billion	High prevalence policy: $m_2 = 2.90$, K = \$38.9 billion
D^*	\$6.9 billion	\$6.9 billion
Z^*	237.3	237.3
t^*	0	0
Present value damages	\$1,189.9 billion	\$1,173.5 billion
Savings from policy	\$344.0 billion	\$360.3 billion

Shown are D^*, critical damage level; Z^*, zoonoses events trigger; and t^*, expected first-passage time, for the low prevalence policy and the high prevalence policy (the expected net present value of damages plus the costs of the policies, where all policies are discounted back to 2014 dollars). Note that $\beta = 6.9$ billion, $\gamma = 0.0124$, $m_1 = 3.206$, $s_1 = s_2 = 2.6$, and $\delta = 0.05$.

and other measures, e.g., the Global Health Security Agenda (29), is likely to be far more urgent. Furthermore, although our approach is similar to those used to optimize global strategies for adaptation to climate change (24), the timeline to execute adaptive responses to the rise in EID events is shorter because the largest impacts of climate change are likely to occur after 2100 (30), whereas significant impacts from pandemics have already been reported (3).

Our analysis of mitigation policies suggests that, for both low prevalence and high prevalence zoonotic EID scenarios, mitigation will be more cost effective in reducing pandemic risk than adaptation to the rise in EID events. Furthermore, mitigation strategies need to be enacted immediately to be optimally effective. Their efficacy is likely heightened because pandemics tend to be zoonotic and zoonoses are increasing as a proportion of all EID events (8) and because programs targeting zoonoses are less expensive to enact than those targeting all classes of EIDs. Like climate change (11, 31), efforts to mitigate the pandemic threat will be expensive, but more cost effective in the long-term than business as usual. Multilateral efforts to mitigate pandemics have already begun. They include so-called one health approaches that focus on reducing contact with animal reservoirs in highly populous regions (19) and targeting farm biosecurity for avian flu and other pathogens (16). They also include development initiatives such as the United States Agency for International Development Emerging Pandemic Threats (USAID-EPT) program, which conducts pathogen discovery in wildlife to identify potential future zoonoses in EID hotspot countries before they emerge, and behavioral change efforts to reduce human contact with these animal reservoirs (7).

There are limitations to the current study that could be addressed by further targeted research. First, the economic damages associated with emerging diseases have been well studied only for a small number of outbreaks. Work that analyzes the individual health costs of patients and the secondary impacts on trade and travel for a range of different-sized EID events would help parameterize models better. Second, our assumptions on costs of adaptive policies globally are based on US spending on surveillance and control for infectious disease outbreaks extrapolated globally, corrected for national GDP. Country-specific data on healthcare spending and the specific portion of that spent on infectious disease control would be invaluable to better parameterize these analyses. Third, studies on the efficacy of mitigation programs in reducing the rate of disease emergence and the thresholds at which their costs outweigh their benefits would be invaluable. The uncertainty in magnitude and timing of EIDs and problems in tracking success of a policy that results in no outbreak need to be overcome.

Despite these challenges, our findings illustrate the urgency with which global initiatives that mitigate disease emergence need to be launched for optimal impact via the significant savings that we find from implementation sooner rather than later. Currently, mitigation programs tend to be funded through national public health measures, international development aid, or national commitments to intergovernmental agencies. Other approaches have begun to examine reducing the risk of disease emergence in agricultural and industrial sectors previously associated with EID emergence (e.g., large agricultural developments; livestock exports; timber, mining, and other extractive industries; and travel and trade). However, the issue of who should pay for these has not yet been dealt with, and some have called for taxes to be levied on these industries (32). Given the high value of the public good of mitigation programs, we propose that international development programs could partner with industry to fund infrastructure (diagnostic clinics, surveillance programs, food supply chains to reduce bushmeat hunting, etc.) around these activities that would help reduce risk of disease emergence. These programs could also promote alternatives to high-risk activities by counting the full cost of pandemic emergence in health impact assessments (e.g., for mines, dams, and other large infrastructure) or through carbon-trading platforms (e.g., for logging and land use change activities). Such approaches may gain more traction by promoting cleaner and greener economic growth and act as a new way to ensure against a growing pandemic threat. Finally, pandemics predominantly originate in low-income tropical countries (8), but once pathogens enter global travel and trade networks, they can have far higher economic impacts on high-income countries (33). Geographical allocation of global resources from high-income countries to pandemic mitigation programs in the most high-risk EID hotspot countries should be an urgent priority for global health security and supports a strong role for international development agencies in pandemic prevention.

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