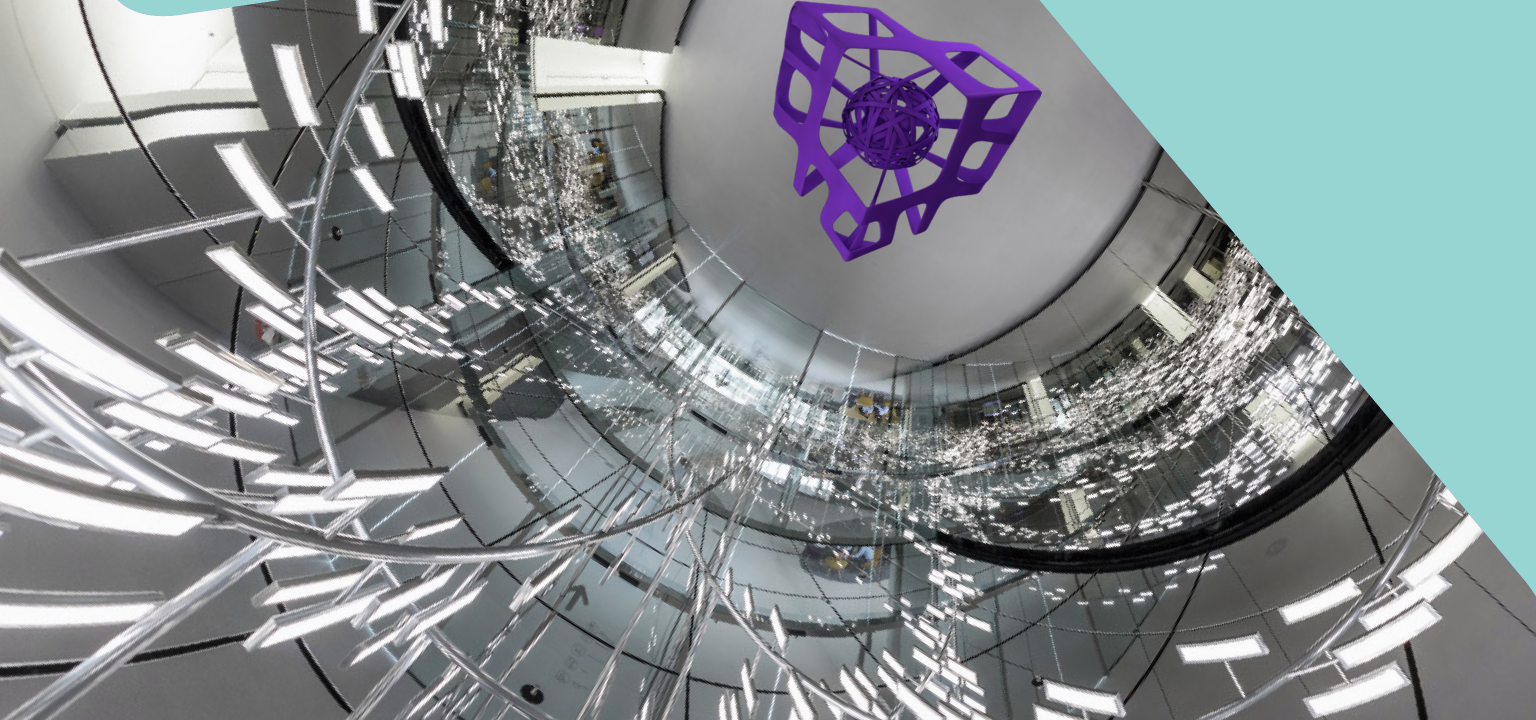
PANDEMIC RESPONSE

SUPERMIND REPORT

The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.



MilliporeSigma

MIT CENTER FOR COLLECTIVE INTELLIGENCE

community biotechnology

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INTRODUCTION

The MIT Center for Collective Intelligence, Community Biotechnology Initiative at MIT Media Lab, and MilliporeSigma convened more than 180 experts and global leaders in science, healthcare, public policy, and other sectors for a three-week exercise to address the following challenge:

How can we develop pandemic resilience—the ability for society to recover quickly from global disease outbreaks—both in resolving the current COVID-19 pandemic and in building the public health and other infrastructure to prepare for future pandemics?

We activated our expert group—or ‘Supermind’, “a powerful combination of many individual minds” (Laubacher et al., 2020)—to share their ideas on how to address this challenge in five domain areas: (1) diagnostics and monitoring; (2) viral transmission control; (3) therapies and vaccines; (4) validating, sharing, and communicating scientific insights; and (5) pandemic preparedness.

Our experts submitted more than 200 contributions—ideas that covered a wide spectrum of topics, from identifying emerging, disruptive technologies to suggesting new modes of global, cross-sector collaboration that could strengthen healthcare systems. Using facilitated dialogue and natural language processing, and with an emphasis on impact and feasibility, we clustered these contributions into emergent, actionable themes, several of which we have highlighted within the document.

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Executive Summary

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Early warning signs of disease spread can be found in sewers, genomes, voices, internet searches, and other digital health breadcrumbs.

Robust and reliable monitoring of infectious disease can provide the advance warning necessary to control and prevent outbreaks. The Supermind identified several surveillance methodologies that can provide the timely information needed to save lives. Analyzing the genomic content from our sewer systems can provide as much as a seven-day leading indicator of disease spread. Studying sewage from planes, trains, and other transportation could signal the need for passenger testing and tracing. A widespread sewage monitoring program could help establish a critically needed population baseline to help us identify new pathogen threats. Genomic epidemiology can help detect the emergence of viral variants that may be evading population herd immunity to motivate the development of new treatments and vaccines. Phylogenetic network analysis of viral genomes could help identify unreported cases in a population. Voice acoustics change when disease impacts respiratory function, so smartphones could be potential COVID-19 respiratory monitoring tools. A host of digital breadcrumbs—from internet searches to networked digital thermometers and device data from wearables—could be integrated into systemic "disease forecasting" approaches to detect community spread days or even weeks early.

Digital contact tracing with privacy protections could suppress the pandemic.

Our mobile phones could contain the data necessary to trace and rapidly identify the contacts of infected individuals so they can isolate themselves from the population, halting spread of the disease. If every adult carried a device with digital contact tracing enabled, such an approach, combined with cutting edge privacy protections, could single-handedly control the pandemic without mass lockdowns or masks. The Supermind proposed several ways to enhance the impact and adoption of digital contact tracing. Data standards could be implemented to create interoperable, privacy focused contact tracing applications that share community data and update in real time. Tracing could be done "bi-directionally"—notifying both people who were recently exposed, along with the infected individuals—which, when done with digital exposure notification, could triple the probability of controlling outbreaks relative to current practice. Giving phones to every adult could not only increase the efficacy of digital contact tracing, but would also help bridge the digital divide for low income communities.

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Accelerate therapy and vaccine clinical trials.

The COVID-19 pandemic will ultimately be controlled with effective therapies and vaccines. Research suggests that only 10% of drugs make it to market after an arduous trial process which often takes decades (Bio, Biomedtracker, and Amplion, 2016). The experts proposed ways to accelerate clinical trials through global, harmonized protocols. Competitive barriers can be removed when possible to encourage the broad sharing of antiviral and vaccine candidate clinical trial data. Data standards should be unified to facilitate cross-institutional agreements. New safety testing methods could be conducted, for example using proteomics to detect warning signs of adverse immune responses, potentially markedly reducing the duration of clinical trials.

Create resilient supply chains.

Manufacturing and supply chains matter. From personal protective equipment (PPE) to diagnostic tests, therapies, and vaccines, our ability to stockpile and rapidly produce the necessary materials, ingredients, and reagents is essential for resilience. Our experts emphasized employing decentralized manufacturing modalities and creating regional and local production hubs for stockpiling and emergency production. Critical materials should have manufacturing redundancy with multiple factories. In the event of emergency, flexible manufacturing is necessary: plans and standards should be in place to pivot production lines or re-purpose existing factories.

Include and empower marginalized and vulnerable communities.

Marginalized communities—including ethnic minorities like African Americans, Latinx, American Indians, immigrant workers, and other indigenous groups—are not only disproportionately impacted by the pandemic, but have also historically been under-represented in pharmaceutical clinical trials and benefited least from translational research. These systemic problems require systemic solutions. The Supermind proposed building equity considerations into all pandemic research funding and implementation and ensuring representation from these communities in randomized clinical trials (RCTs). Community mobilization and education should be participatory at the grass-roots level and involve engagement with trusted local leaders. Effective implementation of policies and programs, like contact tracing, should be done collaboratively and with respect to cultural perspectives and communal needs and priorities. Communication strategies need to be community specific and foster equitable discussions amongst healthcare, governmental, and other stakeholders, taking into account language and accessibility needs.

Build better behaviors.

Non-pharmaceutical interventions can save lives and can, in lieu of an effective therapy or vaccine, control the pandemic. Our experts proposed ideas to change public behavior, like encouraging mask adoption by partnering with fashion forward designers and influencers to make mask-wearing culturally normative. Education programs could be deployed to teach the public basic sterile techniques regarding PPE like masks and gloves. Campaigns to address major risk factors for COVID-19, like obesity, should be launched. Technologies should be developed to encourage good hygiene, like preventing face-touching and avoiding contact with commonly shared surfaces. Social scientists, psychologists, and cultural anthropologists should be mobilized to help shape messages and interventions in ways that people will hear, trust, and follow.

Build trust and dispel fear.

Controlling outbreaks requires trust at multiple levels—among the public, government, public health experts, scientists, and other stakeholders. Successfully empowering the public with trustworthy, accurate, and scientifically validated information can help dispel fear and promote the social cohesion and actions necessary to control the pandemic. Our experts proposed myriad strategies for building trust amongst stakeholders. Participatory research methods could be used to incorporate the perspectives, needs, and concerns of community members. Multi-generational engagement could be fostered by empowering communal youth networks for outreach and distribution of information and services. Concerted efforts should be made to develop reliable, continuous communication methods with vulnerable communities that may, for example, have accessibility issues like poor access to internet or smartphones. National and global institutions that can communicate scientific facts, guidance, and advice should be established or reformed. Scholarly articles could include plain language summaries for the public. Visual designers could collaborate closely with researchers to help demystify scientific findings. Public health officials should have platforms to regularly engage with the public and help manage expectations.

We will expand upon and explore these themes in greater depth throughout this report.

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Laubacher, R., Giacomelli, G. Kennedy, K., Kong, D.S., Bachmann, A., Kramer, K., Schlag, P., & Malone, T. (2020). *Using a supermind to design a supermind: A case study of university researchers and corporate executives co-designing an innovative healthcare concept.* https://cci.mit.edu/wp-content/uploads/2020/04/Using-a-supermind-to-design-a-supermind-A-case-study-of-university-researchers-and-corporate-executives-co-designing-an-innovative-healthcare-concept.pdf.

Appendix 1: Methodology

The Pandemic Response Supermind was activated as a crowdsourcing platform for collective thinking, created as an enabler to help identify critical, unmet needs to address COVID-19 and future pandemics. The platform engaged participants online over a three-week period, allowing a diverse and geographically separated group to work together conveniently, cost-effectively, efficiently, and rapidly.

By bridging specialties, disciplines, industries, and geographic boundaries with technology, the Pandemic Response Supermind Activation aimed to deliver deeper insights and more useful and trusted information to contribute to the current and future role of life sciences in pandemic resilience.

The process used natural language processing (NLP), in addition to facilitated dialogue, to identify themes in experts' contributions. These themes informed questions and prompts throughout the process, ensuring there were not any gaps during the three-week discussion and discovery period.

Week 1: Experts were asked to submit contributions in their domain areas, i.e., areas in which they were most comfortable. Even if a participant brought a perspective that was outside of the life sciences (say for example they were a tech writer), they were asked to weigh in on areas that they might know more about from the news, life experiences, or how their field could intersect or inform the domain.

Week 2: Members of the Supermind were then asked to submit contributions outside of their domain areas. They were prompted to think creatively, and suggest ideas that were outside of the box. The hope was that this would expand the breadth of ideas and push the boundaries of domain bias.

Throughout the process, participants were asked to like and comment on others' contributions to highlight areas of opportunity or signify their support.

Week 3: Participants had the ability to vote on groups of contributions created by clustering the ideas generated in weeks 1 and 2. Prior to the start of week 3, the contributions created during weeks 1 and 2 were clustered into groups. This was done by first using natural language process (NLP). The results of the NLP analysis were then reviewed by members of the CBI/CCI staff and a scientific advisory committee from MilliporeSigma, and 15 meta topics or categorizations were parsed out using two NLP methodologies: 1) topic modeling, and 2) word to vector (word-2-vec). Topic modeling looks at the frequency of words and phrases used, and clusters according to semantic patterns. Word-2-vec takes a large corpus of text, and by noting which words occur close together, is able to represent each word as multi-dimensional vectors. It can take new strings of text and assign them a position in the multi-dimensional space. Text strings can then be clustered with like groups based on their proximity. By doing an initial pass with topic modeling and then comparing this result with word-2-vec, we were able to get our final 15 groups of contributions. The advisory committee then created a description and title for each of these clusters.

The Supermind participants voted on which clusters they believe would have the most impact in building pandemic resilience, both in resolving the current COVID-19 pandemic and in building public health and other infrastructure to prepare for future pandemics.

Throughout the process, we also created social network graphs, which looked at participants by their sector and analyzed what contributions they were commenting on and liking. An interesting insight from this analysis was that participants were liking and commenting on not only contributions within their sector, but also contributions outside their own. Thus, there was significant cross-pollination between sectors.

Appendix 2: Pandemic Response Supermind Activation by the numbers

Total Contributions: 243
Total Supports (Likes): 413
Total Comments: 152
Total Votes: 1,267

Participants by sector

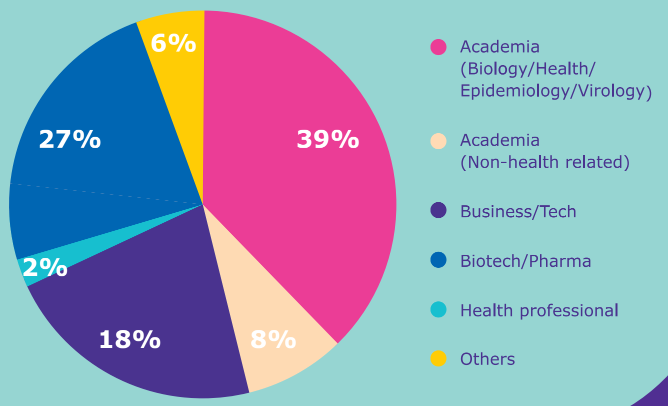


Figure 1:
Participants by sector

Most impactful & feasible groups of contributions for present pandemic

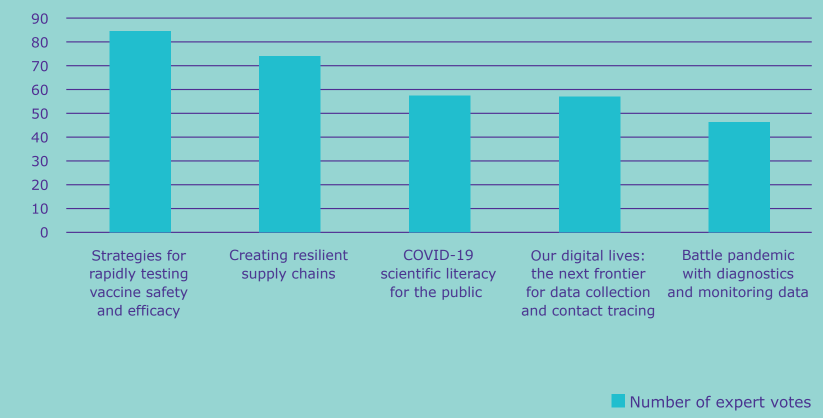


Figure 3:
Most impactful & feasible groups of contributions for the present pandemic

Most impactful & feasible groups of contributions for future pandemic resilience

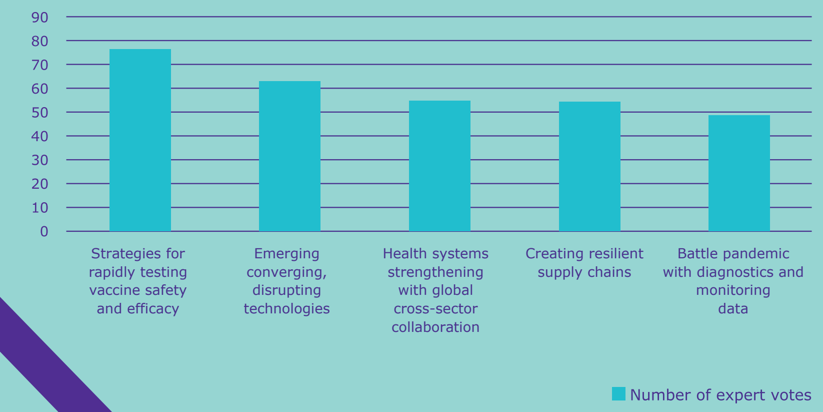


Figure 4:
Most impactful & feasible groups of contributions for future pandemic resilience

Most interacted with contributions

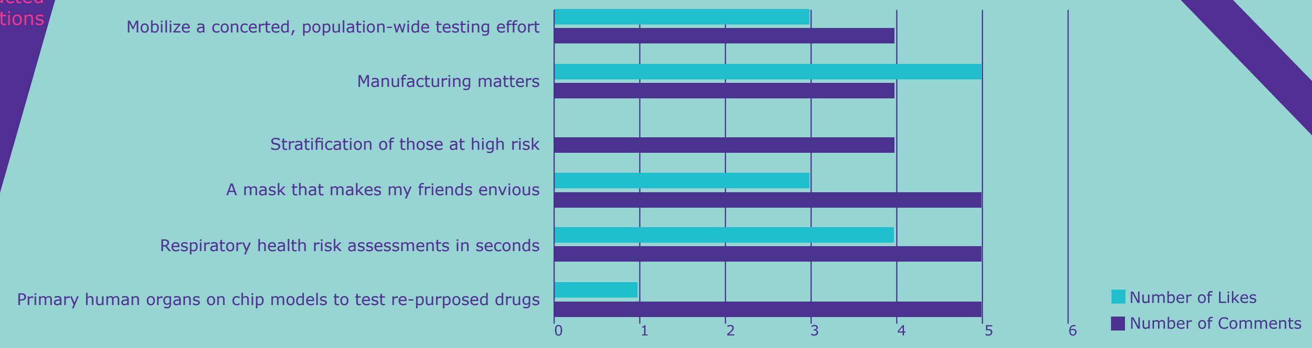
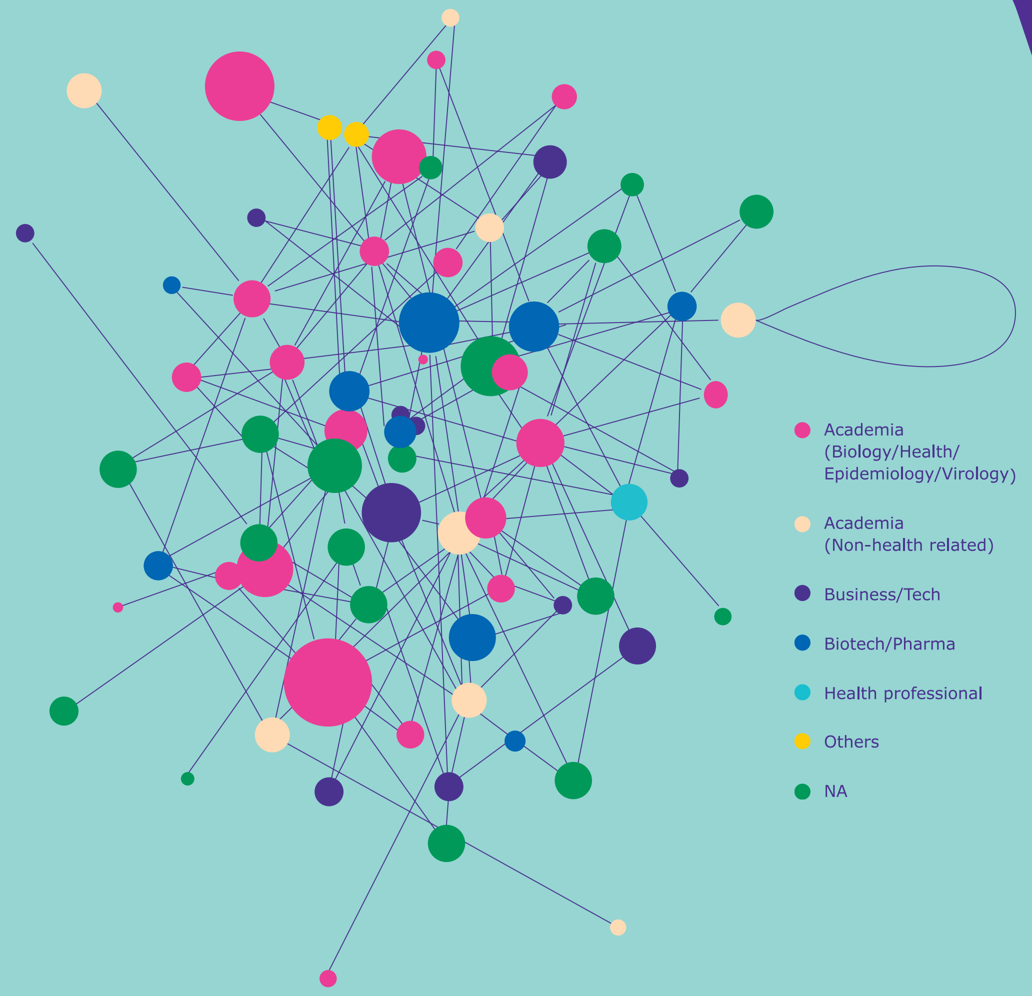


Figure 2:
Most interacted with contributions

Social network graph of likes by participants by sector



Appendix 3: Short list of institutions of the participants

- BI Lahey Health
- Boston Medical Center
- Stanford
- Brandeis University
- Institute of Natural Material Technology, TU
- Lysogene
- Wyss Institute
- University of Ghana
- MIT
- University of Iowa
- Longview Analytics
- University of Cambridge
- Takeda
- Deloitte
- Columbia University
- GenPact
- Boston Children’s Hospital
- University of California San Diego
- Tel Aviv University
- University of Melbourne
- AAFOA
- Sonde Health
- MilliporeSigma

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Viral Transmission Control

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Viral Transmission Control

Beyond the utilization of therapies and vaccines to control the spread of COVID-19, numerous other strategies for reducing and controlling viral transmission are possible. From maintaining physical distance to re-designing air flow in buildings, the employment of non-pharmaceutical interventions can effectively control the pandemic, thus providing critical, life-saving strategies that can be applied at any stage of the outbreak, but particularly before pharmaceuticals can be developed and deployed.

In this chapter, the Supermind explored numerous approaches for reducing the spread of COVID-19 without necessitating the use of pharmaceutical interventions. These strategies require, first, a deep comprehension of viral transmission dynamics; then, based on this understanding, strategies for protecting the most vulnerable populations could be designed and deployed.

Understand transmission dynamics

In order to develop effective countermeasures to reduce viral spread, first transmission dynamics need to be characterized in detail. The Supermind identified a variety of aspects of viral transmission that need to be understood, starting with the molecular dynamics of infection as compared to similar viruses, like the common cold coronaviruses, Severe Acute Respiratory Syndrome (SARS), and Middle East Respiratory Syndrome (MERS). The specific pathways of infection in the body, from the upper airways to the lungs to other mucosal membranes like the eyes, all provide insight into the likeliest modes of transmission. For example, the Supermind proposed studies to measure the particle size and concentration in exhaled breath of viral particles in COVID-19 infected patients to rigorously elucidate infectious aerosol transmission. Understanding the "infection dose," or minimum number of viral particles necessary to cause infection, is of critical importance, both for transmission via inhalation or via viral particles on surfaces (i.e., fomites).

In addition to molecular dynamics, human behavioral dynamics for viral transmission are of vital importance to elucidate. What behaviors are risky? And under what circumstances? The Supermind proposed employing large-scale survey data collection to identify dangerous behavior patterns associated with risk of infection augmented with machine learning. Individualized, highly granular data combined with automated data discovery techniques could help pinpoint what behaviors seem correlated with heightened risk of infection. Data could be generated via interviews, surveys, social media, and by scenario sharing of how, when, and where (e.g., restaurants, gyms, households, etc.) transmission occurred. This data could be maintained in a central resource and analyzed over time to stratify risk. Based upon these insights, efforts could be conducted to drive behavior change, like awareness campaigns and community accountability measures.

More targeted analyses could also be conducted, for example, in settings that are known to have higher risk, e.g., nursing and group homes and meat packing plants. Earlier in the pandemic, it was observed that 40% of COVID-19 fatalities occurred from the elderly in nursing homes (The Economist, 2020). More tailored prevention strategies could then be developed specifically for those settings and to protect the particularly vulnerable. For example, more at-risk segments of the population could be accommodated by the general public and provided additional protections, like having specific times for shopping for the elderly. Furthermore, techniques like genetic epidemiology, which has been a powerful tool in analyzing food-related outbreaks, could also be used to identify work-related infections.

The Supermind also highlighted asymptomatic transmission as a critical area of analysis. Most infections are asymptomatic (Sutton, 2020; Gudbjartsson, 2020; Li, 2020), with modeling of the epidemic in China indicating that 79% of transmissions are caused by asymptomatic individuals. The Supermind proposed executing large-scale, population-wide testing to both understand asymptomatic transmission dynamics and to enable quarantining of as many asymptomatic cases as possible. Such data could guide rational containment and mitigation policies by providing detailed information on the prevalence of the virus in geographic areas, age groups, and socioeconomic strata.

Finally, the Supermind proposed funding and supporting research programs to increase knowledge regarding the importance, dynamics, and impact of healthy ecosystems on disease transmission. As humans expand our footprint into otherwise intact ecosystems, we inherently disrupt their functionality and increase human exposure to novel viruses. Understanding the role of animals in virus transmission could provide insight on a more holistic view of human and planetary health. Both have suffered under the combined impacts of climate change and other anthropocentric pollution. Understanding the relationship between healthy, intact ecosystems and their overall impact on human health could lead to better policy recommendations that could collectively be adopted at the global level.

Address societal inequities and protect the vulnerable

The Supermind observed that the pandemic, like other health crises in the past, has laid bare the historical fault lines and inequities in our health care system and social safety net. Vulnerable populations, like the poor, who often live in high density neighborhoods, or those who have lower access to clean water and sanitation, People of Color, and minorities, are suffering disproportionately. The Supermind proposed longer term and more systemic strategies to address broader societal inequities that will not only help mitigate the impact of the pandemic and reduce viral transmission, but also protect against future system challenges, be they infectious disease outbreaks or other economic disruptions.

The Supermind proposed integrating social determinants of health into pandemic control. Social scientists could be recruited to research the social determinants of health, from housing to food security, education, and a variety of non-health factors that can significantly influence a society's ability to deal with outbreaks and control viral transmission. Lockdowns can be effective methods for protecting the upper and middle class, where options like working from home and virtual commerce are easier to adopt, but would adversely impact poor and vulnerable populations. Sustained engagement with social scientists, anthropologists, and economists early in the response can aid in crafting more nuanced strategies for reducing viral transmission.

Specific strategies for mitigating spread in vulnerable communities could include ensuring healthy food, clean water, screening, treatment, and routine care in underserved and underprivileged communities. Low-income communities could be supported with salary continuation and other economic benefits. Efforts should be made to expand affordable housing, which could help mitigate the impact of overcrowded households, where risk of exposure and viral transmission is high, a common situation for low-income service and agricultural workers. Hand-washing stations could be deployed in homeless communities, like the LarvaMaeX "Hand Washing for All" campaign (Curry, 2020). "Ghost malls," or shopping malls that are going bankrupt, could be turned into shelters for the homeless. Jails or detention centers that house large numbers of inmates who have not been sentenced or have misdemeanors could be restructured to decrease population density and reduce the risk of outbreaks.

Re-designing airflow, ventilation, and spaces

As researchers continue to study viral transmission dynamics, it has become evident that aerosol and respiratory transmission of SARS-CoV-2 is a significant modality of viral spread. Indoor spaces where people speak, sing, or shout (e.g., bars, clubs, concert halls, gyms) have been demonstrated to be high risk for viral transmission. The Supermind proposed strategies for designing improved airflow and ventilation systems, including indoor space designs that are larger and better ventilated, using filtration systems whenever possible. Furthermore, these spaces should ideally be equipped with sensors to better monitor the refresh rate of air. Portable air cleaners could be used to remove infectious aerosols, which may be an improved method for ventilation over dilution methods. While increasing ventilation rates (adding more outside air and decreasing the volume of recirculated air) is an important strategy for diluting and reducing virus concentrations, this may have limitations as the number of people increases, particularly with asymptomatic people shedding virus. Portable air cleaners could provide significant benefit (Miller-Leiden, 1996). Similarly, local exhaust ventilation strategies—removing contaminants at their source, at locations like patient beds, headboards, during patient transport, etc.—could lower healthcare worker exposure and help reduce the need for extensive PPE in healthcare settings.

Finally, pandemic-resilient building codes and vehicle standards could be employed. The Supermind proposed establishing infection control measures in the workplace and transportation on a similar footing to occupational health and passenger safety. Multiple common-sense adaptations of building codes for office spaces, high-density residential buildings, and public transportation vehicles could contribute significantly to reducing the overall ease of transmission and baseline R-naught values for diseases with significant aerosol transmission potential like SARS-CoV-2. Examples include ensuring frequent air replacement through ventilation of enclosed spaces and creation of multiple negative pressure zones within workspaces to limit the ability of aerosols to spread from a single infected person to an entire workspace. Similar ventilation requirements already exist in clinical and laboratory settings and have been demonstrated through Army Corp of Engineers adaptation of hotels to be feasible as a retrofit option to multiple building types. Ensuring that frequently touched materials in public transportation vehicles are selected to minimize surface survival times for viruses and adding stronger ventilation and filtration requirements for busses, trains, and subways would all providesystematic contributions to reducing spread in both initial and ongoing stages of transmission. Because the virus has been demonstrated to survive for only several hours on materials like copper (Doremalen, et al. 2020), commonly touched surfaces like handles, knobs, buttons, and railings could be replaced with copper or brass (a copper-containing alloy) equivalents. Similarly, codes limiting the size of and occupancy of open office spaces would help simplify and accelerate the potential to return to work with greater safety across multiple industries.

Build better behaviors

Large-scale, widely adopted behavior changes by the public can single-handedly bring the pandemic under control. The Supermind identified public education and mass public awareness-raising as critical factors in modulating behavior. Social scientists, behavioral economists, psychologists, cultural anthropologists, and other experts could be engaged to shape messages and interventions in ways people will hear, trust, and follow. Engaging such experts could have significant impact, as the Supermind observed the challenges of the "prevention paradox," where people often do not believe the severity of the situation because they may not have personally been impacted by disease spread and are thus less likely to adopt appropriately preventative behaviors. Sterile techniques like how to appropriately use personal protective equipment (PPE) like globes and face coverings could be communicated to the public using awareness campaigns, art, and other methods, which are also described in greater detail in the "Validating, Sharing, & Communicating Scientific Insights" chapter. Other desired behaviors like maintaining physical distance, using face coverings when in proximity to others, avoiding crowds, especially indoors, and maintaining mask-less contact with ideally only your household, should similarly be communicated, with an emphasis toward engaging vulnerable populations.

Awareness campaigns could be strategically targeted to particularly at-risk populations, like those with obesity or diabetes. Encouraging healthy diet and lifestyle can both prevent and alleviate the severity of disease.

Finally, those who are infected with COVID-19 or may have been exposed to the virus should quarantine to prevent infecting others. The Supermind suggested ways to leverage expertise from entertainment and other industries to design quarantine experiences that could be enjoyable and incentivize the public to isolate themselves. Social isolation is challenging economically and from a mental health perspective, and so experience designers could be important experts to engage to creatively design quarantine for various communities. Novel physical spaces could also be used—for example vacant hotels, which could be effectively used in urban areas or other high density regions for individuals to isolate.

PPE, masks, and other technologies

The Supermind placed particular emphasis on novel designs for face coverings and masks. For example, masks could be designed with vulnerable populations like the hearing-impaired in mind. With over 400 million people world-wide with hearing loss (~5% of the world's population), innovative mask solutions could be developed to enable lip reading, and also the ability for frontline and healthcare workers to show facial expressions. Masks could be coated with gels or other materials with anti-viral properties. They could also be designed with biomaterials for enabling biosensing capabilities and environmentally sustainable production and degradation. Special care could be taken to ensure that they are fashionable and even combined with favorite aromas to make wearing them more pleasurable and even enjoyable.

Finally, the Supermind identified several other technologies to help reduce viral transmission. Digital wearables could be used to detect the proximity of others within a certain radius, informing the person that others are too close. Wearables could also be used to help train people to reduce touching their faces to prevent fomite-based transmission of SARS-CoV-2. Systems for detecting fecal or saliva contamination combined with local UV sterilization could be used to rapidly inactivate viruses, which might be applicable in settings like airplanes, restaurants, or other locales.

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Diagnostics & Monitoring

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INTRODUCTION

Methodologies for widespread and rapid testing and disease surveillance, such as digital contact tracing, can play a crucial role in suppressing the pandemic. The Supermind proposed novel modalities for how to detect COVID-19, including identifying novel biomarkers; where to look for signs of the disease, including in the air, in the sewers, and in our "digital health breadcrumbs;" and also how to quickly build new testing labs and infrastructure. The Supermind also focused on aspects of smart phone technologies for contact tracing, known as digital contact tracing: how to ensure equitable access and increase efficacy and interoperability, while critically protecting privacy.

> **Data from over 45,000 volunteers** ... indicates that voice acoustics could be used to detect and monitor various health conditions

> **Digital health breadcrumbs:** digital signals that can provide health surveillance data for tracking infectious disease

Detecting COVID-19: Novel biomarkers in our voices and in digital health breadcrumbs

The bedrock of public health response for mitigating and suppressing the spread of infectious disease involves widespread and rapid testing. The most common method for detecting active cases of COVID-19 has involved analyzing patient samples for the presence of viral RNA, usually through variants of polymerase chain reaction (PCR). There are, however, other types of biomarkers that could indicate the presence of an infection.

For example, an ongoing clinical study of digital biomarkers involving data from over 45,000 volunteers across the United States and India indicates that voice acoustics could be used to detect and monitor various health conditions affecting brain, respiratory, and motor functions required for healthy speech. In response to the COVID-19 pandemic, respiratory-responsive vocal biomarkers (RRVB) have shown promise to detect and measure COVID-19 associated respiratory impairments that also could be tracked over time to understand disease status and symptom severity. Furthermore, because the methods used to collect and analyze speech samples could be gathered from smart phones, such detection could reduce infection risks by eliminating the need for close contact with healthcare workers. Detecting vocal biomarkers using smart phones could provide cost-effective and near universal access to diagnostics and monitoring, making the allocation and use of these resources more timely and efficient and providing valuable assessment and risk stratification capability when gold standard tools, like viral RNA detection, may not be available or are too slow.

Biomarkers for COVID-19 can also be found in our "digital health breadcrumbs," or digital signals that can provide health surveillance data for tracking infectious disease. Some of these include search history keywords for symptoms; networked digital thermometers tracking fever trends; device usage changes correlating to cognitive, behavioral, and mental health changes that occur with infectious disease; and acoustic biomarkers as described above. Such bio-surveillance techniques have been successfully used to track the flu, including FluNearYou and Healthmap. It is possible that an integrated and systemic approach, fusing complementary digital signals with advanced machine learning and artificial intelligence techniques, could provide a robust monitoring system that could detect community spread of COVID-19 days or weeks earlier than current timelines for testing and patient notification. Current approaches can take longer than a week, rendering diagnostic tests largely useless for containing outbreaks.

Making diagnostic tests and labs accessible and scalable

The lack of sufficient COVID-19 diagnostic testing is still a significant problem in the United States and globally. The Supermind emphasized the critical importance of massive-scale testing to enable the isolation of asymptomatic individuals and proposed several approaches to make viral testing more accessible and scalable.

With tens of thousands of COVID-19 cases confirmed per day in the United States alone, and the significant rate of transmission by asymptomatic individuals that one study estimates to be between 6% to 41% of cases (Bradshaw et al., 2020), universal testing is desired. Large-scale detection of infected individuals without symptoms (either pre- or asymptomatic) is incredibly challenging without ubiquitous testing. An additional benefit of universal testing is the ability to relax social distancing measures, enabling the return of socioeconomic activities while limiting future outbreaks (Bradshaw et al., 2020).

> **Large-scale detection of infected individuals** ... is incredibly challenging without ubiquitous testing

One approach to scale the number of tests conducted is to pool samples from multiple patients in a single test. In such a scenario, a negative test result indicates that no viral RNA was detected in any of the patient samples, thus returning valuable data on multiple patients with only a single test, thus enabling large-scale screening. If, however, a positive result was returned, subsequent rounds of pool testing or testing of individuals from within the pool would be required to determine whom was infected. Pooling samples is particularly effective when rates of community transmission are low.

The Supermind proposed generating the necessary data standards and guidelines for how best to pool samples based on the type of diagnostic test and their prevalence to facilitate regular population-level screening. Such approaches have been successfully conducted in parts of the world, including in China, for example.

Other approaches the Supermind highlighted to make testing more accessible include developing rapid tests that could be conducted at home using saliva samples, which can be easier to collect than, for example, nasopharyngeal swab tests, which require specialized training. The Supermind also pointed to the recent FDA emergency use authorization (EUA) approval to Rutgers Clinical Genomics Laboratory to permit testing of samples self-collected by patients using saliva (Giordano et al., 2020). University of Colorado, Boulder has also recently developed a saliva test with a 45-minute sample-to-results turnaround (Meyerson et al., 2020).

Finally, the Supermind also acknowledged that collecting more samples alone is insufficient; infrastructure to conduct the tests also must be scaled. In the United States, for example, numerous outbreaks across the country during the summer of 2020 have overwhelmed centralized testing facilities, causing a processing backlog. To address this challenge, the Supermind proposed designing highly automated units, like 20-ft. shipping containers, that could be self-sufficient, containing a small number of staff with automated testing solutions capable of handling different diagnostic tests. For example, Open Cell, an organization in London, has designed a bio lab in a shipping container. These mobile labs could be deployed quickly to hot spot areas in close proximity to locations where samples could be collected (e.g., subway stations, hospitals, large factories) to augment existing testing infrastructure.

Similarly, more modular, reagent-agnostic testing systems could provide flexibility and remove points-of-failure in supply chains that potentially rely on single, large manufacturers. The Supermind pointed to entities like OpenTrons, who make open source pipetting robots, along with the Global Biofoundry Alliance and the London Biofoundry, which are also working on developing systems to automate lab protocols and diagnostic testing. Such modular and automated systems would be ideally suited to operate in mobile testing labs that could also be deployed to offer testing for underserved populations like the homeless, or in rural areas that are experiencing outbreaks and require additional infrastructure.

Understanding airflow dynamics ... is critical for designing circulation systems that refresh air and dilute the presence of any viral particles

COVID-19 surveillance for the air, sewage, and our genomes

AIR MONITORING

One area the Supermind identified that requires significant research and study is the analysis of viral prevalence in air, both indoor and outdoor. A recent article from The Atlantic (Tufekci, 2020) similarly highlighted this need. The Supermind proposed rigorous analysis of outdoor transmission in settings like golf courses, outdoor markets, restaurants, and learning environments for schools, for example. A deep understanding of these dynamics could play a critical role in designing public policies for many socio-economic activities that potentially could be conducTed safely outdoors.

Similarly, for indoor transmission, rigorous analysis of air filters or air monitoring devices in schools, workplaces, or transportation systems could also provide critical data, which could influence public health policies. Such monitors could be placed strategically with either sample collection or molecular diagnostics tools in situ. Understanding airflow dynamics inside buildings and ventilation systems is critical for designing circulation systems that refresh air and dilute the presence of any viral particles. Finally, the Supermind highlighted the need to understand the particle sizes and concentration in exhaled breath of COVID-19 infected individuals to elucidate the infection dynamics of aerosol transmission.

SEWAGE SURVEILLANCE

Sewage can be an early indicator of epidemics. The Supermind proposed developing a monitoring program based on metagenomic sequencing of all nucleic acids found in sewage that could establish a baseline against which novel pandemic zoonosis (the process of a virus infecting humans from animals) could be detected. Moreover, particularly dangerous engineered viruses are likely to have telltale signatures of alteration by humans, and those changes could be detected by automated algorithms. This type of sewage monitoring could be done not only in municipal sewer systems but also in transportations systems like airplanes, ships, or trains, which, when coupled with pool testing, could trigger targeted testing and contact tracing.

The Supermind proposed developing a monitoring program ... to sequence all nucleic acids found in sewage that could establish a baseline against which any novel pandemic zoonosis...could be detected

Such systems could provide a vital early warning, with studies showing that sewage screening could provide communities as much as a week's early notice of a COVID-19 outbreak (Peccia et al., 2020). When coupled with exposure notification and contact tracing technologies, local outbreaks could be controlled before they became pandemics. Furthermore, the existence of such an early warning system may provide the additional benefit of deterring malevolent actors from making engineered bioweapons.

Digital contact tracing is sensitive to uptake, but powerful if universal

One of the most promising technology solutions for suppressing the pandemic is digital contact tracing (DCT). Such technologies rely upon individuals having contact tracing applications installed on their smart phones that through, for example, blue-tooth technology, enable the logging of close proximity contacts. In the event of a positive test, all potentially exposed individuals could be instantly contacted so they can then be tested and potentially isolated. Models predict that, if such digital technologies were universal, the pandemic could be controlled without requiring lockdowns or face coverings (U.S. Food & Drug Administration, 2020). However, strong privacy protections would be required for adoption to succeed, particularly in liberal democracies where installing such applications would be largely voluntary.

To help adoption, the Supermind proposed, for example, buying every adult in the United States an inexpensive smartphone with a basic data plan that is DCT-enabled. This could cost approximately $4.2b. Such an approach could also help provide low income communities and frontline workers access to low cost technologies to help keep their families safe while bridging the "digital divide" that has exposed profound inequities in society, including access to life-saving digital tools. DCT applications could also be enabled with "bidirectional" contact tracing, which is predicted to reduce the effective reproductive number (Reff) of SARS-CoV-2 by roughly 0.3 (U.S. Food & Drug Administration, 2020). Finally, to manage the complexities of multiple DCT applications (potentially a unique app for each state in the United States or each country in Europe), particularly when individuals cross state or country borders, the Supermind proposed using interoperable data standards to prevent data silos and to enable connected systems updated in real time.

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4

THERAPIES & VACCINES

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For effective therapy and vaccine discovery and development, it is critical to understand the molecular basis of COVID-19 pathogenesis in terms of mechanisms of viral entry, replication, and host responses. The Supermind proposed approaches in computer-aided rational design and development of safe and effective broad-spectrum antivirals or repurposing known drugs with antiviral activity to combat the next pandemic, and development of antivirals to families of viruses that jump species. The Supermind also focused on various aspects of vaccine development including utilizing adjuvants that lower vaccine doses, inhalation-based vaccines, and approaches to fast track vaccine safety and efficacy evaluation and new ways to conduct clinical trials. Finally, the Supermind proposed ways to create more resilient supply chains for the various reagents and materials critical for manufacturing therapeutics and vaccines.

> **Viruses jump species in two ways**
> ...
> as a spillover event when humans become exposed to zoonotic viruses
> ...
> [or when] viruses mutate or undergo recombination re-assortment

Advances in patient treatment

Since March 2020, physicians' tools have improved considerably with significant advances in treating COVID-19 patients with multiple treatment regimens. These include:

- The antiviral drug Remdesivir, which has become a standard of care, and other repurposed antiviral drugs such as Kaletra (liponavir/ritonavir) and Tamiflu;
- Dexamethasone, a common corticosteroid used in autoimmune conditions and allergic reactions;
- Transfusion of convalescent plasma from recovered patients with high antibody content to treat active coronavirus infection;
- Acterma (Tocilizumab), a drug approved for rheumatoid arthritis which works by blocking interleukin-6 (IL-6), a protein involved in causing overactive immune system that could result in a cytokine storm, a potentially fatal problem where the immune system malfunctions and inflammation goes out of control;
- Monoclonal antibodies generated against portions of spike proteins, which are currently in clinical trials to see if they could provide short-term protection (until vaccines become available) from SARS-CoV-2 by binding directly to portions of the virus that are used to attach and enter host cells, preventing them from initiating the infection cycle.

Antivirals to families of viruses that jump species

Viruses like parvoviruses, coronaviruses, influenza viruses, parainfluenza viruses and arthropod transmitted viruses have shown a propensity to jump species, also known as zoonosis. Viruses jump species in two ways: the first is as a spillover event when humans become exposed to zoonotic viruses that they normally do not encounter. Forest clearances and dam building are examples of these events as they affect vector populations. In the second type, viruses mutate or undergo recombination or re-assortment, altering their ability to infect a variety of hosts.

Each of these virus families have points in their replication cycle that are targets for antivirals. For instance, for influenza viruses, the "M2 protein" has been a main target, but resistance has been developed to a class of antiviral medications known as "adamantanes." Combination therapy is required to reduce establishment of resistant mutants, ideally via rational design based on the 3D crystal viruses that have jumped species, followed by in vitro selection with selected molecules to predict escape mutants and then designing drugs for escape mutants and combination therapy to reduce their establishment.

Search for broad-spectrum antiviral drugs

Unlike broad-spectrum antibiotics such as penicillin, available to treat multiple bacterial infections, we currently do not have any broad-spectrum antivirals to treat respiratory track diseases arising from various viral infections. The Supermind proposed screening novel molecules through computer-created virtual libraries and the libraries of known drug compounds for their ability to inhibit viral replication through either viral protease or polymerase inhibitors or by preventing viral entry into the host cells by specific host enzyme inhibitors. This approach has potential for pan-pathogenic applications to develop broad-spectrum antivirals to combat future pandemics.

Next-generation adjuvants for scalable vaccine production

While the United States Food and Drug Administration (FDA) has traditionally been cautious around the adjuvants used in vaccines, the Supermind proposed utilization of novel, next-generation protein-based adjuvants that may reduce the effective dose of the vaccine by a factor of 10–100, and vastly accelerate manufacturing and scale-up. Additionally, long-term protection may require a more powerful immune response than can be achieved using traditional vectors. The fastest vaccine modalities are nucleic acids (DNA and mRNA) which are traditionally not very immunogenic—but they also make it very easy to co-deliver adjuvants in gene-encoded form.

Designing an inhalation-based vaccine

The Supermind proposed novel methods for improving delivery of a mRNA vaccine for SARS-CoV-2 to the lungs. Through the design of an efficient and rapid process to generate biomolecule-carrying aerosols with minimum disruption to their internal structure, this concept could provide a method that minimizes waste of important vaccine biomolecules. While other nebulization processes can destroy biomolecules, a major breakthrough for biomolecule delivery could be deliverings directly to the lungs. If successful, it would provide validated technology to produce an optimized mRNA vaccine for SARS-CoV-2 for delivery to the lungs. As such, this inhalation-based vaccine technology could offer several advantages including being non-invasive, direct delivery and reduced cost, resulting in improved access to potentially life-saving formulations.

Approaches to fast track vaccine safety and efficacy evaluation and new ways to conduct clinical trials

Vaccine trials often take a long time to uncover serious adverse effects. The Supermind has suggested the application of modern biotechnology tools to detect the adverse events early, to allow vaccine trials to proceed more quickly and safely with tools like modern proteomics.

The safety risks for SARS-CoV-2 vaccines fall under three broad categories: 1) *Acute anaphylaxis* in response to the antigen or the adjuvant; 2) *Vaccine-induced allergies* or *autoimmune diseases*; and 3) *Antibody-dependent enhancement* (ADE) effects that can make future SARS-CoV-2 infections worse.

Acute issues typically occur within minutes of vaccination, and therefore can be rapidly identified in Phase I and Phase II trials. Determining adverse reactions due to allergies and autoimmune disorders are the main reason that trials take a long time. However, it should be possible to detect warning signs of adverse immune response without actually causing them in people. For instance, allergen tests can be carried out before and after vaccination to identify unexpected shifts in allergen profiles. Proteome protein arrays and mass spectrometry methods can be used to detect the development of autoantibodies, allowing potential autoimmune issues to be identified in early vaccine subjects who do not go on to develop any diseases. These data can then be used to build custom assays for early diagnosis of potential side-effects in Phase III trials, eliminating the potentially lengthy follow-up period.

Antibody-dependent Enhancement (ADE) has been observed in Severe Acute Respiratory Syndrome (SARS) and Middle Eastern Respiratory Syndrome (MERS). In cats, for example, a feline coronavirus produces a mild disease, but if re-infected with a variant virus a fatal autoimmune disease can occur which, in part, is associated with ADE (Vennemma et al. 1990; Vennemma et al. 1998; Corapi et al. 1992; Hohdatsu et al. 1998). The Supermind proposed an assay to test ADE by comparing virus entry in three engineered cell types, all based on a common parental cell. These cell types would be designed to have variations of the "FC receptor," a protein found on immune cells, and the "angiotensin-converting enzyme 2" (ACE2) receptor, which is utilized by the SARS-CoV-2 virus to infect cells. By infecting these cell lines and testing their responses, one could identify an ideal vaccine candidate that elicits high neutralizing activity while having no or little infectivity on a cell line expressing FC receptors but not ACE2 receptors.

Accelerating and improving clinical trials

The Supermind also proposed a novel approach to speed up Phase III clinical trials for vaccines, using population-level statistics. One could capitalize on the high prevalence of SARS-CoV-2 in many American communities, such that an effective vaccine would be expected to shift the dynamics of local spread. The vaccinated subjects may develop a strong Immunoglobulin G (IgG) response within a few days, enabling efficacy measurements as early as five weeks into a clinical trial. In contrast, traditional clinical trials rely on measuring the protection conferred to each clinical trial subject, which may require more than one year of observation to obtain sufficient statistical validity.

In a pandemic crisis situation, traditional processes must be accelerated. There is a need to implement new thinking in clinical trial processes—like real-world trials, Bayesian Statistics, etc.—on an emergency basis, in parallel with the traditional Randomized Clinical Trial (RCT) approach to collect data very broadly across candidates, by removing competitive barriers, both geopolitical and institutional.

The Supermind noted pros and cons regarding the ethical dilemma of accelerating vaccine trials by infecting healthy volunteers with SARS-CoV-2 virus following vaccine administration. Instead of vaccinating hundreds to thousands of people and waiting to see if they naturally catch the virus and whether the vaccine would be effective in neutralizing the virus, the idea would be to purposely infect a smaller number of healthy vaccinated volunteers with the virus in a controlled setting to see if a vaccine offered protection (Lambert, 2020). If successful, such studies could fast-track vaccine evaluation, as well as our understanding of COVID-19 immunity. Arguments for and against this "human challenge trial" approach need to be evaluated and a decision would need to be made by regulatory authorities.

Finally, the Supermind noted that communities of color have historically been excluding from pharmaceutical clinical trials. Given the disproportionate impact the virus is having on communities of color, the clinical trial programs for promising therapies must include adequate representation from those communities to ensure we are developing treatments that are efficacious for those hardest hit by COVID-19 (CDC, 2020).

Creating resilient supply chains

The Supermind noted that the development of therapies and vaccines will only make a significant impact if sufficient manufacturing capacity exists and can be rapidly deployed. For example, when the antiviral drug Remdesivir was approved by the FDA for "emergency use authorization," there were only enough doses to treat 5,000 patients and the pharmaceutical supply chain was not equipped to deliver the drug in sufficient quantity (Gilead, 2020). Similarly, raw materials for the SARS-CoV-2 diagnostic kit manufacturing were also in short supply, resulting in large delays in viral RNA testing.

The push for vaccine development on an accelerated timeline has resulted in multiple modalities being pursued simultaneously, including RNA vaccines and antigen (recombinant) based vaccines, each of which has different manufacturing requirements. The Supermind proposed ways to improve supply chain resiliency by increasing local capacity to produce some of the most commonly used reagents and ingredients in a selected number of regional hubs. The Supermind also proposed the development of "innovation teams" that could be assembled under emergency conditions that could be connected to existing "maker" or grassroots innovation communities to aid in local production. Existing manufacturing capacity could also potentially be re-purposed, if relevant standards could be made available along with operating procedures and expertise. This type of flexible and decentralized manufacturing, along with manufacturing redundancy with multiple factories for critical reagents and ingredients, could significantly increase supply chain resiliency for therapeutic and vaccine deployment.

> **Using population-level statistics**
> ...
> enabling efficacy measurements as early as five weeks into a clinical trial

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5

Validating, Sharing, & Communicating

SCIENTIFIC INSIGHTS

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As new scientific insights about the pandemic are generated, how do we ensure they can be effectively validated, confirmed, shared, and communicated to the public and other stakeholders? These insights can span key aspects of virus biology, its impact on human health, and ways in which the virus spreads in a variety of settings and environments. Rapid research, validation, and communication of research to policy makers and the public is crucial for pandemic response. Yet, obstacles toward achieving these goals are myriad, from slowing the spread of misinformation to building and restoring trust between the public and scientists, public health officials, policymakers, the institutions that comprise these, and other stakeholders.

In this chapter, the Supermind proposed strategies and creative ways to:

- communicate clearly to educate the public on verified science;
- engage communities directly to build trust;
- promote evidence-based journalism;
- re-design, re-purpose, or build new institutions that engender public trust;
- share data and incentivize rapid research;
- and rapidly validate and curate scientific insights while removing barriers to access.

"

If you could tell the story
of this pandemic, what would it be
...
How could it be changed
...
What's your ideal ending
...
How do you see it being accomplished

Communicate to the public clearly, consistently, and creatively

To communicate effectively to the public, the Supermind suggested several strategies that borrow from approaches used for other types of information dissemination. For example, when communicating guidance on a behavior change like mask-wearing or social-distancing, it is critical to convey the suggested behavior with a simple rationale that clearly illustrates its benefits and consequences – and to do so repeatedly, consistently, and with a unified voice. Countries that have managed the pandemic effectively thus far have often featured a consistent scientific communicator who engages regularly (at times, daily) with the public, sharing simple and clear guidance. Conversely, conflicting stories from authorities can fuel mistrust among the public, as evidenced, for example, by the confusion and politicization surrounding mask-wearing in the United States. The Supermind further emphasized that communication skills can be as important as research skills for scientists, noting that a range of solutions for pandemic suppression, such as using face coverings, downloading digital contact tracing applications, or taking vaccines, will be ineffective if the public is unable to understand their importance and efficacy and change their behavior or act according to guidance.

The Supermind also proposed strategies for storytelling and other modes of creative communication. Basic storytelling questions should be considered including, for example, "If you could tell the story of this pandemic, what would it be? How could it be changed? What's your ideal ending? How do you see it being accomplished?" While seemingly simple questions, Supermind participants noted that, without a clear story and vision, ideas and plans can fragment. Other modes of storytelling, like television shows, movies, or performative art could also be interlaced with scientific information important for public health.

In recent years, there has been an increase in direct-to-the-public science communication by scientists, or "scicomm." A movement led in large part by women in science, scicomm has used popular media, including Twitter and live events like Story Collider, to convey science in new and compelling ways to the public. While scicomm training has been incorporated in some university degree programs, there remains untapped potential to use this approach as a means of increasing the number and diversity of scientific voices reaching their respective communities with critical scientific information.

Scientific insights could also be creatively and effectively communicated in partnership with data visualization designers. Data visualization design has evolved into a dedicated field study and practice, and experts in this field have become well-versed in interpreting complex data and conveying it clearly through the use of attributes like color, form, motion, and shape. The Supermind proposed creating a platform or community space to facilitate collaboration between researchers and data visualization experts to support the creation of charts, maps, and graphics to better illustrate complex science for public consumption.

Engage communities extensively, and with help from trusted leaders

The Supermind highlighted consistent and coordinated community engagement as a critical strategy for building trust. For example, scientists and public health experts could begin by developing education strategies for trusted leaders to inform their communities. Strategies like connecting effective science communicators with trusted influencers to disseminate messages via social media was also proposed, like the #BeatTheVirus campaign. The Supermind noted that outbreaks in areas where there is little trust in government make such grassroots exercises a necessity, and that empowering people and giving them fact-based evidence can help dispel fear.

Furthermore, community-based participatory research (CBPR) methods directly engaging localized participants could be used to bridge gaps between scientists, policymakers, and the public. CBPR methods incorporate the perspectives, needs, and concerns of community members as policies and interventions are being designed and tested. This allows for and informs careful consideration of normative cultures in different communities when developing science communications, which the Supermind also noted for its importance. Knowing potential sources of resistance in advance and designing solutions to overcome them, while making people feel heard, can improve pandemic response. Doing so has shown to increase the acceptance levels of the community for the ultimate solution or intervention, as evidenced via public participation in environment policy in the Netherlands (Hofman).

The early inclusion of diverse stakeholders, particularly communities who are not typically involved in planning activities, could help to build trust. This could be particularly important for marginalized communities, like, for example, African American, Latinx, and American Indian communities in the United States, who have been disproportionately impacted by the pandemic. Effective resources are more likely to be created through collaboration and community engagement that respects community cultural perspectives and represents their needs and priorities. The global health community has long relied on public engagement events and the use of crowd-sourced media such as cartoons, music, and theater to spread information about best practices and health threats.

The Supermind also highlighted ways in which school systems could help, through their curriculum, to better aid community members and the public to develop media literacy and, in particular, to distinguish between reliable and unreliable sources. Organizations like the "News Literacy Project" have helped teachers with general media literacy, while organizations like "Science in the News" provide models for how scientists can engage directly with their communities to address technical issues in the news. Science curricula could also include more programs on "pandemic sciences" at a young age.

Promote evidence-based journalism

One of the significant challenges of the pandemic has been the rapid cycle and release of unverified, conflicting information. The Supermind noted that telling humanized stories along with scientific facts and stats can help the public absorb the information. One idea was to help media companies establish scientific advisory boards and encourage social media companies to identify proven misinformation and directly combat misinformation bots.

Amongst the scientific community itself, researchers could also be responsible for identifying erroneous or misleading science communication from peers. Previous public awareness campaigns like "See something? Say something" could be applied culturally amongst scientists. The scientific community should also vigorously debunk conspiracy theories, ideally with calm, professional, substantiated, and convincing explanations, potentially working with professional communicators. When engaging with the public, basic tactics could be employed like not repeating or negating a lie - for example, instead of answering, "Is this just like the flu?" with, "This is NOT the flu," instead use a positive response like, "This is a new and dangerous disease."

> **Data visualization design has evolved** into a dedicated field of study and practice
>
> ...
>
> attributes like color, form, motion, and shape can influence perception of information.

Re-design, re-purpose, or build new institutions that the public can trust

What happens when scientific authorities have their trustworthiness called into question? The Supermind highlighted, in particular, balancing trust in institutions that have traditionally communicated about infectious disease to the public, like the World Health Organization (WHO) and the United States Centers for Disease Control and Prevention (CDC) (Madrigal, Meyer). One route involves reforming the existing institution and redesigning its communication practices, which could include more regular communication. The Supermind noted that, during the 2009 influenza pandemic, the CDC provided regular public communication and for the current pandemic ideally would be engaging with the public on a similarly regular, if not daily, basis.

Another proposed alternative would be to build new institutions or repurpose existing ones to fill the void. For example, a new organization could provide a clearinghouse of vetted and agreed-upon communication, validated by the scientific community, focused exclusively on information dissemination. Universities could also fill the void and reclaim science communication narratives by coordinating closely among labs, departments, and university communications teams to build trust with the public.

Share data and incentivize rapid research

The Supermind highlighted the need to incentivize rapid reproduction of critical research during a pandemic and noted that enabling data-sharing across institutions could help these efforts significantly. Unifying data standards and creating cross-institution agreements could aid the large-scale analyses of complex data sets. Furthermore, removing other competitive barriers could incentivize the broad sharing of clinical trial data, thus potentially accelerating therapeutic and vaccine development processes.

The Supermind also proposed methods for rapidly translating research into meaningful capabilities for clinical and public health availability by developing pre-defined and standardized sets of non-exclusive licensing terms that guarantee fundamental economics and rights to both inventor and commercial entities. Such provisions could fall under a subset of "pandemic emergency powers" that would include funding mechanisms and organizations to support the initial research reproduction phase. By supporting that critical validation, technology de-risking and licensing process, the government would likely catalyze the rapid mobilization of private capital to carry the development process forward. Finally, the Supermind emphasized that equity considerations should be built into all pandemic research funding, given that translational research and other mechanisms to cure disease have historically left vulnerable and marginalized populations most impacted by the virus behind.

Rapidly validate and curate scientific insights while removing barriers to access

The Supermind observed that, during the pandemic, we have seen numerous scientific papers published without the necessary, or usual, rigor–an observation that applies even to top journals. Given the critical role journals play in disseminating ideas and observations, supporting rapid publications is essential but can create an unfortunate compromise of review standards. In order to address these issues, creative incentives, including economic benefits, could be established to reward qualified peer review research and dramatically expand the amount of peer review, thus accelerating the review cycle. This could help in reducing the media exposure of un-validated preprints which can provide undesired amplification of unproven science.

The Supermind also highlighted the critical importance of reproducing key scientific findings. While academia currently incentivizes publishing, such an approach strongly favors novelty over reproducing already-published work. Such reproducibility research could be incentivized with rapid funding to those capable of validating findings, which can also help expand the workforce and create jobs.

Finally, the Supermind proposed creating different types of portals for greater access to scientific research. There could, for example, be a central site unifying COVID-19 research where publication data could be shared quickly, encouraging the reproduction of certain experiments. Artificial Intelligence (AI) and Machine Learning (ML) approaches could be used for curation purposes to group and find linkages between publications in real-time. Such groupings could be curated specifically for certain attributes–for example, research that is more actionable by public health experts and policy makers. To increase access, paywalls for pandemic science and technologies could be removed and journals could be incentivized to share more data openly. Plain-language summaries in addition to abstracts could be required, thus removing technical jargon and enabling lay readers and amateurs better access and ability to understand the latest research. A portal could also be created with free access to information on science-based best practices, which could include proper use and disposal of personal protective equipment (PPE), activities now widely used by the public.

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6
Pandemic Preparedness

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Pandemic preparedness

The COVID-19 pandemic has led to hundreds of thousands of deaths and trillions of dollars in economic damage. To mitigate the impact of future infectious disease outbreaks, significant strategic effort must be undertaken locally, nationally, and globally to create more resilient systems across sectors of society.

In this chapter, the Supermind shared strategies to enable national and global coordination, ways to use games and models to assess risk, ideas for early warning systems for detecting infectious disease outbreaks, methods for sharing key pandemic data, ways to create resilient supply chains, agile manufacturing, and strategic stockpiles, and strategies for bolstering hospital systems.

Coordinate globally and nationally

Responding and preparing for global outbreaks of infectious disease requires coordination and institution building at global and national scales. The Supermind proposed the exploration of a "North Atlantic Treaty Organization" (NATO)-like agreement across nations that could specify, for example, what resources each member commits in case of attack – except responding to, instead of military threats, pandemic threats. This should include developing countries, just as the US and richer European nations agreed to protect comparatively poorer Eastern European countries under NATO. Such agreements could redefine the role of global organizations like the World Health Organization (WHO) and include more detailed preparedness plans, ongoing disease surveillance, inter-agency coordinating, data sharing, and more sophisticated pandemic response coordination.

From a national perspective, the Supermind proposed the creation of permanent institutions for responding to pandemics; for example, a federal-and-state-level "Permanent Pandemic Response Facility" (PPRF). Similar to the US Emergency Petroleum Reserve facilities, a PPRF could entail: (1) physical facilities to accommodate pandemic patients; (2) placement of physical pandemic assets with an agreed upon expenditure and revenue sharing function for upkeep; (3) mandatory training for medical students, nurses, and other health care workers in pandemic response techniques; and (4) the establishment of a certification in pandemic response for low-level staff intervention to provide the human capital infrastructure allowing physicians and nurses a faster conversion to pandemic treatment when they are required. The PPRF would require stable funding but would ultimately help avoid the massive fiscal shocks associated with pandemic responses.

Use games and models to assess risk

To better understand the nature of future pandemics and other system-level threats, the Supermind proposed a variety of modeling and risk assessment strategies. For example, games could be developed to explore possible "Black Swan," or unpredictable, rare, catastrophic events (Aviashi, 2020) to raise awareness of systems thinking, resilience, and collaboration. Modeling could also assess the systems impact on health care and health outcomes to assist in post pandemic planning. Risk assessment tools could be developed with the aid of computational tools to monitor viral genome sequences in real time and search for hints of viral mutations that would increase risk to the human population, particularly transmission virulence. Such risk assessment tools could be based upon data generated from a variety of genomic early warning systems and could inform the development of therapies and vaccines.

Establish early warning systems

The establishment of robust early warning systems is essential for enabling rapid and decisive response to infectious disease outbreaks. As described in the chapter on Diagnostics and Monitoring, ubiquitous metagenomic sequencing of sewers, paired with automated algorithms for screening sequences, could enable the reliable and rapid detection of pandemic viruses, including the potential detection of bio-engineered threats.

Ubiquitous, "low-cost", rapid diagnostics would also facilitate the population-wide detection of viral community spread. The Supermind proposed strengthening the capacity for low and middle-income countries to develop diagnostic tools for a long-lasting legacy of skill and technology transfer with sustained global engagement. Similarly, the proactive distribution of rapid, point-of-care diagnostics in underserved communities could aid in the mitigation of unfolding outbreaks.

Digital bio surveillance technologies and projects like "Healthmap," "FluNearYou," and "COVIDNearYou" have been invaluable in early detection of major outbreaks but will also be critical in monitoring isolated outbreaks of COVID, flu, and potentially newer viruses. The Supermind strongly supported investment in these digital detection systems, including analyzing internet searches of symptoms, and other crowdsourced "digital health breadcrumbs" like digital thermometer data, device use changes that correlate to cognitive, behavioral, or mental health changes that occur with infectious disease, and other biomarkers. An app-based alert system could allow individuals to report their health conditions (e.g., temperature, pain, fatigue, cough, cold, etc.) into a central database that, when coupled with artificial intelligence and machine learning techniques, could perform pattern recognition to trigger alerts or actions at a variety of scales (individual, community, local government, etc). Such a solution could be bi-directional, giving users indications to see a doctor while preserving anonymity.

Finally, from a global and planetary health perspective, the Supermind proposed developing a "sentinel system" to better define the global hotspots where the initial introduction of a novel pathogen is likely to occur, and how these hotspots change over time. This sentinel system could collect and analyze a wide range of data in real time on environmental changes, for example: changes in rain patterns, agricultural practices, human encroachment on wildlife, deforestation, etc. This data, combined with data on patterns of infection, could help define conditions that are most conducive to "leakages" of zoonotic pathogens into human population, akin to an "infectious disease forecast," analogous to weather forecasting.

Trusted, open data for planning and coordination

Planning, decision-making, and coordination require trusted sources of data. The Supermind highlighted the need for an internationally respected authority to provide reliable facts, guidance, and advice that is non-political, non-commercial, and a trusted source of evidence-based information. A variety of health, macro-economic, and pandemic-related data could be made open and accessible and with interoperable data standards to enable the identification of system weaknesses and enhanced coordination and planning among nations and other diverse actors. Improved data standards could enhance common understanding and alleviate confusion between countries as they devise both national and global mitigation strategies. Such activities could be conducted by the WHO or via a new global institution.

Such open data could be represented by "data dashboards" for the research community and policymakers, but also could be framed for the public in clear and accessible ways. Pandemic research and other data may be too technical for the public and should be communicated clearly or enhanced, for example, via visual design techniques and other methods discussed in the chapter on "Validating, Sharing, & Communicating Scientific Insights." When communicated well, such data could inform matters of significant importance for the public, including behavioral guidance like mask-wearing, or policy considerations like when to open and close certain businesses and for what duration, but ideally in a highly customizable fashion based on community values and needs.

Resilient supply chains, agile manufacturing, and strategic stockpiles

From personal protective equipment (PPE) and healthcare equipment (e.g., ventilators) to ingredients and materials for manufacturing diagnostics, therapies, and vaccines, these critical pandemic assets should be strategically stockpiled and a part of robust and resilient supply chains. As has been highlighted in the chapter on "Therapies and Vaccines," decentralized production and rapid bio manufacturing is critical for economic resilience and pandemic preparedness. Global supply chains must be protected against disruption to prevent shortages of critical reagents.

The Supermind proposed providing impartial, fast testing capabilities to deliver feedback to organizations ready to pivot their manufacturing lines when needed. National and global task forces could be marshalled to monitor global supply chains. Laws could be passed to mandate that PPE and other healthcare equipment be locally sourced, similar to the "Berry Amendment" for the military. In addition to global supply chains, local supply chains should be established for critical materials, including for all equipment in the National Emergency Stockpile. Manufacturing processes that are common to products that are manufactured locally could be identified in preparation should they need to be quickly pivoted to new production lines to produce equipment in case of an emergency. To increase resiliency, there should be multiple domestic manufacturers of critical PPE and other healthcare equipment. Networks of Do-It-Yourself (DIY) and other community-driven labs and makerspaces could form regional nodes for rapid manufacturing of needed equipment at high volume and rapid speed. Strong channels of communication and support for these organizations coupled with collaborations with science research institutions and local industrial fabricators could enable the translation of designs to rapid scale pathways such as injection molding. Effort should be made to upgrade standards of PPE from cloth and surgical masks to respirators to properly protect our health and safety professionals.

Finally, the Supermind proposed building the logistics for population-wide testing, therapeutic, and vaccination infrastructure. As an example, in the early phases of a pandemic, plasma recovered from patients can serve as a valuable therapeutic. A plasma collection and distribution system could be developed that utilizes the neutralizing antibodies from recovered patients prior to the development of therapeutic antibodies that could be manufactured at scale. This plasma collection and distribution system could be based on blood banks, the infectious disease departments of general hospitals, pandemic dedicated hospitals, and physicians treating mildly symptomatic quarantined patients. The system could be set up at a national for regional level, under the sponsorship of, for example, the Center for Disease Control (CDC) or WHO. Such an approach could provide therapeutic coverage over the first several months of a pandemic, providing a bridge to synthetically produced antibodies, antivirals, and ultimately vaccines.

Strengthen hospitals

The Supermind identified hospital systems, in particular acute care hospitals, as being in need of improved coordination for pandemic preparedness. For example, focused national task forces could be established to coordinate local government, local hospitals, and industry to assist with procurement of basic supplies (e.g., PPE), while more specific task forces with experts from a range of representative fields could aid in the deployment of more innovative, cutting-edge solutions.

Hospital readiness and effective response is also reliant upon having reliable and transparent data. Supermind participants that assisted in natural disasters like hurricane Katrina and hurricane Sandy noted that information gaps, poor funding, and poor planning resulted in incomplete information on what materials were in stockpiles and a lack of a distribution schema to ensure strategic deployment of materials. Superior funding and strategic plans should be established to bolster hospital preparedness.

Engaged communities enhance pandemic preparedness

Successful pandemic response requires engagement by all sectors of society, from public health leaders to policymakers, government officials, and the general public. The Supermind highlighted the need for robust community engagement to ensure broad awareness of pandemic planning, including an understanding of the realistic scenarios that might unfold during infectious disease outbreaks. Scientists could spend more time informing the public about their decision-making processes, and ideally involve the public using participatory research methods to increase adoption of pandemic policies and guidelines. Participatory research methods incorporate the perspectives, needs, and concerns of community members as policies and interventions are being designed and tested. Doing so has been shown to increase the acceptance levels of the community, as evidenced, for example, by the co-design of environmental policies in the Netherlands (Hofman, 1998).

Furthermore, engagement could involve developing culturally appropriate resources for diverse and marginalized communities, like African American, Latinx, and American Indian and other Native communities that have been disproportionately impacted by the pandemic. Effective resources can be created through collaboration and engagement that respects cultural perspectives and represents communal needs and priorities. Such engagement could involve, for example, information distribution via callers with megaphones at food markets, inserting print materials in a range of indigenous languages in food distribution sites, or other culturally appropriate means. These information and engagement systems should also be designed to be continuous and long-lasting, fostering equitable discussions amongst stakeholders.

Finally, young people could be introduced to epidemiology and pandemic concepts in their K-12 education. The Supermind proposed a "COVID corps" to empower students to begin talking and thinking about pandemic planning and to also think creatively and design solutions to pandemic challenges. Educators could also strategically link pandemics to climate crisis, where young people already display significant engagement and activism, to solidify the link in public discourse and help students better navigate challenges with social distancing and other remedies.

Rapid response forces for pandemic response

In addition to preparing strategic stockpiles and supply chains, the Supermind also emphasized the importance of building human capacity and teams in the form of rapid response forces that could be mobilized to accomplish a variety of tasks. For example, nation-wide volunteer task forces could be trained and deployed to assist in community education, food distribution, contact tracing, and other activities. A "medical reserve force" for healthcare workers, modeled after the "army reserve," could be specifically trained in pandemic procedures and organized to work in field hospitals. Maker forces could be deployed in resource-limited settings to drive innovation and capacity to fabricate materials and devices. A global, multi-purpose, "pandemic rapid-response supermind" could also be organized. Such a collective intelligence resource comprised of, for instance, spare data scientists, coders, designers, management consultants, and technological resources like cloud computing power and internet network capacity, could be networked to help drive the creation of innovative solutions to local problems. This network of people and machines—or, "superminders"—could be funded via catalyst philanthropy and public health and security funds. A digital collaboration platform could be utilized by the "super-minders" to facilitate both synchronous and asynchronous co-creation to support core pandemic response activities.

Reduce planetary stresses to mitigate pandemic risk

Planetary health stresses, destruction of ecosystems, and climate change can all increase the likelihood of zoonotic viruses. To combat these threats, the Supermind proposed funding the cessation of forest clearance, particularly tropical forests, which can impact animal habitats and lead to human exposure to new viruses. Additionally, zoonotic infections have arisen from the consumption of "bush meat," dam building, which can affect vector density, and the disturbance of forest habitats. Financial incentives could be created to prevent the continued devastation of tropical ecologies and to discourage the eating of bush meat.

Health systems should also prepare beyond zoonoses to include other planetary health stresses and climate change. Preparation for similar events with catastrophic potential could be synergistic and could draw upon best practices from COVID-19. The Supermind proposed developing a planetary health framework and health system adaptation guidance from global institutions (e.g., WHO, World Bank) to prepare and resource health systems in all countries. Finally, these health systems could be staffed to include human and veterinary resources who can think and act in a holistic fashion with consideration to the entire biosphere: humans, animals, and the environment.

Preparing for future pandemic threats

The Supermind identified several sources of future pandemic threats and proposed ways to combat them. For instance, "superbugs," or strains of bacteria, viruses, parasites, and fungi that are resistant to antibiotics and other medications commonly used to treat infections represent a significant future pandemic threat. To combat "superbugs," the Supermind proposed utilizing open source phage libraries to identify potential targets. Parvoviruses, which include canine, feline, and rodent varieties, have also demonstrated a propensity for multiple species cross transmission. Parvovirus preparedness could include the development of generic antivirals targeted against various stages of the virus life cycle and

development of diagnostics for viral detection, particularly in food supplies where rodent parvoviruses can proliferate. Funding for such panviral drugs and virus development should be prioritized to combat a spectrum of viruses, including coronaviruses, influenza viruses, parainfluenza viruses, and arthropod transmitted viruses.

Additionally, phrophylactic strategies include the development of "safe decoys" for all known receptors used by viruses before pandemics strike. Because the known families of mammalian viruses rely on a limited number of receptors, of which over 80% are proteins, it is possible to engineer and evolve decoy variants of these receptors that will be highly resistant or immune to viral evolutionary escape. Such protein therapeutics could be delivered directly to the lungs as a prophylactic alternative, or compliment, to vaccines.

Finally, engineered pandemics are also a significant threat to be taken seriously. The Supermind proposed preventing engineered pandemics by screening all DNA synthesis orders for essential fragments of potential pandemic agents, but to do so discreetly without disclosing what sequences are being screened to avoid information hazards. Such a secure global system would:

- Minimize the number of people with access to known pandemic agents;
- Securely guard against new potential pandemic agents without drawing attention to them;
- Refrain from delaying legitimate research in any way

This could be done by merging cryptography with new bioinformatic approaches to screening for particular sequences, enabling discretionary identification of biosecurity risks while preserving progress in life sciences and biotechnology research.

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PANDEMIC RESPONSE

SUPERMIND REPORT

The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.